ERRATA:

Page 581, line 1: Read "degreased" for "decreased."

Pages 686 and 687: Reading matter on these pages is transposed.

ENDOCRINOLOGY

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INTERNAL SECRETIONS

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THE INTER-RELATION OF THE THYREOID AND HYPOPHYSIS IN THE GROWTH AND DEVELOPMENT OF FROG LARVAE

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In attempts at establishing the function of the ductless glands, investigators are limited to relatively a few kinds of experiments. One can administer a particular gland to an animal or transplant the gland into the animal in the hope of bringing about a condition wherein the subject receives more than the normal amount of the hormone being studied. One can extirpate a gland from an animal and then administer to it preparations of the type of gland removed, and one can remove a gland of one type and administer prepared glands of another type. Still further, various combinations and modifications of the above kinds of experiments can be attempted. The unsatisfactory elements in ductless gland investigations are difficulties of controlling the experiments and the greater difficulties of interpretation of the results.

In administering ductless glands one must admit that the preparations are abnormal to begin with. The glands used are dead and only hormones that are relatively stable can be preserved. Even here we have no absolutely certain method of

*The senior author succumbed to broncho-pneumonia on Jan. 30, 1920.

checking our findings and must usually reason by inference and deduction in the interpretation of results. Further, as has previously been pointed out, experiments with prepared glandular substances are more often pharmacological than physiological, especially when extracts obtained by any agent other than physiological salt solution are used. The body itself can hardly be expected to prepare from its own glands extracts requiring strong sulphuric acid, ether, acetone, alcohol and so forth. It is one thing to bring about certain reactions by the use of such preparations and quite another to prove that similar reactions are normally brought about by the living gland within the animal's body. However, we are on reasonably safe ground when we can, by administering preparations of a particular gland, prevent the occurrence of symptoms that would otherwise result from extirpation of the gland in question.

Transplanting a ductless gland into an otherwise normal animal would seem at first sight to be a method whereby hypersecretion could be brought about and the animal thus provided with more than the normal amount of hormones from the gland in question, but a usually ignored fact is that the host exerts a controlling influence upon the transplant, as well as the transplant upon the host, so that an equilibrium often results. We have transplanted thyreoids into embryos for example (Hoskins and Hoskins '19a) and observed later that they "took," so that the animals possessed an anatomical excess of thyreoid tissue, but were apparently able to regulate the amount of thyreoid hormones secreted by their own and the transplanted glands, because no symptoms of "hyperthyreoidism" resulted.

After a ductless gland has been extirpated there is often a considerable readjustment among the other structures of the body, so that of the resulting symptoms, some are due directly to the loss of the gland removed while others are caused only indirectly by the removal, and it is usually not possible to distinguish between these categories. Metabolic processes are so complex that phenomena occurring together may be merely concomitantly and not causally related. As an example of this complexity we may consider the results of thyreoidectomy wherein there occurs a physiological (perhaps pathological) hyperplasia of the hypophysis, so that the resulting symptoms are

brought about presumably both by the thyreoid deficiency and by hyper-activity of the pituitary, and it is very difficult to tell from such an experiment the normal function of the thyreoid. At best in such cases we can only say that there is some relation between certain processes and the gland in question.

METHODS AND MATERIAL

In the following experiments with hypophysis feeding we have administered a commercial preparation of the anterior lobe of beef pituitary (Armour & Co.) to otherwise normal larvae of Rana sylvatica, and to larvae of the same species from which the thyreoid had been removed in the embryonic stage before it could have begun to function. This preparation consists of dry substance of the anterior lobes of the hypophysis, put up in tablets of milk sugar. The tablets are composed of two grains of bovine anterior lobe pituitary substance dried in a vacuum (representing 10 grains fresh gland) mixed with three grains of milk sugar. A. C. Henderson of the Armour and Company laboratory states in a personal communication of June 4, 1919, "Our anterior pituitary substance is made from carefully selected material and is, we might say, entirely without iodin; at least there is not any more than would be found in muscle substance, which means practically none at all. It is absolutely free from thyreoid tissue."

Dr. E. C. Kendall of the Mayo Foundation, who kindly analysed this material for us, reported that each tablet of two grains of dried anterior pituitary substance contains .0035 mg. of iodine, either organic or inorganic, a content of one part in 40,000 which would be 1:200,000 in the fresh gland. Dr. Kendall is of the opinion that the iodine present is soluble, and if so, considering the amount of water in the larger aquaria, the dilution of the iodine was 1:570,000,000, a concentration much less than is necessary to stimulate metabolism in tadpoles (Swingle '19) if inorganic iodine is used.

Even if the iodine did not go into solution, only a very small fraction of .0035 mg. of it was ingested by each larva in one dose, yet in most cases an effect was noticeable within twenty-four hours after the first dose was administered.

The active principle of the hypophysis, whether it contains iodine or not, apparently is soluble, as shown by the fact that

the thyreoidless larvae continued to develop after their jaws began to metamorphose, and they were thus compelled to stop eating the tablets.

In several different experiments, most of which we have not yet described, it was found that eggs collected early in the season developed into larger animals than those taken later, or taken early and kept for a time in cold storage before being used.

In each experiment the controls and the experimental larvae were of the same age and size and were taken from the same mass of eggs.

In addition to the hypophysis tablets the experimental larvae received Spirogyra in abundance, and the controls received milk sugar and Spirogyra. The water in the aquaria was changed the day after each administration of the tablets or sugar.

The larvae were under daily observation and were measured from time to time as indicated.

Before being autopsied, the animals were fixed in Bouin's fluid.

The experiments were performed in the Anatomy department of the University of Pittsburgh.

I. Effects of administering a preparation of the anterior lobe of the pituitary to normal larvae.

Experiment 1. April 27, 1919.

Fifteen animals were selected for hypophysis feeding and 15 of the same size kept for controls. Each set was kept in one aquarium in which they had an abundant supply of normal food. In addition to this food, one pituitary tablet was given daily to the experimental group, while the controls received milk sugar. The treatment was continued from April 27 to May 13, 1919, making a total of 17 tablets given in this way.

Experiment 2. April 28.

Three sets of 13 animals each were chosen for this experiment. Those of the first group (A) were taken at intervals from the aquarium in which they were receiving their normal food, and placed in a small jar of water, containing one pituitary tablet. They were left in this jar for 24 hours, during which time they ate a portion of the tablet. Five treatments were

given on the following dates: April 28-29, May 5-6, May 13-14, May 15-16, May 22-23.

The second group of tadpoles in this experiment (2B) was used at first as a control for group 2A, to make sure that the effects observed in the latter were not due to the fact that the animals were temporarily deprived of their ordinary food. When group 2A was placed in the aquarium containing the pituitary tablet, group B was also taken from its aquarium and put in a small jar containing water and a few cracker crumbs. The animals were left there as long as those of group A were feeding on the pituitary substance, and then returned to the aquarium, where they received normal food. As no effect resulted from these periods of light feeding, the control was discontinued and the animals used in another way. They were left in a small jar containing water and a pituitary tablet for periods of one hour each. Nine such doses were given between May second and sixteenth.

The third group of tadpoles (C) for this experiment was composed of normal animals kept on an ordinary diet of leaves and algae.

It will be seen that in these experiments care has been taken to avoid starving the animals. In number 1, an abundant supply of normal food was always present with the hypophysis substance, and the animals ate freely of it as well as of the tablets. In 2A the effect of 24 hours at a time on light diet was checked by a control, as above described; and in 2B the periods of removal from the normal food were too short to have any effect in themselves. The effect that the sugar content of the tablets might have had was checked by the giving of milk sugar to the control larvae.

RESULTS OF EXPERIMENTS

Experiment 1.

At the beginning of this experiment the animals measured as follows:

15 for hypophysis feeding:

Body length, 9-10 mm., average 9.4 mm.

Total length 20-23 mm., average 21.1 mm.

15 for controls:

Body length, 9-10 mm., average 9.4 mm.

Total length, 20-22.5 mm., average 20.7 mm.

The first noticeable effect of the hypophysis feeding was a marked wasting of the bodies of the animals, which gave them the appearance of starved tadpoles. As has been said, the possibility of starvation has been carefully excluded from this experiment, and this emaciation differs from that produced by starvation in the time of its appearance. A normal tadpole kept without food does not show noticeable changes in form for four or five days, and is not strikingly wasted until several days later. The emaciation following hypophysis feeding is seen within 48 hours after the experiment is begun. Within a few days, however, the animals seem to recover from the first effect of the dose, and their bodies fill out again to the normal form. While the wasted appearance of the body lasts, the animals are sluggish in their behavior. Later, however, they become more lively than the normal tadpoles, and show a high degree of irritability, so that the slightest jarring of the aquarium starts them all to swimming about very actively.

By May 3, 1919, one week after the beginning of the experiment, the measurements taken showed that the hypophysis-fed animals were growing faster than the controls. These measurements are:

Hypophysis-fed—B. 10-12 mm., aver. 10.5; total 25-29 mm., aver. 26.7 mm.

Controls—B. 9-10 mm., aver. 9.8; total 20.5-23 mm., aver. 21.9 mm.

The greater length of the tails of the hypophysis-fed animals is particularly noticeable. In them the tail made up 61 per cent of the total length, while in the normal tadpoles it was only 55 per cent of the whole.

On May 8th the measurements showed still greater difference between the two groups of animals, as follows:

Hypophysis-fed—B. 10-12.5 mm., aver. 11 mm. Total 28-36 mm., aver. 31.5 mm.

Controls—B. 9-11 mm., aver. 10 mm. Total 20.5-25 mm., aver. 22.5 mm.

In addition to the size difference, which is largely due to

the unusual length of tail, marked changes in appearance may be seen in the hypophysis-fed animals. Figure 1, drawn four days later, represents a tadpole of the average size on May 8th (Body 11 mm. Total 32 mm.) and a normal but older tadpole of the same total length is shown in figure 2. The hypophysis-fed specimen shows a decided approach to the adult form. The body has become thinner both laterally and dorso-ventrally, showing that the intestine has been reduced in length. The anal canal has also shortened, the legs are well developed, and the pigmentation is like that of a frog. All these changes show that the animal has passed its maximum size and begun metamorphosis. The normal animal of the same length shows none of these signs of approaching metamorphosis. Its intestine and anal canal have not begun to shorten, its hind legs are represented by buds of tissue, and it retains the larval pigmentation. Figures 1 and 2 also illustrate the abnormal relation of tail and body in the hypophysis-fed specimen.

On May 13th all the hypophysis-fed tadpoles in this experiment were undergoing metamorphosis. The measurements showed a decrease in length, the approach to the adult form was noticeable in all the animals, and one tadpole had three legs. Five tadpoles, all of which had passed their maximum size, were found dead on this day, and the hypoyhysis feeding was discontinued.

No fully developed frogs were obtained from this experiment, though several members of the group reached a condition just short of the frog stage. Their bodies were frog-like, but a stump of tail of a few millimeters remained. The animals seemed to have been somewhat weakened by the treatment, so that they could not survive metamorphosis. Those that reached the stage at which they were able to leave the water had undergone a great shrinkage, but died before their tails had entirely disappeared. There is, of course, a reduction of the size of a normal animal in passing from the larval to the adult stage, but it is not quite so great as that seen in hypophysis-fed tadpoles. One member of this group died on May 14, and five more on May 20. All of these had four legs, and the tails had begun to shrink. On May 25 an animal which was already leaving the water died, and on May 30 the last two were killed. One of

these, also, had practically completed metamorphosis, and was leaving the water. The other still had a considerable stump of tail.

During this time (May 13-30) the control animals had developed much more slowly and did not reach their maximum length (B. 15, total 40 mm.) until early in June. The representative normal tadpole preserved on May 20 still retains the larval form of body and the hind limbs are but slightly developed, the digits of the foot being barely distinguishable. No completely metamorphosed frogs were found until June 9th, ten days later than the day on which the last of the hypophysis-fed animals left the water. On June 17th, when the experiments were ended, one of the normal animals was practically in the frog condition, but others were no farther advanced than the hypophysis-fed animals had been on May 13.

The precocious metamorphosis of hypophysis-fed tadpoles naturally gives rise to abnormally small frogs. The first of this group to reach the adult condition is shown in figure 3, and the first control frog in figure 4 (Plate II). The hypophysis-fed animal is normal in appearance except for its size. Its length (fixed) was only 8.4 mm., while that of the normal frog (somewhat below the normal average) was 10.4 mm. (fixed). The minimum length of the other hypophysis-fed frogs from this group was 8 mm.

Group 2A

It was in this group that the effects of hypophysis feeding were most marked. The animals were fed for 24 hours at a time on an exclusive diet of the pituitary tablets. The toxic effect of the first dose was very noticeable. The animals became much emaciated, and floated at the surface of the water, often on their backs. They remained in this condition for several days, and although they ultimately regained their normal shape, their growth appeared to have received a check from which it did not entirely recover. There was no period when the animals of this group were larger than the controls. The disproportionate growth of the tails which was seen in experiment 1 was less marked in this group. In the interval between the first two doses (April 29-May 5) the average length of these tadpoles increased as follows: Body from 8.4 mm. to 8.8 mm.; total from

18.8 mm. to 21.5 mm. The control tadpoles, in the meantime, had grown from 8.5-18.9 to 10.5-22.4 (body and total length in mm.). The second dose, given May 5-6, had no toxic effect on the animals. Between May 6 and May 15, there was an increase of 1.2 mm. in their bodies and .9 mm. in their tails. On May 16 the effect of the feeding on the form and development of their bodies was clearly apparent. Figure 5 (Plate III) drawn at this date, is to be compared with figure 6, its control. The most noticeable abnormalities appear in the lateral view of the hypophysis-fed tadpole, from which may be seen that the intestines are already reduced, giving the animal a much smaller abdomen than is seen in the normal specimen. This shortening of the intestine is one of the later metamorphic changes in a normal animal, but occurs in hypophysis-fed tadpoles at a relatively early date, before the legs have developed to any very great extent. The legs of the animal shown in figure 5 do not correspond in their development to the condition of the intestine, but are much more advanced than the legs of the control (fig. 6), although the latter is considerably the larger of the two.

Between the dose of May 16 and that of May 22 the tadpoles increased very little in size. The average length on May 16 was: Body, 10 mm.; total, 23.6 mm.; and on May 22nd, Body, 10.5 mm.; total, 26.1 mm. This was their maximum length, and by May 26 the anal canal had shortened and metamorphosis had begun. Figure 7 shows the smallest animal of this stage of development which we obtained from any of these experiments. Although the body of this animal was only 8 mm. long, the reduced abdomen and anal canal, the well developed legs, and the pigmentation shows that it has already begun its metamorphosis.

As might be expected from the small size of the tadpoles of this group, the frogs developing from them were below the normal size. As in experiment 1, few survived metamorphosis. Those that did so range in size (fixed) from 7 to 10.5 mm., with an average length of 8.8 mm. They had an average volume of 0.15 cc. while the volume of the normal frogs was from 0.20 to 0.30 cc.

Group 2B

The animals in this experiment received less of the pituitary substance than those in either of the experiments just described, and the effect of the treatment was correspondingly smaller. There was no emaciation following the early doses, and the first result to be seen was a stimulation of the growth of the tail and hind legs, and the reduction of the abdomen, due to shortening of the intestine. By May 15, two weeks after the beginning of the experiment, the hypophysis-fed animals have, on the average, considerably longer tails than the controls, while the bodies remain practically the same in the two groups. The measurements taken on this date were: Hypophysis-fed: Body 11 mm., total 30.4 mm.; controls: body 10.9 mm., total 23.7 mm. Individuals may be found, however, among the hypophysis-fed animals, which show normal proportions as far as length is concerned. One of these is shown in figure 8, and is to be compared with figure 6, which represents a normal tadpole of the same length. The two show a striking contrast in outline, and in the development of their legs. Figure 8 is typical of the hypophysis-fed tadpoles at the time when the effects of the treatment are first noticeable. Comparison of this figure with figure 1 shows that although the animals of experiment 2B were stimulated by the hypophysis feeding, the changes indicative of metamorphosis took place more slowly than in the earlier experiments. Although most of the animals completed their metamorphosis early, a few showed very little effect from the feeding. An example is shown in figure 9, and its control in figure 10. The hypophysis-fed tadpole has a slightly longer tail than the normal one, and its legs are longer, but there is no external evidence of changes in the intestine. The two drawings were made on June 3, when many of the hypophysis-fed tadpoles of this group had completed their metamorphosis.

The frogs that developed from this group ranged in length from 9 to 11 mm., with an average length of 9.9 mm., as compared with the control frogs, which varied in length from 11 to 14 mm.

Discussion of Part I.

The effects of hypophysis feeding on normal young tadpoles may be divided into two groups: the toxic and the stimulating,

as has been noted for thyreoid feeding. To the former group belongs the emaciation which immediately follows the first dose of the pituitary substance. Abderhalden '15 noted the toxic effect of pituitary extract. This effect is temporary, and does not recur after later doses. The animals appear to acquire a tolerance for the hypophysis substance. This may be the result of the repetition of doses, alone; or it may be that larger tadpoles have a greater resistance to the toxic effect. Late in the season an attempt was made to produce this effect on a normal tadpole, in order that a figure of this stage might be drawn. No such result was obtained, however, and this suggests that a tolerance may develop normally in the tadpoles with increasing size. No emaciation was produced in group 2B, the members of which were larger at the beginning of the experiment than those of the other group. In this case, however, the dose was small, and may have failed to affect the animals on that account.

2A. Although these animals recovered from the toxic effect of the first dose, their growth was considerably retarded.

The more interesting results of hypophysis-feeding are seen in various indications of stimulation. The most constant of these is the relatively rapid growth of the legs and tails of the treated animals. This effect is seen in animals which have received but a small amount of pituitary substance and are apparently not otherwise affected by the treatment, as well as in those which have had so much hypophysis that their general growth has been retarded.

The early shortening of the intestine occurs in almost all the animals, although a few in group 2B were not affected in this way. This result occurs relatively much earlier in the history of the hypophysis-fed tadpole than in that of the control; and hence it is more precocious than the development of the legs.

Moderate doses of the pituitary substance cause a stimulation of the growth of the body as well as of the legs and tail.

Metamorphosis as well as growth is hastened by pituitary feeding, in proportion to the amount of the substance administered. The process takes place relatively early in hypophysis-fed larvae, so that abnormally small frogs develop, and such larvae never become as large as the size attained later by the

controls. The maximum length reached by any of our hypophysis-fed larvae was 36 mm. as compared with 40 mm. for the maximum of the controls. After metamorphosis the hypophysis-fed animals were from one-half to two-thirds as large as the control frogs, and were about three-fourths as long, as is described above.

While we do not believe that the iodine content in our preparation of pituitary was sufficient in itself to bring about the results obtained, such may be the case. But whether it is or not, the substance used was normal pituitary, and the results indicate a similarity of its action to that of thyreoid.

The normal presence of iodine in the hypophysis of mammals has been claimed by some previous investigators and denied by others. Thus Bauman '96 found no iodine in the human hypophysis, but Schnitzler '96 found a trace of it. Wells '97 reported finding 0.05 mg. of iodine in 1.22 grams of dried human hypophysis. Simpson and Hunter '09 could not find iodine in Armour and Company's ox pituitary preparation nor in the fresh pituitary of sheep following thyreoidectomy, but detected a trace in fresh normal sheep pituitary. They state that their method would detect iodine in the amount of 0.005 mg. in 1.2 grams of dried substance. Denis '11 could not find iodine in the human pituitary either before or after the administration of iodides. MacArthur '19 likewise did not find iodine in beef pituitary. Thus it appears that while iodine is present normally in the hypophysis of mammals, it may be at times either absent or in concentration too small to be detected by the technique employed.

Smith '18 states that anterior hypophysis substance and boiled lettuce fed to normal tadpoles causes a rapid growth just before the larvae begin to metamorphose and hastens this process, as compared to larvae to which liver and boiled lettuce is given. This difference in size is very much less than the variation within the two groups of larvae in Smith's experiments, and may not be of any significance. The liver may have had some effect upon the growth of the control larvae and if so they were not normal and the results obtained need confirmation. In our experiments the larvae to which anterior pituitary substance was administered began their metamorphosis before

they had become as large as larvae of this species normally grow, and as a result, the frogs which were formed are smaller than normal. Since Smith did not mention any such effect on the size of his frogs, and since he did not notice any effects in the early part of his experiments, it is evident that the preparation of hypophysis used in his experiments was different in its action from our preparation.

II. Effects of administering a preparation of the anterior lobe of hypophysis to thyreoidless larvae.

For this experiment twelve thyreoidless larvae were selected as shown in the accompanying table. They varied in length from 42 to 53 mm. and in volume from 0.90 to 1.45 cc. Each was placed in a separate aquarium and treated as described under "Material and Methods." They were all kept under observation from 9 to 31 days, receiving from 9 to 21 doses of the hypophysis substance.

The normal control larvae, 50 in number (see Pl. IV.) had all passed the period of metamorphosis before most of the hypophysis feeding experiments were begun. These controls grew and developed normally and do not require description. They varied in maximum size before metamorphosis from a total length of 36 mm. to 41 mm. and volume of 0.50 cc. to 0.80 cc. After metamorphosis the control frogs varied from 13 mm. to 14 mm. in body length and from 0.30 to 0.45 cc. in volume. The hind legs were about 14 mm. long before metamorphosis and 15 to 18 mm. afterwards. It is easy to tell when metamorphosis proper is beginning by noting when the anal canal begins to shorten. Skeletal changes have already begun before this time, but there is no particular point in the skeletal growth that signifies metamorphic change, since the growth of the skeleton is at first very gradual. For a recent discussion of these normal changes see Hoskins and Hoskins '19b.

Thyreoidless larvae differ from normal larvae in many particulars as Allen, Hoskins and others have already described, and only a brief description will be given here. (See Pl. IV and VI.) These larvae that have had their thyreoid removed in the early embryonic stage, grow in volume and length more rapidly than normal, but if kept in normal conditions and given normal food, will not metamorphose at least for two years, although

the control animals taken from the same eggs will change into frogs within four to eight weeks from the time the eggs are laid. These thyreoidless larvae ultimately become two to four times as large as normal larvae, but their skeleton shows little tendency to calcify or to ossify. Their legs develop only as rudimentary appendages a few millimeters in length.

It is interesting to note that Hahn '12 found four gigantic larvae occurring naturally in otherwise normal cultures of Rana esculenta, but unfortunately he did not study their thyreoids. It is highly probable, however, from Hahn's description that the thyreoids of his monsters were atrophied because the changes which he does describe are much like those occurring in thyreoidless larvae. He attributed their gigantism to hypertrophy of the pituitary.

In thyreoidectomized larvae, as in other animals, there results a hyperplasia of the pituitary after thyreoid removal, but the pituitary is not able to make good the loss of thyreoid secretions.

At the beginning of the hypophysis feeding the thyreoidless larvae resembled those previously described.

DESCRIPTION OF EXPERIMENTS

A. (Pl. V and table.)

This larva was about twice the size of a normal larva when the feeding began, its total length being 50 mm., nose-anus length 20 mm., hind limb buds 2 mm. and volume 1.50 cc. It received 18 daily doses of one-half tablet each, only a small amount of which it ate, as described above, and was observed for 20 days.

An effect of the medication was evident within 24 hours, at the end of which time the tail had shortened 10 per cent and the volume had diminished 12 per cent. The animal had become more active, as was true in all the following experiments after a single dose of hypophysis. If one approached or touched the aquaria, the larvae swam rapidly about and were difficult to catch, whereas before the medication began they were rather unresponsive to ordinary stiumli. The same effect was produced by Smith '16 by extirpating the hypophysis.

After two days the tail of animal A had decreased an additional 9 per cent in length, the volume had decreased 3 per cent,

and the hind limbs had lengthened 25 per cent.

Between the sixth and eighth days the anal canal disappeared, the animal's body now being 17 mm. long.

Between the fourth and twelfth days the tail underwent a secondary growth period, giving the animal a total length of 48 mm. The hind limbs had grown to 15 mm., which is the average leg length of young frogs. The volume had, during this period, decreased to about two-thirds of the original. On the thirteenth day the left foreleg broke through the operculum. By this time the shape of the body and head was definitely that of a frog. The pigmentation and other skin changes also were those of normal metamorphosis. Two days later the other foreleg appeared. It came through the toughening skin with considerable difficulty. On the seventeenth day the total length was reduced again to 44 mm. The tail did not, however, have the appearance of a normal larval tail of the same length, being but half as wide dorso-ventrally and half as thick, showing evidence of impending disappearance. The body was still 17 mm. in length, but had become very much thinner. The hind limbs were 20 mm. long, were somewhat disproportionately thick, and were short also in relation to the size of the body. The volume was not measured at this time, but it appeared to be further decreased.

On the twentieth day of the experiment the animal was found dead in its aquarium, too much swollen for accurate measurement. It was much larger than a normal young frog, as was to be expected from the size of the larva at the beginning of the experiment. The animal had the shape and pigmentation of a frog, but a long narrow tail still persisted.

Autopsy showed the gastro-intestinal tract to be almost completely metamorphosed, the liver being greatly reduced in size and the gall-bladder enlarged as occurs normally; the gills were small and the lungs well differentiated, as were the kidneys, gonads and brain. In general it may be said that metamorphosis was between 80 and 90 per cent completed.

A. A. (Pl. V, VI, and table.)

At the beginning of the experiment the total length of this larva was 42 mm., the body length 19 mm., the hind limb buds 2 mm., and the volume was 0.98 cc. It was thus about a third

larger than the average of the control larvae. It received 15 half-tablet doses of the pituitary substance during the first 18 days of the experiment, and was kept under observation for 31 days. In the first four days the tail increased 3 mm. in length, but the volume decreased to 0.75 cc., a loss of about 23 per cent, due partly to expulsion of intestinal contents.

By the sixth day the length had not changed, but the hind limbs had doubled in length and the volume had increased very slightly. By the ninth day the anal canal had shortened 3 mm., the hind legs had grown another mm. and the volume had decreased to about 66 per cent of the original.

On the next day the nose-anus length had still further decreased to about 74 per cent of the original and the hind legs had increased to 5.5 mm. On the twelfth day the total length was 41 mm., but the tail was very narrow dorso-ventrally, the volume had increased to 0.75 cc., the hind limbs were 6 mm. and the pigmentation was changing toward that of a frog.

Three days later the tail had increased 1 mm. and the hind limbs 3 mm., and the head and body were changing in shape toward that of a frog. On the nineteenth day the animal looked like a frog except for its long narrow tail. Both forelegs had appeared. The medication was stopped at this point.

Three days later the tail had shortened by 3 mm., the body length had increased 1 mm., the hind limbs were 16 mm. in length and the volume had been decreased to 51 per cent of the original. On the twenty-seventh day the tail had shortened again by 3 mm., and the hind limbs had increased in length another mm. The larva frequently tried to protrude its head from the water, so it was placed in an aquarium one end of which contained shallow water. From this time to the end of the experiment the animal, unless disturbed, remained in this end of the aquarium with its head out of water. On the thirty-first day the animal, which had practically become a frog, still had a very narrow and thin tail 20 mm. in length. Its volume had decreased to 36 per cent of the original, a decrease equal to the maximum loss suffered by a normal larva during metamorphosis. On this day while being examined it jumped from the observer's hand and was killed by the fall.

Autopsy showed a fully differentiated gastro-intestinal tract,

the liver being even smaller than that of normal frogs, and the gall-bladder rather larger than normal. The gills had not been reduced in size as much as occurs in normal metamorphosis, although the lungs were well developed and functional. The kidneys appeared normal, the ovaries were quite large, and the brain was as fully differentiated as that of a young frog. Metamorphosis seemed to be complete save for the fact that the tail had not fully disappeared and the gills had not been very much reduced in size.

B. B. (Pl. V and table)

This animal had received but three doses of 2 grains each when it died on the fourth day. The total length had been reduced 4 per cent, its body length 7.5 per cent and its volume 33 per cent. Since the animal when measured on the previous day was almost as long as when the experiment began, it may have shrunken between the time it died and the time it was removed from its aquarium. A part of the loss in volume was due to discharge of fecal matter. At autopsy the viscera were still in the larval condition.

B. (Pl. V and table.)

This larva received eight daily doses of 1 grain and on the ninth day while being anaesthetized to be drawn, it died and was fixed. An effect of the pituitary substance was noticeable twenty-four hours after the experiment began, when it was seen that the entire length had changed from 46 to 47 mm., the body length from 20 to 20.5 mm., the hind limb from 1.5 to 2 mm., all signs of growth, but the volume had decreased from 1.30 to 1.15 cc.

On the next day the animal was the same length, but its volume had decreased to 1.10 cc. and the hind limbs had increased to 2.5 mm.

On the fourth day the tail had lengthened another mm., and the hind legs 0.5 mm., but the anal canal had decreased 1.5 mm., and the volume 0.10 cc., the latter being now 23 per cent less than at the beginning of the experiment. By the seventh day the anal canal had disappeared and the body was beginning to change in shape. On the ninth day the larva had decreased in total length to 47 mm., and in nose-anus length to 16 mm.

The volume was 0.85 cc. or about 65 per cent of the original. The hind limbs had grown to 7 mm. and the fore limbs beneath the operculum were 3.5 mm. long.

Autopsy showed that the gastro-intestinal tract was changed about half way to that of the frog stage. The liver had formed its three lobes, was being freed from the coil of gut which in the larval stage is embedded in it, and the gall-bladder had increased in size. The gills showed little change, but the lungs were large and air-containing. The kidneys and ovaries showed no peculiarities. The latter were large, but as Allen and we have shown, thyreoidless larvae develop large gonads. The brain showed differentiation beyond that of the thyreoidless larval type.

C. (Pl. V and table.)

This animal reacted in about the same way as A. It received 18 one-half tablet daily doses of the anterior pituitary substance and was found dead in the aquarium on the twentieth day, from drowning or other cause.

Within 24 hours after the first dose the larva began to decrease in volume. As in most of the experiments the tail increased in length at first, but rapidly decreased in size, and after 10 days, in length also. On the tenth day the total length was still 1 mm. greater than at first, but the nose-anus length had lessened by 24 per cent from shortening of the anal canal and the volume had decreased by 44 per cent. The hind legs were now 8 mm. long.

On the seventeenth day the total length had decreased to 40 mm. and the body length to 15 mm. The hind limbs were 13 mm. long and the left foreleg had broken through the skin. The volume was not measured, but was seen to be less than before. The shape of the head and body and the pigmentation were definitely those of a frog, and the mouth and jaws also had metamorphosed. The skin had become toughened to such extent that the right foreleg could not break through it, and on the next day a small incision was made in the skin to release this leg.

On the twentieth day the animal, a frog to all intents and purposes except for a narrow tail of 30 mm., was found dead. It was somewhat swollen, so the volume could not be taken, but

the animal had decreased in size more than the average normal larva during metamorphosis.

Autopsy showed that the viscera were nearly completely metamorphosed, as in animal A. The kidneys and liver were especially small. The ovaries were large and the brain well differentiated. The other viscera also were those of a normal young frog.

D. (Pl. V. and table.)

This larva received 13 doses of pituitary substance, and reacted about the same as did larva C., but somewhat more rapidly, and in seven days its metamorphosis was further advanced than that of the other. Its volume by this time had been reduced by a third, its nose-anus length by a fourth, and its hind legs had lengthened to 5 mm.

By the twelfth day the total length and volume were rapidly decreasing, the hind legs were 13 mm. long and one foreleg had appeared. As in animal C, the other foreleg had to be liberated by operation because the skin had toughened, and like animal C, this animal was found dead in the aquarium two days later.

At autopsy its viscera were seen to have metamorphosed to the same extent as in animal C, except that the gastro-intestinal tract was not quite so completely differentiated, and the gills were somewhat further reduced in size.

E. (Pl. V and table.)

This larva received 21 one-half tablet doses and reacted as did D. In nine days it lost 45 per cent of its volume, its tail decreased in size and its head and body began to resemble those of a frog. In twelve days one foreleg broke through the skin and a few days later the other appeared. By the seventeenth day, except for a narrow tail the animal appeared quite like a frog. By the twenty-second day the volume was down to 40 per cent of the original, the hind limbs were 12 mm. long, the tail was still present but was becoming smaller and the body was fully reduced to the size, shape and color of a frog. The thin ventral and dorsal fins of the tail had nearly disappeared, giving this appendage a near-rod shape.

Autopsy showed a completely metamorphosed gastro-intes-

tinal tract, including a very small liver and very large gall-bladder. There were small gills, large air-containing lungs, small kidneys, large spleen, spherical and well differentiated testes and a well differentiated brain.

F. (Pl. V, VI and table.)

This animal received 15 half-tablet daily doses, and it reacted very rapidly to the medication. There was at first an increase of 2 mm. in the length of the tail, but a decrease in the volume of the body. In five days the volume decreased from 0.93 cc. to 0.80 cc., the legs grew from 2 to 7 mm., and the anal canal shortened 2 mm. The body during this time had become slender from discharge of fecal contents and from contraction and shortening of the gut. By ten days these changes had gone on still further, and the animal had the general shape and color of a frog.

By the fifteenth day one foreleg had appeared, but the tough skin seemed to have prevented the appearance of the other. Except for this, and the presence of the tail, the animal resembled a fully formed frog. The tail had begun to shorten and its dorsal and ventral fins had almost completely disappeared. The volume of the animal had decreased to 60 per cent of the original, and the hind limbs had lengthened to 18 mm.

At autopsy were found a practically differentiated gastro-intestinal tract, gills that had decreased somewhat in size, lungs that were very large and full of air, small heart and kidneys, spleen and ovaries well developed, and brain fully metamorphosed.

G. (Pl. V and table.)

This large thyreoidless larva was kept in this group of animals to serve as a control and was fed algae and milk sugar, although such procedure was not really necessary since Allen, Hoskins and others have shown that thyreoidless larvae retain the larval condition under normal circumstances, and as shown in section I of this paper, milk sugar alone has no direct effect upon metamorphosis. This animal (G) was kept for 15 days in a dilute sugar solution and fed on algae. It continued to grow, but showed no signs whatever of metamorphosis. Its growth was somewhat more rapid than that of average thyreoid-

less larvae of the same age kept on a normal diet, but was little if any more rapid than the maximum growth of such larvae.

At the end of the experiment this animal had increased in total length from 47 to 52 mm., including an increase in body length of 3 mm. The volume had changed from 0.98 to 1.40 cc., a growth of 43 per cent as contrasted with a decrease in volume of 30 to 60 per cent suffered by the other larvae. This animal was thus from two to three times as large as the larvae that had received 15 doses of pituitary substance.

Autopsy showed its viscera all in the larval condition as previously described for thyreoidless larvae (see Hoskins and Hoskins '19b). The brain was especially small and undifferentiated, whereas the ovaries, which are not retarded by thyreoidectomy, were well developed and contained oöcytes visible on the surface of the gonad.

H. (Pl. V and table.)

This animal received 9 daily 1 grain doses of the anterior pituitary substance, and reacted about the same as the other thyreoidless larvae after the same amount of medication. The length decreased slightly, the anal canal disappeared, the volume decreased about a third and the hind legs grew to 10 mm. The animal was then killed, fixed and autopsied. The forelegs under the operculum were 4 mm. long. The shape of the body and the pigmentation of the skin were changing to those of a frog. The mouth had just begun to change. The stomach was being formed, the gut was shortened to about half the larval length, the liver was still large, but had formed its three lobes and was decreasing in size, having freed itself from the coil of gut formerly embedded within it. The gall-bladder had enlarged. The gills were still large, but the lungs were fully expanded and air-containing and the kidneys had decreased in size. The testes were spherical and well developed, and the brain was about half way between that of a larva and a frog.

I. (Pl. V, VI and table.)

This larva also received nine doses of the preparation and reacted about the same as did H, except that its loss in volume (55 per cent) was greater, and its tail became relatively smaller. Its leg growth was relatively the same as that of H.

At autopsy its liver, stomach, kidneys, lungs and spleen were found to be completely metamorphosed. The intestine was about three-fourths reduced to the frog type, the gills were slightly reduced, and the brain had become nearly differentiated.

J. (Pl. V, VI and table.)

This animal was treated similarly to I and reacted in the same manner, except that its loss in volume (35 per cent) was not so great.

The viscera were in practically the same condition as those of I.

DISCUSSION OF EXPERIMENTS OF SECTION II

In the above experiments it was noted that in most cases the length of the animal increased slightly during the first day or two of the hypophysis feeding, before involution began. In one case (AA) this added length persisted for ten days, although in this, as in other cases, the volume of the tail was steadily decreasing regardless of length, because of a shrinkage both dorso-ventrally and laterally. In this involution the tail did not react quite the same as it does in natural metamorphosis, the muscles and cartilage being more resistant than the skin and connective tissue.

The volume began to decrease in every case within twenty-four hours, and in all but one experiment, the decrease was continuous. A considerable portion of this loss in the first few days was due to discharge of feces, as occurs naturally with the shrinkage of the gut. The total loss in volume suffered by the larvae was quite as extensive as occurs naturally, being 63 per cent in one case.

One animal (AA) continued to metamorphose for thirteen days after the medication was stopped, indicating either that the absorbed pituitary substance persisted for some time in the larva or else that it had started some process within the animal that was able to continue after the intake of pituitary ceased. In all of the cases in which the jaws of the larvae began metamorphosis (AA, A, C, D, E, F) the animals quit eating the pituitary substance and could have been influenced after that time only by the extract soluble in the water of the aquarium

or else by a persisting effect of the substance eaten previously. The animals' ceasing to eat the tablets may account for the failure of their tails to disappear entirely.

The effect of the medication on the viscera was evident earlier than the effect on the somatic structures so far as macroscopic changes could be noted. There occurred on the first day the decrease in the size of the abdomen referred to above and the anal canal began to disappear usually within three or four days, being entirely gone, in some cases, in five days.

At autopsy the viscera were found, in every case, to be further advanced in metamorphosis than were the somatic parts as a whole, although the skeletal development was well advanced. The gastro-intestinal tract differentiated fairly early, being nearly half completed in nine days. The shrinkage of the liver that occurs normally during metamorphosis was very marked in these experiments, in one animal (E) becoming actually smaller than the gall-bladder. The gonads which are not directly affected by metamorphosis resembled those already described for thyreoidless larvae. The kidneys and spleen underwent their usual metamorphic changes in most of the animals of these experiments, but the gills tended to persist for a longer time than they do in normal metamorphosis. The lungs are not affected directly either by thyreoidectomy or natural metamorphosis, as we have shown in a previous publication, and there was no effect on them in these experiments. In all cases they were noted at autopsy to be expanded and to contain air, but this is true also of the lungs of undifferentiated larvae. The brain, which in thyreoidless larvae develops much more slowly than normally, was markedly stimulated in its growth by the hypophysis feeding, and after but nine doses given to animal I, for example, the brain had changed almost completely to the shape found in young frogs.

The skeleton, as indicated by the growth of the legs, showed considerable variability in its response to the pituitary substance. Animal F (Pl. V) developed a larger skeleton in a shorter time than did E, although at the beginning of the experiment it was the smaller of the two animals. The skin developed in some cases more rapidly than did the legs, and in C, D and F the right foreleg was unable to break through it.

The action of the pituitary substance in these experiments was somewhat less extensive and less rapid than has previously been described for the thyreoid in experiments of the same kind.

GENERAL DISCUSSION

It has been believed for many years that the thyreoid and hypophysis are able, to a certain extent at least, to function vicariously. This idea was expressed by Rogowitsch '89, who noted hypertrophy of the hypophysis in rabbits, following thyreoidectomy, an experiment probably first performed by Raynard '34 and repeated since by a very large number of other investigators. In cases of pregnancy (Paton '13) and in naturally occurring myxoedema, there has also been noted pituitary hypertrophy (Boyce and Beadles '93). Ascoli '12 has shown, on the other hand, that after removal of the hypophysis of mammals the thyreoid tends to atrophy, and Adler '14 and others have verified this finding in the amphibia. In addition to the above mentioned effects of removing either the hypophysis or the thyreoid, many other changes have been described for other organs and tissues, and changes in either the thyreoid or hypophysis can be produced by experiments other than removal of one of them. Livingston '14, for example, noted hypertrophy of the pituitary after the spaying of rabbits. Jackson '17 found that the hypophysis of rats decreases in size during inanition; Cushing and Goetsch '15 described a similar decrease in the pituitary of woodchucks during hibernation; in both cases the hypophysis returned to normal when the animals were given a normal diet.

The effect on the hypophysis of thyreoidectomy in mammals has been seen since the experiments of Rogowitsch '89, by Hofmeister '94 and more recently by various workers (see Vincent '12, Biedl '13, or Paton '13). Viguier '11 obtained the same effect in lizards, and Hoskins and Hoskins '18, Rogers '18 and Larson '19 have noted it in amphibia. Hence the relationship between the thyreoid and the hypophysis indicated by this kind of experiments probably obtains in all classes of animals.

Response to feeding thyreoid substance has been investigated in many kinds of animals and with fairly uniform results. When large doses are administered the animals are poisoned, but when properly regulated amounts are used there occurs a

stimulation which, however, has been interpreted differently by different investigators. This effect in mammals has recently been discussed by Hoskins '16, Herring '17, and Kojima '17, and in protozoa by Shumway '17. The classic studies of Gudernatsch '12, '14, have shown the remarkable stimulating effect of thyreoid extract when fed to amphibian larvae. Morse '14 found the action to be due to the iodine content of the thyreoid. He was unable to obtain it with inorganic iodine, but did obtain it with iodized blood albumen. Lenhart '15 stated that the effect on frog larvae was proportional to the iodine content of the thyreoid substance used, but he also was unable to get the same results with inorganic iodine. Lenhart pointed out further that the effect in hastening metamorphosis was of a general nature and not due to any specific differentiating property of the thyreoid. Romeis '15 using Lugol's solution likewise was unable to bring about precocious metamorphosis of frog larvae by administering inorganic iodine. Abderhalden '15 showed that the result could be obtained with thyreoid substance thoroughly digested and later, Swingle '18, repeating the experiments with iodine, was able to stimulate metamorphosis in normal frog and toad larvae and in those which had had their thyreoids removed. He hastened metamorphosis in frog larvae with M/1,100,000 iodine solution ('19). Allen '19 produced the same kind of stimulation in amphibian larvae which had had both the thyreoid and hypophysis extirpated.

From the above experiments, and especially from the work of Kendall '19, it seems highly probable that the active principle in the thyreoid is some iodine compound, and, as far as amphibia are concerned, inorganic iodine appears to be as capable of markedly stimulating metabolism as thyreoid substance itself. There are possibly various other organic and inorganic substances able to produce the same effect, if, as Kendall points out, it is simply in the nature of catalysis.

Experiments with the hypophysis are by no means so uniform in their results as are those with the thyreoid. There is an admitted relation of the hypophysis to carbohydrate metabolism as discussed recently by Keeton and Becht '19, and to skeletal and other growth (Cushing '12), but the exact details of these relationships are still in dispute. In higher animals, re-

moval of the hypophysis (Cushing '12) is incompatable with life, although larval frogs are able to live without it (Adler '14, Smith '16 and Allen '16, Hoskins and Hoskins '19a), and Houssay '17 was able to keep alive some adult frogs from which the hypophysis had been removed.

From 1897 to 1916 there was about an even division of opinion as to whether pituitary feeding would or would not give positive results (for discussion see Schiff '97, Biedl '13, and Hoskins '16), but since then most of the papers published on the subject agree that at least with the feeding of the anterior lobe of the hypophysis, a definite stimulation of growth can be produced. This has been claimed for protozoa (Flather '19), worms (Wulzen '16), birds (Winternitz '16, opposed by Pearl '16) and mammals (Robertson '17 and Marinus '19). Numerous other papers on the subject will be found abstracted in the files of Endocrinology, 1917-20.

Massay '08 tried to prevent the usual symptoms following thyreoidectomy of dogs, by hypophysis-extract injections, and obtained negative results. Larson '19 with somewhat similar experiments reports that these symptoms can be prevented from occurring in thyreoidectomized rats by hypophysis feeding, but Allen '19a, states that he obtained negative results when he administered beef pituitary substance to thyreoidectomized tadpoles. As described above, anterior pituitary substance will bring about almost if not complete metamorphosis of thyreoidless frog larvae.

As to the effect of feeding hypophysis substance to normal tadpoles, Gudernatsch '12, '14, reported negative results with hypophysis extract carried from New York to Vienna and kept in the laboratory at room temperature. Abderhalden '15 performed a few experiments with an extract of thoroughly digested hypophysis substance and found it very toxic to his tadpoles, but noted that in a few cases it seemed to stimulate their development. He regarded his results as indefinite. Smith '18, states that anterior pituitary substance stimulates growth of frog larvae just before metamorphosis and then hastens this process.

That we were able to bring about early metamorphosis in normal frog larvae by the administration of anterior pituitary

substance is not surprising, in view of the fact that hypophysis substance has previously been shown to stimulate metabolism and the fact that such stimulation is sufficient in itself to hasten metamorphosis of amphibians. As Lenhart '15 pointed out, in the numerous experiments wherein early metamorphosis of tadpoles has been induced, what really occurs is simply the hastening of a natural process. Nothing fundamental takes place during this hastened change of form that does not happen naturally at a lesser rate.

Concerning the manner of action of pituitary substance fed to animals, we have no certain explanation. We cannot as yet determine whether the action upon the metabolism is direct or whether the substance acts by stimulating some gland or other structures of the body. It is doubtful whether the influence of the hypophysis fed to normal tadpoles is exerted entirely upon the thyreoid because, as we described above, the same sort of phenomenon is seen when this substance is administered to larvae which have been deprived of their thyreoids. Moreover, the action is not simply a stimulation of all general metabolic processes, because thyreoidless larvae will live for months or years on a normal diet without undergoing metamorphosis, whereas they begin to metamorphose within twenty-four hours if anterior pituitary substance is administered to them. The hypophysis of these thyreoidless larvae has undergone a distinct hyperplasia, apparently in an attempt to make up the deficiency of thyreoid secretion, but it is not successful, and in these experiments the pituitary preparation may act through the animal's own hypophysis. Smith '18 was unable to cause metamorphosis of hypophysectomized larvae by hypophysis feeding, but as Allen '19b shows, larval amphibia which have been deprived of both thyreoids and hypophysis go nearly, if not completely, through metamorphosis if inorganic iodine is administered to them. But it is also true that the normal larvae in our experiments reacted more completely to pituitary feeding than did those which were without thyreoids, and more completely than did Allen's larvae which were without both thyreoids and hypophysis, react to iodine. Hence it seems probable that when the thyreoids and hypophysis are present their activity during metamorphosis is augmented by the administration of thyreoid, iodine, or pitu-

itary, and in the absence of one or both of these glands, the above mentioned substances are able to supplement their activity to a considerable extent. It is quite possible that Allen's larvae and our thyreoidless larvae failed to metamorphose completely because of the fact that when their jaws metamorphose they cease eating the administered substances. Swingle '19, however, caused normal and thyreoidless larvae to metamorphose by placing them in a dilute solution of iodine, so it is probable that this halogen is absorbed in quantities sufficient to produce the effect noted. It has long been known that the skin of amphibia is pervious to substances soluble in water.

In the metamorphic processes produced in thyreoidless larvae by pituitary feeding, there was some variability of the minute details of these phenomena as described above. In some larvae the skeletal growth was relatively more rapid than in others, and the changes occurring in the different viscera were variable, the entire process not being quite so well co-ordinated as in normal metamorphosis.

Finally, as stated in the introduction, the results obtained by feeding preparations of dead ductless glandular substances to animals may be pharmacological rather than physiological, and may not represent the normal functions of the animal. This is certainly true of feeding inorganic substances such as iodine.

SUMMARY AND CONCLUSIONS

We have found that a preparation of the anterior lobe of beef hypophysis, which contains some form of iodine, 1:200,000 of fresh substance, when administered to normal frog larvae will bring about a precocious metamorphosis, resulting in the production of frogs the size of which varies with the size of the larvae at the beginning of the experiment. If the original larvae are very small, they never become as large as the controls and the resulting frogs are small. Such frogs have little vitality. If permitted to remain exposed to the air they die and dry down almost flat, losing their shape, and there remains but a very small percentage of the original volume. We have not yet studied these small frogs microscopically, but they appear to have a relatively high water content. Pituitary substance is more toxic to small than to larger larvae.

When the pituitary preparation was administered to thyreoidless larvae which would otherwise have remained in the larval form more or less indefinitely, a beginning of metamorphosis occurred within twenty-four hours; it progressed somewhat more slowly than in the other experiments just mentioned; but it ultimately became nearly complete by the time the animals were either killed or died spontaneously.

From these experiments the hypophysis, in its relation to amphibian metamorphosis, is to be ranked with the thyreoid as shown by the well known work of Gudernatsch.

We regard the results obtained as due to a stimulation of natural general metabolic processes, either directly or indirectly, but the exact nature of this action is not known. The effect is both progressive, as seen especially in the skeletal and cutaneous development, and retrogressive, as seen especially in the digestive tract and tail.

It is very doubtful that the action of the anterior pituitary substance is due merely to its iodine content, although such may be the case. Other tissues with traces of iodine will not produce the same effect as the pituitary.

It is quite possible that the initial stimulation in hypophysis feeding is exerted upon the calcium and phosphorus metabolism as is indicated by skeletal changes in these experiments, although intestinal transformation also begins very early.

The hypophysis and the thyreoid are closely related physiologically and can to some extent function vicariously.

Recent investigations by various workers with amphibian larvae have developed the following facts concerning the thyreoid and hypophysis:

1. Removal of the thyreoid hastens growth, causes hyperplasia of the hypophysis and prevents metamorphosis.

2. Removal of the hypophysis retards growth, retards development of the thyreoid, prevents metamorphosis, and retards development of cutaneous pigment.

3. Feeding thyreoid or hypophysis (or iodine) to normal larvae hastens metamorphosis.

4. Feeding thyreoid or hypophysis (or iodine) to thyreoidectomised larvae brings about metamorphosis.

5. Feeding hypophysis to hypophysectomised larvae stimulates growth but does not cause metamorphosis.

6. Feeding iodine to larvae with both the thyreoid and hypophysis removed causes metamorphosis.

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PLATES I to VI

TABLE

PLATE I.

Fig. 1. Hypophysis-fed tadpole. (Ex. 1) 15 days after beginning of experiment. Body 11 mm. Total 32 mm. X 2.

Fig. 2. Normal tadpole. Body 13.5 mm. Total 32 mm. X 2. Both drawn from the living animal.

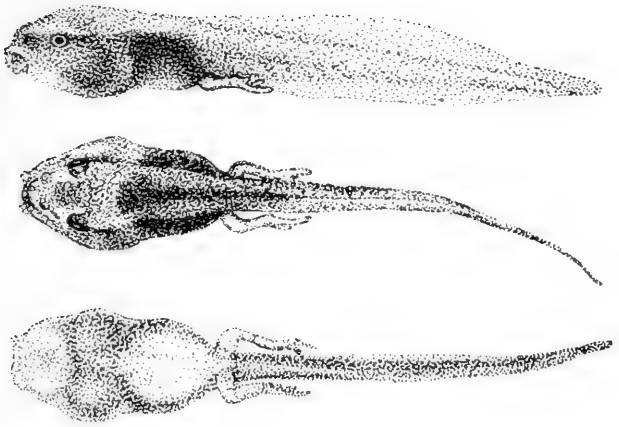


Fig.1

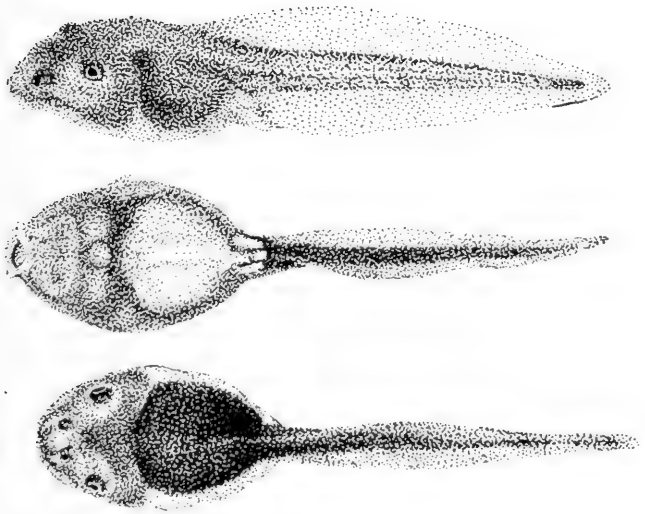


Fig.2

PLATE II.

Fig. 3. Hypophysis-fed frog. (Ex. 1.) 28 days after beginning of experiment. Body 8.8 mm. X 2. Drawn from the living animal.

Fig. 4. Normal frog. Body (fixed) 10.4 mm. X 2.

Fig 3

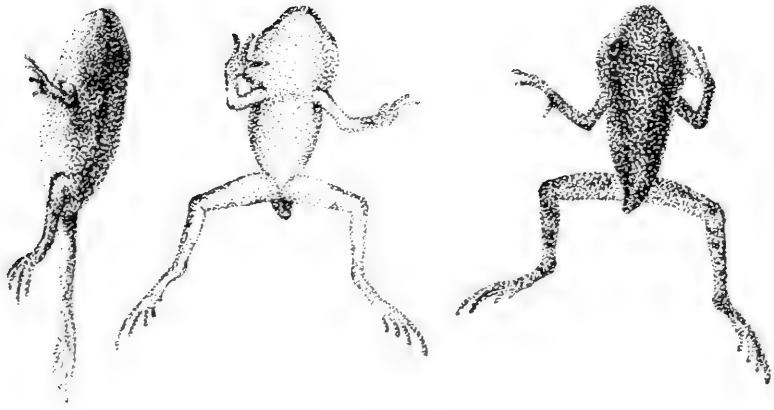


Fig 4

PLATE III. All drawn X 2 from the living animals.

Fig. 5. Hypophysis-fed tadpole (2 A) 18 days after beginning of experiment. Body 9.5 mm. Total 21 mm.

Fig. 6. Normal tadpole. Same age as above. Body 12 mm. Total 28 mm.

Fig. 7. Hypophysis-fed tadpole (Ex. 2 A) 28 days after beginning of experiment. Body 8 mm. Total 21.5 mm.

Fig. 8. Hypophysis-fed tadpole (Ex. 2 B) 13 days after beginning of experiment. Body 12 mm. Total 28 mm. Compare with Fig. 6 for tadpole of same length.

Fig. 9. Hypophysis-fed tadpole (Ex. 2 B) 31 days after beginning of experiment. Body 15 mm. Total 35 mm.

Fig. 10. Normal tadpole. Same age as in Fig. 9. Body 15 mm. Total 33 mm. (Later the controls became larger than the hypophysis-fed larvae.)

Fig. 5

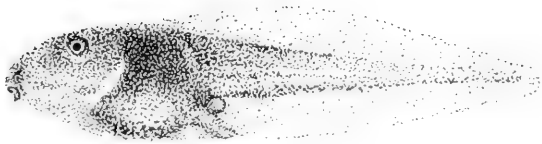


Fig. 6

Fig. 7

Fig. 8

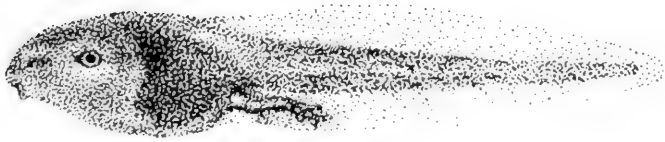


Fig. 9

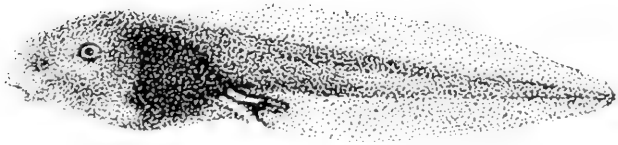


Fig. 10

PLATE IV.

Figures D to J. Normal Rana sylvatica natural size photographed in alcohol after fixation. The larvae (D to N) had reached their maximum size and were on the point of beginning a rapid metamorphosis when fixed. Note the shrinkage in size that has occurred during metamorphosis (B to J).

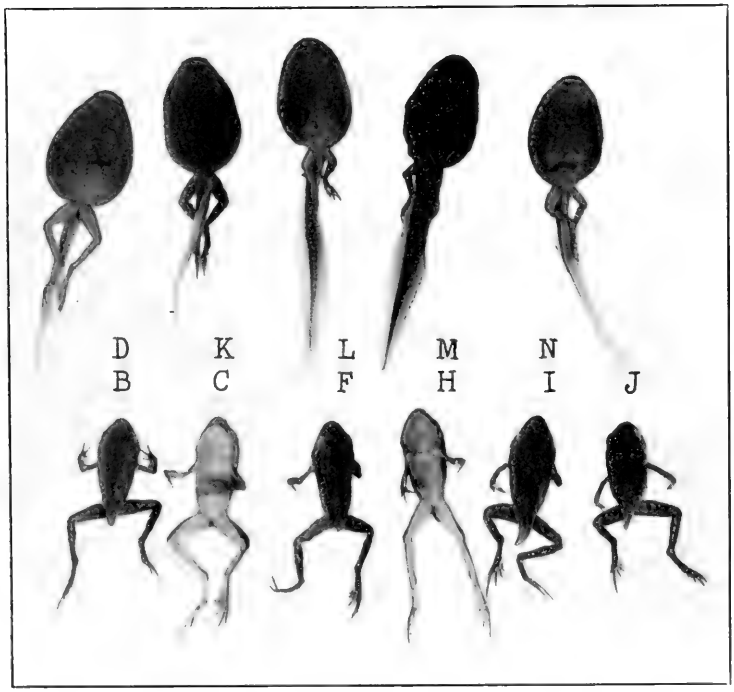

D
B
K
C
L
F
M
H
N
I
J

PLATE V.

Figures A.A. to J. Thyreoidless Rana sylvatica, natural size. Photographed in alcohol after fixation. For size and number of doses of anterior pituitary substance administered see Table. Note G. which received no medication. The development is roughly proportional to the amount of pituitary given, and the size of the frogs is proportional to the size of the larvae before medication. A, C, and D died in the aquaria and became slightly swollen.

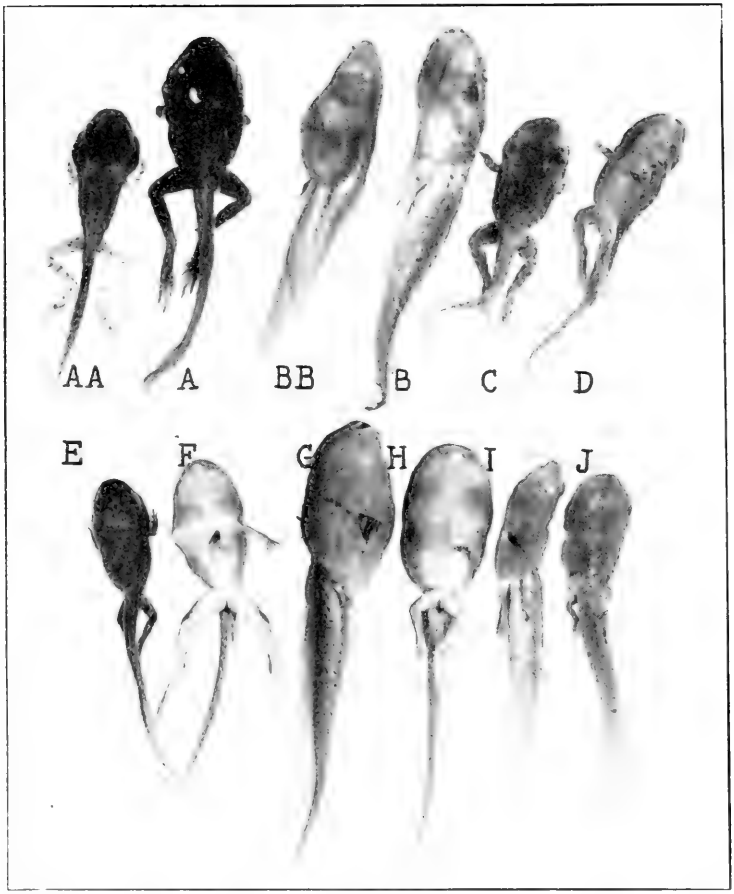
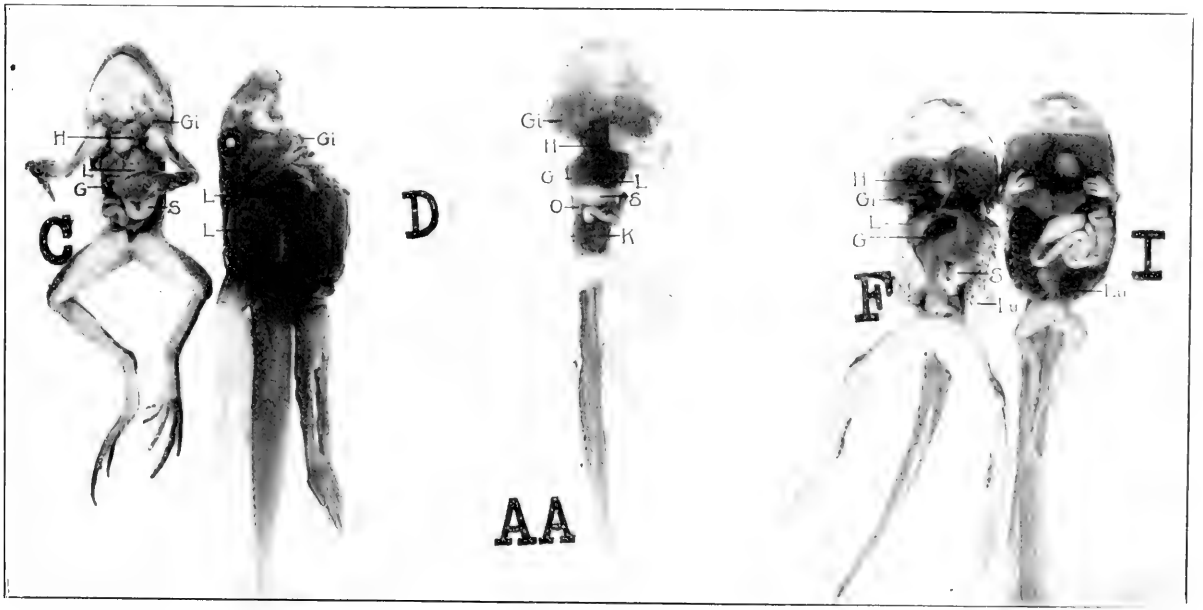

AA
A
BB
B
C
D
E
F
G
H
I
J

PLATE VI.

Thyreoidless and control larvae and "frogs" of Rana sylvatica treated with anterior pituitary substance. Same animals as in Plate V. but dissected. X 3. C and D—Controls; AA, F and I—Thyreoidless.

Abbreviations: G.—Gall-bladder, Gi.—Gill, H.—Heart, K.—Kidney, L.—Liver, Lu.—Lung, O.—Ovary, S.—Stomach.


C
H
Gi
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F
I

TABLE SHOWING THE EFFECT OF TREATING THYREOIDLESS LARVAE WITH ANTERIOR PITUITARY PREPARATION.

	Beginning	2 days	4 days	9 days	10 days	12 days	15 days	22 days	31 days	Doses
	mm. cc.	mm. cc.	mm. cc.	mm. cc.	mm. cc.	mm. cc.	mm. cc.	mm. cc.	mm cc.	
A.A.	42-19.0-2.0-0.98	43.5-19.0-	45-19.0-0.75	45-16.0- 5-0.65	45-14- 5.5-0.65	41-14- 6-0.75	42-14- 9-0.75	40-15-16-0.50	36.5-15-17-0.35	*15
A.	50-20.0-2.0-1.50	41.0-20.0-2.5-1.20	41-20.0-3-1.10			48-17-15-0.96	44-17-20-**			18
B.	46-20.0-1.5-1.30	47.0-20.5-2.5-1.10	48-19.0-3-1.00	47-16.0- 7-0.85	**					8
B.B.	47-20.0-2.5-1.20	48.0-20.0-	45-18.5-3-0.80	*						3
C.	43-21.0-2.0-1.35	43.5-20 5-2.5-1.20	44-18.0-3-1.00		44-16- 8.0-0.75		40-15-13-**			18
D.	42-18.5-1.5-0.90			41-14.0- 5-0.60		39-14-13-**				13
E.	44-19.0-1.5-1.00			41-14.0- 5-0.55		38-14-11-		36-14-12-0.40	*	21
F.	45-19.0-2.0-0.93		47-17.0-7-0.80		45-16-13.-0.70		42-17-18-0.56	*		15
G.	47-19.0-2.0-0.98		48-21.0-2-1.06		51-21- 2.0-1.08		52-22- 3-1.40	*		0***
H.	53-23.0-2.5-1.45		54-20.0-5-1.22	50-19.0-10-1.05	**					9
I.	46-20.0-2.0-1.05		43-16.0-3-0.80	41-14.5- 7-0.50	*					9
J.	44-19.0-2.0-1.00		43-16.0-3-0.85	42-14.5- 7-0.65	*					9

N. B.—The first number, total length; the second, nose-anus length; the third, hind-leg length, all in mm.; and the fourth, volume, in cc.
*Killed. **Died. ***Control thyreoidless.

PITUITRIN TEST

By
M. ASCOLI and A. FAGIUOLI

From the Institute of Internal Pathology, University of Catania
(Director, Prof. M. Ascoli)

In a previous article (1) the *adrenalin test* has been described. The subepidermal (s.e.) introduction of 0.05 c.c. of a 1:1000 solution of adrenalin (2) provokes the appearance of a swelling which, after a few seconds, or sometimes immediately, assumes a dark blue color, as if ink had been injected. Sometimes the periphery of the spot is red. The swelling then becomes surrounded by an alabaster-like halo, which grows in intensity and extent, often sending out irregular shoots in one or more directions. Around the white halo appears in turn another red halo, more or less intense in color and width. Frequently, a contraction of the pilomotor muscles of the skin occurs, which gives the appearance of goose-flesh to the alabaster zone.

The reaction in its complete form is therefore composed of the three following elements: 1. *Blue central spot*, 2. *White Halo*, 3. *Red Halo*. Having reached its utmost development in half an hour, after a stationary period, within an hour or so the reaction gradually disappears, the blue spot changing to red, leaving a slightly swollen red papule which in succeeding days goes through the usual stage of pigmentation.

By using a more dilute solution, for instance 1:200,000—1:1,000,000, the reaction is less intense, but nevertheless always manifest and preserves the same general type. It differs, however, by the absence of the central blue spot, generally substituted later on by a small red mark. This and the white halo around the alabaster swelling comprise in this case, the whole picture; the red halo is not always pronounced. The more dilute the solution, the later, up to 20 minutes and more, is the appearance of the response.

By further dilution the reaction becomes weaker, until it gets to be identical with the *indispensable* control reaction with distilled water. This water injection causes simply a white swell-

ing and a halo, which is not white but reddish. Briefly, the swelling becomes colored, afterwards to fade again with (always relatively) variable duration and intensity of the single phases in different subjects. A small reddish brown papule remains for one or more days and changes to a small brown spot (3).

The reactivity of the subepidermal adrenalin test in ordinary circumstances is usually included between dilutions of 1:200,000 and 1:000,000 (Parke, Davis vials). In some pathological conditions, however, it may be diminished or increased. We found it subnormal (viz., negative with these dilutions) in some cases of Addison's disease and of chronic adrenal insufficiency; increased (viz., positive with further dilutions, up to 5-20 millions), in some cases of disturbances of the menopause, of arterial hypertension, of Flajani-Basedow's disease and in some cases of pregnancy. Children give a weak reaction. Cases of profound anemia do not react.

Comparing in 26 cases the sensitivity to adrenalin administrated subcutaneously (s.c.) (1 cc. of 1 per thousand solution) and subepidermally (s.e.), we have had 21 cases of normal reaction in the s.e. test, no reaction to the s.c. test and likewise in two cases of s.e. hyper-reaction. In two cases of exaggerated s.e. reaction, there was only an increase of a few cm. of the arterial pressure to the s.c. test. Finally, in a case of scleroderma with arterial hypertension with normal s.e. test, the s.c. injection produced a marked reaction (notable increase of pressure, dizziness, tachycardia, tremor, traces of glycosuria). The failing cutaneous response may perhaps depend upon the sclerodermic lesion, although not macroscopically appreciable in the place of injection.

Another s.e. test, not hitherto described, is that with *pituitrin*. After what has been recorded the description of it is easy. Using the commercial solution, the reaction is identical with that obtained with a solution of adrenalin, about 1:200,000. Under ordinary conditions there is still a positive reaction with dilutions of about 1:500 of the commercial vials of pituitrin (Parke, Davis), but there is a delay in the appearance of the characteristic feature, the white halo about the swelling. We have found the reaction strengthened (positive even in dilution of 1:1000 and more) in arterial hypertension, in affections of the

pituitary body, in some cases of Flajani-Basedow's disease and reduced in some cases of chronic adrenal insufficiency.

Worthy of special mention is the circumstance that, if at times there may be a coincidence between the exaggerated or reduced reactivity to the two substances, in the great majority of cases *the pathological reactions to adrenalin and pituitrin are clearly shown dissociated and even opposed.*

We have pointed out that the solution of adrenalin at 1:200,000 gives approximately the same reaction as the vials of undiluted pituitrin; it has also been noticed that, although the reaction to adrenalin does not appear when the standard solution is diluted over five times (1:1,000,000), pituitrin, on the contrary, still maintains its special action when diluted to 500 volumes. The cause of this contrast is perhaps to be sought in the different points upon which the drugs exert their action, these being the neuromuscular junction in the one case and the muscle fibres themselves, in the other.

1. Ascoli (M.) and Fagiuoli (A.), Pharmacodynamic subepidermal tests, Accademia dei Lincei, 1919. After communication of this note we had occasion to read the review "The adrenin tests for thyroid disorders" in Endocrinology, Vol. II, No. 4. On page 463 the following passage appears: "This result was found to be remarkably constant. Not only does a 'hyperthyroid' patient react constitutionally to a subcutaneous dose, but also locally to an intradermic dose of one minim of 1-4000 solution of adrenin. This latter reaction depends upon the excessive contraction of the smooth muscle in the small vessels of the skin, supplied by the sympathetic, and is characterized by a central large area of blanching surrounded by a peripheral zone of reddening due to the neighboring secondary vasodilatation. In the blanched area a characteristic goose flesh is often seen. The reaction in a thyroid patient (exophthalmic goitre or toxic adenoma) lasts for 1½ to 2¼ hours as compared with ½ to ¾ hour in the normal subject. Whether the reaction will be found in other than thyroid cases has not yet been determined." We could not yet procure the original work of Goetsch, "Newer methods in the diagnosis of thyroid disorders: pathological and clinical. B. Adrenalin hypersensitiveness in clinical states of hyperthyroidism," N. Y. State Jour. Med., 1918, **18**, 259.
2. One stretches between two fingers laterally a small piece of skin of the anterior abdominal wall; where the skin is more distended, one introduces the point of a very fine needle attached to a small glass syringe, graduated in at least 1/20 cc. An essential condition is that the needle be pushed quite superficially under the epidermis, so that it is *clearly* visible underneath the skin: the injection must not be intradermal, but *subepidermal.* We insist on this point because the neglect of it may jeopardize the success of the result. One presses slowly the piston until 1/20 cc. of the desired solution is injected. As a measure of control in every experiment an injection of sterile distilled water at a distance of about 5 cm. must be made.

3. The practice of the simultaneous control injection of distilled water, as a test of the general reactivity of the skin *is never to be neglected.* Usually it presents the described type. At times, however, abnormal reactions are observed, which must be known. At times the swelling remains white for a long time (60-90 minutes); exceptionally the phenomenon of the goose flesh may appear. The quantity of liquid introduced and the depth of the injection are, moreover, important and must be considered. The involution time of the red papule, usually about 48 hours, is also variable. Unlike the s.e. injections of adrenalin 1:1000, and pituitrin undiluted, which cause almost no pain, dilutions with water are painful.

A PLEA FOR SYSTEMATIC RESEARCH WORK IN THE ANATOMY, NORMAL AND MORBID, OF THE ENDOCRINE SYSTEM

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The above title may cause some reader to ask whether there really is anything wrong with regard to method in the present anatomical study of the endocrine organs. Indeed the great progress that our knowledge of the endocrine system has made during the last decades as well as the great profit that science has already reaped in this department are rather proofs of the contrary. Perfectly aware of this and of the importance that the methods of research so far used will doubtless have in the future as well, we must not shut our eyes to the fact that this study has its weak point, which forms a positive risk to the sound development of the new branch of science. This weak point is the want of a close anatomical insight into the organs in question.

First of all, I wish to show here that without such a deepened insight great departments of endocrinology must either remain completely inaccessible to us or at all events without sufficient stability.

It is a well known fact that *direct* lesions of endocrine organs occur, and frequently a certain clinical syndrome has more or less unanimously been considered to be connected with such lesions of one organ or another. To discern such direct lesions, at least when they are somewhat pronounced, our present knowledge has often proved sufficient. But, both in connection with exophthalmic goitre, Addison's disease, acromegaly and diabetes —to mention only some of the most studied ones—occur, as is well known, "formes frustes," in which the want of precision in our present anatomical knowledge is perceptible.

Another circumstance is, however, of still greater importance here. It is a commonly acknowledged and well-grounded experience that the endocrine organs are closely connected with each

other functionally; so that a disturbance in the function of one of these organs involves, according to the circumstances, a more or less profound disturbance in the function of a larger or smaller number of the others. Whether this state of things is characteristic only of the endocrine system or whether after more careful research anything of this sort will be also proved for other organs of the body, is another question, which it is not necessary to enter into here. It is sufficient here to establish that in such cases we must reckon not only with direct, but also with *indirect* disturbances of the endocrine organs.

But, indirect disturbances of the endocrine organs might not occur only in the cases in which the injurious factor ("noxe") has affected one or other member of the endocrine system. On the contrary, certain observations make it probable that in the case of other sorts of disease as well, the organs in question do not remain unimpaired. Thus, for instance, in the case of diphtheria and other infectious diseases, such an influence in many cases is established. It does not at present even seem absurd to presume that every disease of some duration and seriousness more or less affects the whole endocrine system, as is in fact, under such circumstances, always true of the thymus gland.

It may now be presumed that indirect changes of one kind or another, which up till now have for the most part not attracted any attention, are by no means always qualitative, perhaps not even chiefly so, but that there may also be, as in the case of the thymus gland, essentially quantitative changes. *But for the purpose of fixing quantitative changes with only a fair degree of certitude, our present knowledge of these organs is decidedly too limited.*

This circumstance may at least partly account for the fact that we have so little information about these indirect changes in the endocrine organs. Very often the system in question may even now be left without attention at the post-mortem examination and when really examined, no conclusions or only very vague ones are arrived at in the absence of an adequate acquaintance with the normal state of the respective organs. Which of us is able at the present time to tell how much or how little of the medulla of the adrenals is present in a man or woman at a certain age before the limits of the normal are exceeded?

What is our present knowledge of the extent to which the so-called gland of puberty is to be found at a certain age in a normal human sex gland? Or of the relation between the quantity of acinar and trabecular tissue in the normal thyroid? Or of the normal total number and size of the islets of Langerhans in the pancreas at a certain age? There is no end of questions of such a kind that crowd upon us in this sphere without our being able even to sketch an answer.

We may try to become acquainted with the real significance of the conditions outlined above: that at every disturbance of an endocrine organ, other endocrine organs too must be affected, that in other diseases these organs probably are also concerned without its being in our power to determine either the participant organs themselves or the degree to which they are afflicted. It really means that neither dissected material nor experimental work can, as matters now stand, by any means be made duly profitable to science.

As suggested above, in the first place normal data of comparison are a pressing need. Whether there is an increase or a diminution, whether too much or too little, can only be decided when we know sufficient about the range of the normal variation under corresponding circumstances as to age, sex, etc.

Our ignorance begins in connection with the mere size (the weight) of the organ. It is true that, even in the present literature, there is no lack of such *indications,* but I do not know a single one which, in the case of man, can even tolerably serve the purpose in question. They all suffer principally from two defects. First, in most cases mere averages are given. Nowadays, I suppose, no investigator holds the opinion that with regard to any organ averages can be given of such a nature that what does not agree with that standard should not be regarded as normal. Under such circumstances, averages are of comparatively little use. The important point is to determine as exactly as possible the normal range of variation. Mainly in order to give an orientation as to the position of an individual value within (or outside) the normal range the average may be of importance.

Secondly, the quality of the primary material hitherto published is mostly far from being sufficient for the present purpose. Generally, only the cases where obvious morbid alterations

of the organ in question were found or could be expected, have been excluded from consideration, while other cases of disease were considered available for statistical estimate of the normal organ. It is, however, quite evident that for the very purpose of creating a normal basis upon which eventual indirect organ lesions, affected by disease, can be recognized and evaluated, values thus acquired are quite useless. Only such organs as come from individuals who have suddenly died in full health and not by disease are available for the purpose. In the case of human beings, principally organs from murdered people, executions, accidents or suicides (1) will thus come into consideration for determining the normal range of variation. It may be unnecessary to point out that even in such cases the circumstances may give rise to criticism and exclusion of some cases. Anyhow, it does not seem necessary to enter into that question in this connection.

The mere determination of the limits within which the size of the organ—the weight of the organ—normally varies, is, however, only one condition for gaining available values in the following analysis of the organ. Generally, one will not make much progress by using merely the size of the organ. It is well known that a change in size may, under different circumstances, have quite a different bearing. A goitre represents sometimes an increase, sometimes a decrease, in the function of the thyroid. A reduction of the pancreas has a very different significance according to whether it has affected the exocrine or the endocrine component of the gland; an increase of the hypophysis or the adrenals, according as one or other of the heterogeneous components of the respective organ is affected, etc.

For this reason *we must elaborate for every endocrine organ special methods which admit of a quantitative—numerical—determination, with sufficient accuracy, of the material components of the organ.* In what manner such a method can be evolved for a particular organ can be gathered from a paper (Ztschr. f. angew. Anat. u. Konstitutionsforsch. Bd. 1.), where the writer set up the problem of fixing numerically the quantity of the cortex and the medulla of the thymus gland and the number and size of the Hassall's corpuscles.

Every organ has no doubt in this respect its own peculiar problems, a complete view of which can be obtained only by very

close attention to the subject. Some of these problems, however, are so obvious that they may be indicated without further investigations.

Thus, for instance, in the hypophysis, with accurate elimination of the connective tissue, the amount of each of the three principal portions ought to be ascertained. In the anterior portions the number of the different cell types, in the intermediate portion the number and size of the cysts with and without colloid should be approximately settled.

In the thyroid the weight of the true parenchyma similarly with deduction of the bulk of the connective tissue is to be ascertained; again, in the parenchyma the amounts of the trabecular and adenomatous territories, respectively, should be fixed apart from the acinar portion; and in the last mentioned part the number and size of acini with and without colloid should be calculated.

Similarly, in the parathyroid glands the true parenchyma, the trabecular and cystic tissue should be treated separately. Here, moreover, we meet with the task of approximating the relative and absolute numbers of the acidophil granulated cells.

With regard to the pancreas, the next object should be to ascertain the quantity of the endocrine and the exocrine parenchyma as well as to calculate the number and size of the islets of Langerhans.

In the adrenals the quantity of the cortex and the medulla as well as of the different zones of the cortex requires to be expressed numerically. Perhaps it will not prove quite impracticable with morphological methods to approximate the percentage of lipoids and adrenine in the organ, which would evidently be of the greatest consequence for estimating the state of function of an individual organ.

Concerning the sex glands, it is of special importance to ascertain the amount of endocrine tissue, in doing which for the ovaries, the corpora lutea and the other so-called lutein tissues should be considered separately. To settle the number and size of the ovarian follicles lies, as Valberg (1915) (2), has shown, within the bounds of possibility even in the case of a relatively large material. To figure the state of the spermatogenesis with fair accuracy seems, at all events in the case of a human being,

where the process passes on so irregularly, a difficult task; but it would, however, evidently be of great importance.

In all these enumerations we cannot stop at apparent or relative values; the real and absolute amount of every element of tissue treated must be approximately fixed. We must not forget that a relative increase of a structural element is perfectly compatible with an absolute reduction and vice versa, as I have stated in my above cited paper on thymus methods in general.

These hints may suffice to illustrate the type of problems which should, in the first place, be taken into account. It is not my object here to plan in detail the work on every organ with internal secretion.

That such problems can really be solved without insuperable obstacles is shown, inter alia, by a series of investigations on rabbits carried out from this point of view and dealing with most of the organs in question; these are recorded in another place (3). Similar investigations of the hypophysis and the adrenals in the albino rat have lately been published by Jackson (1917, 1919) (3a). Indeed, this author has even gone further in his analysis than I have suggested above, as he successfully treated both the frequency of mitoses and the size of parenchyma cells and nuclei.

Certainly, the cases mentioned here deal with the organs of animals and even of relatively small animals. Highly welcome as such researches are, not least as a basis for experimental work, the difficulties in procuring available material and analyzing the voluminous organs increase considerably, however, when the subject of the investigation is man. And it is precisely concerning man that we are in greatest need of the norms in question.

In the case, however, of at least one human organ of this kind, the thymus gland, I have found that investigations of this sort, even in the case of human beings, need not be considered impossible (4).

In the course of the last fifteen years, thanks to the liberality of several Swedish colleagues, I have been able to collect about 120 human thymus glands from post-natal life and about 60 specimens from intra-uterine life, which satisfy fairly well the demands made above. In analysing this normal thymus material, I have obtained norms for the different epochs of pre-natal and

post-natal life, against which can be tested values that have been gained with the same method in pathological cases. In this way it can be directly decided whether an organ from a case of disease shows any abnormality with regard to the absolute quantity of cortex or medulla, or to their reciprocal amounts, or with regard to the relative or absolute number of Hassall's corpuscles of one size or another. At present about 400 pathological cases have thus been analysed. The result as to certain categories of cases (exophthalmic goitre, "thymic death," certain acute infectious diseases, congenital lues) have already been published (5). The others are being prepared for publication. It seems to me as if certain of the results already gained are not only of an importance that is abundant compensation for the trouble taken, but also that they could scarcely have been obtained with the same degree of certainty by any non-numerical method.

I have now touched upon the second phase of the method of proceeding that I recommend here. It is evident that as soon as normal material, sufficient both in quantity and in quality, has been numerically analysed in the manner described, any case of disease, analysed in the same way, can with far more ease and, what is of still greater importance, with far greater certainty than at present, be estimated in all the respects that have been objects of the analysis. Just as in the case of the thymus, *by following the attained norms, we shall be able to decide whether a value from a case of disease falls within or outside the range of the normal and in what direction an eventual displacement has occurred.* It is a matter of course, that under these circumstances, too, the manner of proceeding can never be purely mechanical, but that the sane judgment of the investigator is always a decisive factor.

We shall also see how much here depends on the adequacy of the normal test material both from a qualitative and quantitative point of view. One single case, erroneously interpreted as normal, may be sufficient to give an undue extent to the normal range. And only as greater experience is obtained, are we able to conclude whether the range has been too limited in one set or other. It is also a matter of importance that, after all, for most of the organs in question a sex difference exists; we shall thus have to take into account both differences of sex and differences of age.

No doubt our claims as to the nature of the normal material will increase as our experience grows. Indeed, once the method of work that I plead for here prevails, this will come naturally.

It is, however, important that the method should, from the very beginning, be at once so exhaustive, so elaborate and with such careful foundations that it can claim to possess some stability or can even very soon become a standard for succeeding work. For, otherwise it is to be feared that with every improvement of the method that is found necessary, all the previous analytical work may be found inferior or defective and have to be done all over again. For this very reason I think methods that have been, as it were, improvised to answer the purposes of some special investigation do not come up to the mark. Every organ must be made the object of a comprehensive revision which takes into consideration not only the normal but also the morbid organ structure, the various functional changes, faults caused by shrinkage or swelling and otherwise during the technical treatment, etc. And before such a method is seriously put to practical use, its precision must have been duly tested. Furthermore, all this must be done for every separate species that is to be dealt with.

Here, indeed, an association of investigators for systematized co-operation, such as I have recommended in my paper upon constitution research work, would be of great use. *Would it not be rather a great thing for the Association for the Study of Internal Secretions to put upon its program the task of elaborating and standardizing such methods?*

In proportion as, by means of a numerical working-up of different morbid cases and their comparison with a normal test material, our knowledge increases, the obstacles to our going deep in this branch of science will disappear. In my opinion, there can be no doubt that this research work must be done sooner or later, and the sooner the better for science.

I am not disposed to try to prophesy what positive results will come from such a deepening of our present knowledge. Only, before I come to an end, I should like, more by way of example, to indicate some questions which will then be ready for exact treatment.

From different quarters the suggestion has proceeded that the mental diseases, or at least certain of them, are connected

with troubles in the endocrine system. Except for the experience that has been obtained with Abderhalden's method, results which can hardly be described as decisive, I do not know of any exact attempt to test this interesting hypothesis seriously. The method of working here recommended seems to pave the way for such a test.

The correlation between the brain and the endocrine system may also possibly be elucidated to some extent in that way. That such a correlation really exists is well known. In this connection it is enough to point to the splendid effect on the mental state that thyroid medication has had in certain cases of athyreoidism; or to remind the reader of the characteristic psychical habit in exophthalmic goitre, a habit which, after a successful reduction of the struma, may again give way to a normal state of mind, or to mention the changed mentality of the castrate, compared with the sexually normal individual. The instances could easily be multiplied. I think that the exact anatomical study of the endocrine system here opens the way to the biological aspect of mental activity, which should not be overlooked.

And a further point: only as far as we obtain an analogous exact knowledge of the organs with internal secretion in our experimental animals, can we lay a solid foundation for experiments designed to influence these organs therapeutically; and it is evident that this opens wide fields to us.

And, finally, by the kind of work recommended here an important preparatory step would be taken towards the realization of the still greater program of an anatomical constitution research, a subject to which I have tried to draw the attention of anatomists in the paper quoted several times above.

Indeed, each of the branches of work mentioned here alone is great and important enough to make the method of work recommended seem amply profitable. In order not to be misunderstood I might be allowed to make a further observation. I am far from thinking that the problems mentioned, or analogous ones, can be solved by this method *alone*. I would only emphasize that without a deepening of our anatomical knowledge by exact quantitative work we may never be able to solve them at all.

A systematic numerical study of the anatomy of the endocrine system is thus a necessary condition for an exact treatment

of the important problems that are to be solved in this field.

Upsala, September, 1919.

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ADRENALIN IN ASTHMA. A CASE OF CHRONIC ADRENALISM

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The effect of the continued use of adrenalin has been so seldom reported that every well marked case demands the publication of its record. Accordingly we are submitting the following notes on a case occurring in the medical service at the Kansas City General Hospital.

Case History

Female—Age 24—Married.

Chief Complaint: Asthma; Wheezing; Shortness of breath, paroxymal in type; Cough.

History of Onset: Six years ago the patient began to have coughing spells. These spells began in November and in the following January the wheezing began. The asthma has been practically continuous ever since. These attacks are the same throughout the year. They are always worse when lying down. At the time this trouble started the patient was pregnant and was working in onion beds. The patient has noticed that when she eats eggs, pears, peaches, and other fruits the attacks are made worse.

Menstrual History: She had had two children. Up until three years ago the menses were normal, but in the last three years she has had only two menstrual periods.

History of Use of Drugs: Since this trouble started six years ago the patient has been using adrenalin for the attacks, using about 7 c.c. daily. If deprived of the drug she became frantic. She also was addicted for a time to the use of chloroform inhalations. Up until a year ago she was also a user of morphine, the amount used not known. These habits were the results of attempts to relieve the almost constant dyspnea.

Physical Examination: Female appearing about 30 years of age, in good flesh (neither obese nor emaciated) walking about the ward. Her breathing can be heard for some feet away; she uses the accessory muscles of respiration.

Head: Scalp, ears and nose negative.

Throat: The tonsillar pillars are injected and covered by adhesions to the tonsils.

Eyes: The sclera is clear and both pupils are equal and react to light and accommodation.

Neck: Palpable glands at angles of jaws. Thyroid palpable.

Chest: Lungs—There is lack of expansion on both sides. The patient uses the accessory muscles of respiration. Tactile fremitus is decreased. The chest is hyperresonant. Both expiratory and inspiratory sounds are prolonged with various types of dry whistling rales throughout the respiratory cycle.

Heart: Cardiac dullness seemed normal. The heart tones are strong and regular and no murmurs are heard. Pulmonic second sound seems exaggerated. The blood pressure at the first examination was systolic 155, diastolic 140. At other times it was 160-98.

Abdomen: Because of voluntary rigidity of abdomen, the patient is hard to examine. There are no palpable masses of liver or spleen or notable tenderness.

Skin: Both arms and legs are scarred by the use of the hypodermic needle. On the forearms and ankles there are girdles of this scar tissue about four inches wide.

Extremities: Reflexes are normal.

Death: Patient died suddenly and unexpectedly. Her last dose of adrenalin had been 2½ hours before (1 cc.). Before death the patient was very nervous and noisy, throwing things about the room. She was found dead, lying on the floor, and when found appeared anemic. It had been discovered that patient had adrenalin and a hypodermic outfit and was self-administering the drug while in the hospital and for this reason she had been taken from the ward and put in a locked room.

Previous Entrance to Hospital: Entered Aug. 10, left Aug. 12, 1919. Entered Oct. 3, and left the same day, 1919. No record of findings on these entrances.

Laboratory Findings: Kidney function test, phenol-sulphonephthalein—15% excreted the first hour; 35% excreted the second hour.

Blood Findings: Red cells, 5,120,000; white cells, 8,400; hemoglobin (Tallquist) 80%.

Differential Count: Polymorph. neutrophiles, 53%; small lymphocytes, 27; large lymphocytes, 16; eosinophiles, 1; mast cells, 3.

Cultures: Cultures from sputum after giving KI gave growths of streptococci.

Post-mortem Findings—

Chest: The pleural cavity contained no free fluid. Both lungs were anthracotic. The left lung appeared normal. On cut section it showed areas of collapsed lung tissue intermingled with areas of compensatory emphysema.

The right lung was partially collapsed. There were adhesions from the lower border of the lower lobe posteriorly to the diaphragmatic pleura.

No obstructions along the respiratory tract were found. Cut section across the bronchi and their branches showed them to be patent.

The lumen contained some thick tenacious mucus.

Heart: The heart was slightly larger than normal. It was in systole, the left heart being firm and contracted. The right heart was dilated to a slight extent, with some hypertrophy of its musculature. The valves were normal. The coronary openings were patent and sclerotic. The aorta was normal in size, but contained several sclerotic plaques along the ascending portion and the arch.

Abdomen: No free fluid was found. The liver was enlarged and pushed downward and on cut section showed extensive fatty degeneration.

The stomach appeared normal. The spleen was twice the normal size and on section showed nothing abnormal. No pathological condition was found along the bile tract. The pancreas was normal. The intestinal tract was not otherwise abnormal but was very much congested. The appendix was normal. Both kidneys were congested and there were some drops of pus in the calyces of the right.

Sexual organs: Both ovaries were sclerotic, but the tubes appeared normal. The uterus was small and was in normal position.

Vascular system: All the large vessels were filled with fluid blood and no clots were found. There were small sclerotic patches along the aorta (round, not stellar).

Reaction to Drugs

An attempt was made to ascertain the patient's reaction to the various antiasthmatics and glandular extracts. As will be seen from the accompanying charts, atropine and amylnitrite lowered the diastolic pressure, thus increasing the pulse pressure and affording some subjective relief. Pituitrin simply increased the blood pressure, and gave no relief. Corpus luteum (P. D. & Co.'s ampoule) gave no relief. Adrenalin gave varying results, of which two charts are given. Apparently the subjective relief was due to the increased pulse pressure.

The attempt to secure an autogenous vaccine failed, because of some slip at the laboratory.

The use of a nonspecific vaccine (typhoid, 50 millions) caused no reaction and no change in the subjective symptoms.

The patient was kept fairly quiet by exhibiting 15 minims of adrenalin per os every three or four hours. But this did not prevent her stealing chloroform or morphine whenever the opportunity presented. However, she did not secure enough of these to affect materially her condition; and the picture is one of the adrenalin habit—if it may be so called.

Whenever the patient was deprived of the adrenalin for a

half day, she would become frantic, and if allowed to go on would develop a cyanosis of lips and fingers, with a loss of the radial pulse—a condition so alarming that the attendants hastened to use the adrenalin and relieve her.

DISCUSSION

Sajous states that "the prolonged use of adrenal preparations may induce chronic adrenalism, manifested by marked cardiac disorders, especially of the myocardium, dyspnea after slight exertion, tachycardia, high blood pressure, polyuria, icteric staining of the conjunctiva, and marked increase in weight." In our case, we noted cyanosis and circulatory failure on three or four occasions when we had attempted to stop the use of adrenalin, and to substitute other drugs. But at no time did we find evidence of myocardial disorders other than the decreased force, or pulse pressure. She was not obese.

Erlanger and Gasser believe as a result of animal experimentation that large doses of adrenalin do long-lasting damage to the circulation, if they do not actually carry the pressure down to a dangerously low level. "Peripheral constriction persists for hours." The heart develops irregularities under adrenalin. "The failure of the circulation is to be attributed to the extreme slowing of the blood throughout the body by the constricting action of the adrenalin on the arteries. It is concluded that the cause of the failure is the same as is operative after temporary partial obstruction of the vena cava or the aorta. This conclusion is justified by the fact that the most striking lesion found in animals dying as a result of any of these three procedures is alike in all cases, and consists of tremendous engorgement of the capillaries and venules of the villi of the intestines." Our findings would seem to be in accord with these experimental conclusions. For no lesion sufficient of itself to cause death was found. Even the collapsed lung would hardly do more than lower the vitality of the patient.

The small plaques found in the aorta show the beginning of the sclerosis, which we had expected to find in much greater measure.

It is interesting to note that the use of adrenalin even by the mouth gave some relief. The subcutaneous route also gave

systemic effects, so thoroughly was the patient sensitized to the drug. And as Cushny and other pharmacologists point out, the effect of the administration of the drug on the blood pressure varied from time to time.

Finally, we would call attention to the almost paradoxical effects on the blood pressure: namely, the increased peripheral resistance as shown in the diastolic pressure, and the weakened muscular power of the heart as shown in the decreased pulse pressure. This of course is in accordance with the statements of experimental pharmacologists.

SUMMARY

The history is recorded of a case of 6 years' duration in which the patient had taken approximately 7 cc. of adrenalin daily, for the most part with a hypodermic needle. She had occasionally used morphine and chloroform. Sudden death occurred. Aside from collapsed right lung and beginning aortic sclerosis, the chief post-mortem findings were congestion of the abdominal viscera, similar to that found in animals dead from adrenalin administration.

Addendum Note: Since the writing of the above, a case history of sudden death in an asthmatic has appeared (5). In this instance the patient was given frequent doses of adrenalin intravenously just before death, and the post-mortem examination showed the same congestion of the intestinal mucosa noted in our case. This congestion is probably the chief effect of the adrenalin.

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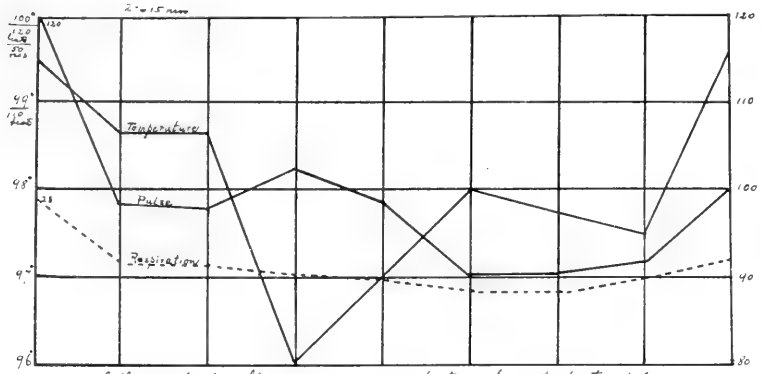
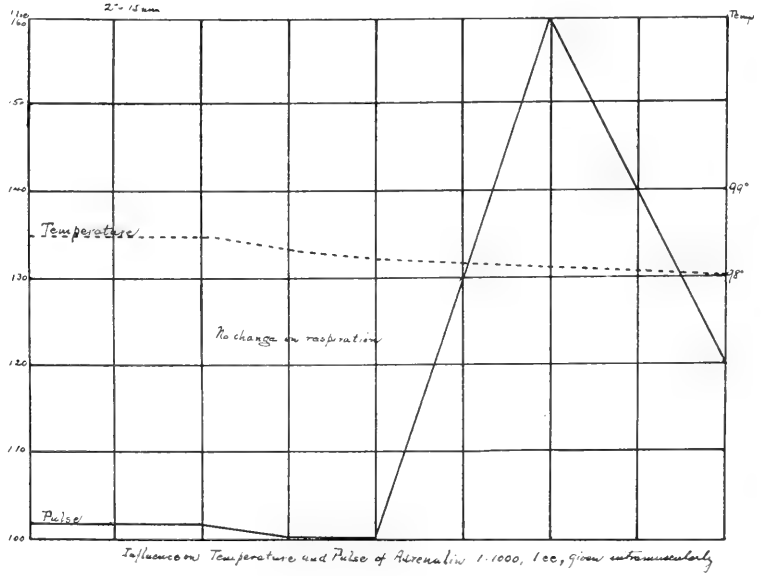
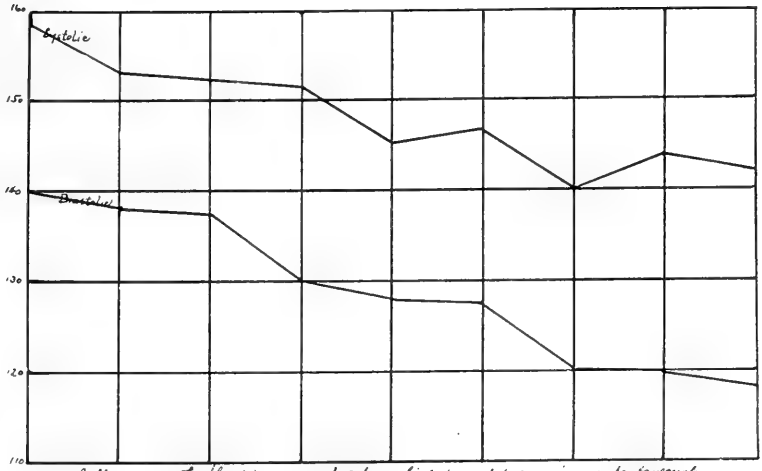


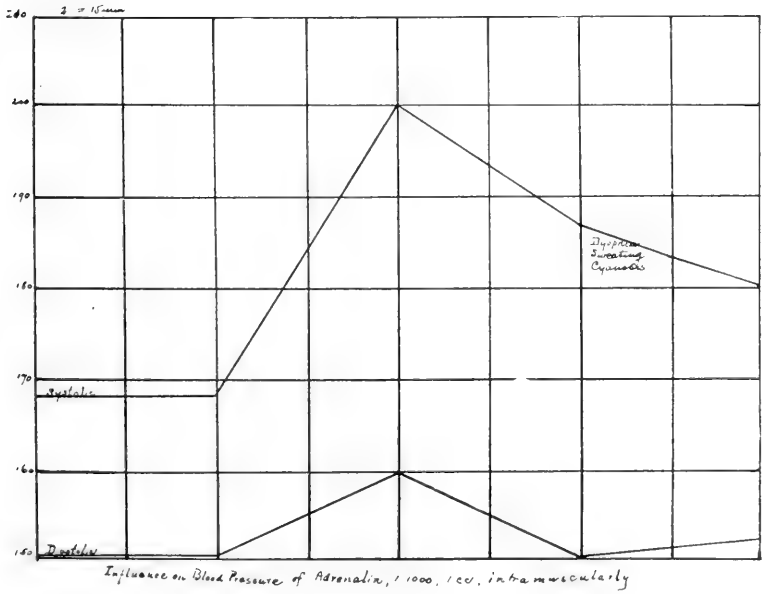
Influence of adrenalin, 1 cc 1:1000, given subcutaneously on temperature, pulse, and respiration



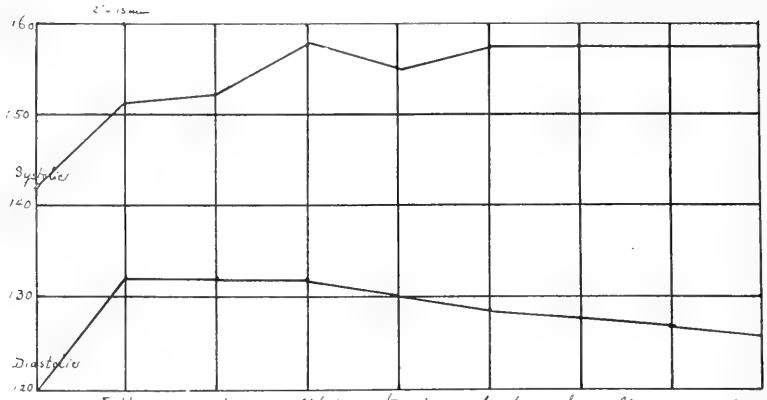
Influence on Temperature and Pulse of Adrenalin 1:1000, 1 cc, given subcutaneously



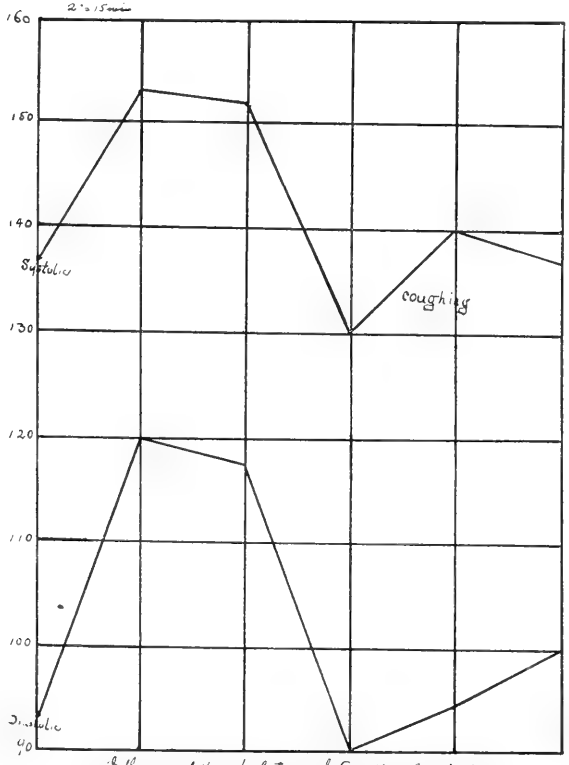
Influence on the blood pressure of adrenalin 1 cc of 1 1000 given subcutaneously



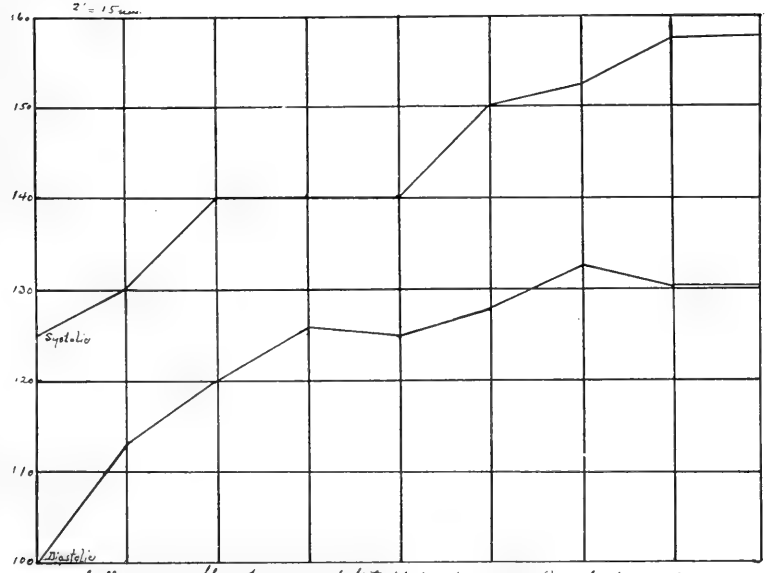
Influence on Blood Pressure of Adrenalin, 1 1000, 1 cc, intramuscularly



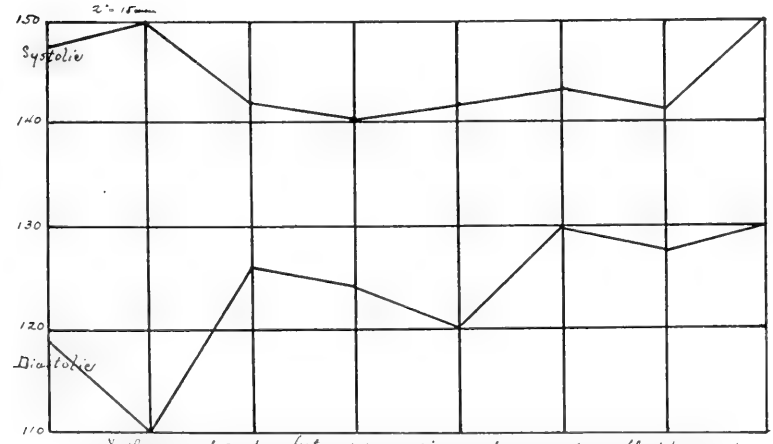
Influence of atropine sulphate, gr. 1/50, given subcutaneously, on blood pressure.



Influence of the inhalation of 5 m. Amyl nitrite on Blood Pressure



Influence on blood pressure of pituitrin 1 cc (surgical), subcutaneously



Influence of corpus luteum, 4gr ". given subcutaneously, on blood pressure

THE INFLUENCE OF THYROID FEEDING UPON THE PHYSIOLOGICAL ACTION OF THE PANCREAS

By Hirotoshi Hoshimoto, M.D.

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In the course of my experimental studies on the effect which thyroid feeding exerts upon the pancreas of white rats, certain interesting changes of the physiological actions were recently observed. I will attempt to describe them here very briefly; the full results of my investigation in the experimental hyperthyroidism will be described in detail and published subsequently.

Upon investigation into the biological activity of the pancreas, only the diastase is found to be contained in this gland in active form, while the other, i.e., proteolytic and lipolytic ferments, exist in an inactive state as trypsinogen and steapsinogen, and they must first be activated before they develop their own activity.

The test by Wohlgemuth's method shows the diastatic activity of the pancreas of normal, fully grown white rats fed on bread and milk for several weeks as follows:

D. 38° 30′=25,000-33,000 (the average 28,825) in nine normal male rats.

D. 38° 30′=16,700-50,000 (the average 26,620) in five normal non-pregnant female rats.

D. 38° 30′=24,717 the average of all rats of both sexes.

The amount of pancreas diastase per 100 mm. body-length was calculated to be:

D. 38° 30′=8,370-16,750 (the average 13,217) for male rats.

D. 38° 30′=7,800-18,560 (the average 12,511) for female rats.

D. 38° 30′=12,864, the average of all rats of both sexes.

During continuous feeding with adequate doses (0.5-0.1 gm.) of dry ox thyroid (containing 0.4 mg. of iodine per gm.) profound decrease of the diastatic activity of the pancreas occurred in the white rats of both sexes, giving the low value of:

D. 38° 30′=16,667, 13,900, 10,869, 9,240, 5,560, 1,262.

This result compared with the average value of normal rats, the decrease is estimated as 40, 50, 62, 67, 80, and 92 per cent.

My personal observations show that thyroid substance (extracted into physiological saline solution) does not at all check the amylolytic action of the diastase obtained from pancreas of rats; the diminution of the diastatic activity of pancreas should be ascribed to the actual diminution of the diastase contents of pancreas.

With regard to the relation of the decrease of diastase content to the morphogenetic change—diminution of acidophil granules—within the pancreas cells, which was found for the first time by M. Kojima in 1916, I confirm this result to coincide generally in the degree of diminution and its period of occurrence.

Administration of thyroid in relatively larger doses brought forth generally more profound decrease of pancreas diastase than that due to smaller doses.

But the individual difference in resistance against the toxic influence which thyroid substance exerts (disposition to hyperthyroidism) plays a more important role in this respect. Even in the same group of rats treated with similar doses of thyroid, some of them showed only slight decrease of diastase, while others showed marked decrease in relatively earlier stages of the experimental process.

The symptoms of thyroid intoxication are decrease of appetite, vanishment of liveliness, loss of body-weight, dyspnoea, and hypersalivation, the last of which should be regarded as a certain sign suggesting approaching death.

The decrease of diastase was not always accompanied by a poor appetite. On the first day of my experiment when the appetite was not yet affected and no emaciation visible, the diminution of diastase was already observed, and more so usually in the third week, in spite of good or rather abnormally augmented appetite. The decrease of diastase—for example that of 80 or 90 per cent—took place only in the rats which were suffering from extremely poor appetite, and showing other severe symptoms, such as dyspnoea, hypersalivation, etc.

The quantity of acid in the stomach does not agree with

that of diastase in the pancreas. The quantity of diastase in the intestinal juice obtained from the upper half of the intestines, i.e. from the duodenum and jejunum, was also estimated.

After the thyroid feeding the intestinal juice becomes milky, less yellowish, and more thick, showing a relatively lower value of diastatic activity, while in the case of fasting it appears very clear, deeply yellow, and less thick, giving comparatively higher value of diastatic activity. Even in normal rats it varies between:

D. 38° 30′=645 and D. 38° 30′=1,290, but has never gone lower than 645.

In some of the thyroid-fed rats the diastase of the intestinal juice was decreased to the low limit of normal rats, as also was the pancreas diastase, the former showing:

D. 38° 30′=320-133 and the latter 10,200-1,390, while in other cases it appeared as entirely normal or sometimes higher than normal, notwithstanding the decrease of pancreas diastase.

It must not be overlooked here that in such cases where intestinal juice contained normal or increased amount of diastase, appetite was never decreased, but rather augmented, and that such evidences were observed generally in the very early or in the later stages of continuous thyroid feeding and the diminution of the intestinal diastase was always accompanied by bad appetite and other severe signs.

Special attention was also given to the quality of the contents of the cecum and colon as well as to excreted feces. In the thyroid-fed rats the content of cecum was often very soft and yellowish white, showing many fat drops or crystals under the microscope, but none of the rats had suffered from diarrhoea. Excreted feces were always in natural form, even though they were sometimes quite soft, and in a few cases contained many fat drops, but such was the case only when the pancreas diastase was extremely diminished.

It has been found by M. Kojima that the pancreas of thyroid-fed rats after a certain duration of feeding becomes enlarged, and this was confirmed afterwards by P. T. Herring. I was also able to observe this in my experiments. The decrease of diastase contents was observed often in such enlarged

pancreases, when both the amount of food consumed and intestinal diastase were rather increased.

The diminution of pancreas diastase may be found sometimes also in emaciated rats, the general metabolism being shifted into pathological condition by certain exogenous or endogenous factors, exhausting or poisoning agents. Among my rats in reserve a female which after birth was giving its milk to eleven young, was very much emaciated and showed profound decrease of pancreas diastase. The same fact was observed in an emaciated male rat, its liver being occupied by more than twenty parasitic cysts.

Although a more or less marked loss of body weight, mostly owing to a rapid disappearance of fat, is well known as the constant results of thyroid feeding, I cannot explain the decrease of pancreas diastase as due simply to the disturbed general metabolism. The pancreas diastase begins to decrease even in the early days of thyroid feeding, although the general metabolism appears as entirely normal, there being no decrease of appetite, no loss of body weight, no vanishment of liveliness. The next fact contradictory to this explanation is that the diastase content of the intestinal juice is often of high value in spite of the diminution of pancreas diastase as already mentioned, while the decrease of pancreas diastase resulting from the decadence of the general metabolism accompanies generally a similar decrease of diastase in the intestinal juice.

The decrease of pancreas diastase in thyroid-fed rats cannot, therefore, be ascribed solely to the disturbance of general metabolism. At least in certain periods of thyroid feeding, when appetite is not affected, and intestinal juice contains much diastase, I should explain this as due to direct stimulation of thyroid autacoid upon the biological actions of pancreas, forcing it to discharge its ferments more quickly than in the normal condition.

P. T. Herring, describing the action of thyroid upon the general metabolism, has well compared it with a forced draft on the fuel in a furnace. My observation upon the pancreas has brought evident proof that thyroid acts in a similar way, as Herring stated, upon one of the digestive organs.

In connection with this description, a few words may be

added to explain the relation of diminution of pancreas diastase to the disappearance of glycogen in the liver of thyroid-fed rats. I have found that after 18 hours fasting almost 90 per cent of the glycogen disappeared in the liver of normal rats. Following decreased assimilation of carbohydrate in the alimentary canal, glycogen diminishes very rapidly in the liver. The disappearance of glycogen in the liver as the result of thyroid feeding, is observed in the rats which have poor appetite, consuming only a little bread and milk per day, but it is still evident in rats in the later stage of thyroid feeding, when the appetite is regained or rather augmented, i.e., the amount of food consumed is more than doubled and the pancreas is already enlarged, containing greater quantity of diastase than in normal rats, while the diastatic activity of intestinal juice is normal. It seems evident that the diminution of pancreas diastase takes only a small part, or sometimes no part, in decreasing the glycogen in the liver. This can be ascribed to the direct influence of thyroid upon the liver (or upon its nerves) or to the increased general metabolism, stimulated by the excess of thyroid autacoid.

Certain clinical observers such as W. Falta, A. Schmidt, Salomon and Amalgia, Schüler, and A. Bittorf noticed steatorrhoea in several cases of Graves' disease. How this symptom develops there is no decided opinion, but most of the observers agree. Falta ascribed it to insufficiency of the internal secretion of pancreas produced by the influence of thyroid, while Bittorf asserts that the insufficiency of the external secretion of pancreas causes such a symptom. The discussion on this problem is based upon clinical observations upon the effect of pancreon administration or on the quality of feces.

Toulay has estimated the diastase in the urine in case of Graves' disease, but failed to confirm the decreased activity of the external secretion of the pancreas.

No investigator has successfully studied the biological actions of pancreas itself to explain this phenomenon. The question whether this may be caused by the deficiency of external secretion or due to disturbance of the internal secretion of the pancreas is yet to be decided.

Another important point among the investigators exists in the question whether the lesion of the pancreas itself is due to the excess of the thyroid influence (hyperthyroidism) or to the agent which produces chronic lesion in the thyroid gland.

During my experiments I have observed under the microscope many fat drops and crystals (stained by Sudan III) in the feces excreted by some of the thyroid-fed rats, the pancreas diastase being extremely decreased, while in the feces of normal rats when fed on bread and milk, not any fat drops were observed (these having been of course previously fed on a similar diet).

From these observations I can assert without hesitation that steatorrhoea may be caused by hyperthyroidism (excess of the thyroid autacoid in the body), and the deficiency of the external secretion of the pancreas plays an important role herein.

SUMMARY

Nine normal male and five normal, non-pregnant female white rats were fed for several weeks on bread and milk. The diastase content of the pancreas varied (Wohlgemuth's method) from 25,000 to 35,000 units in males and 16,700 to 50,000 in females. The average for both sexes was 24,717. Feeding dry thyroid in dosage of 0.5 to 0.1 gm. resulted in a marked decrease of the diastatic activity of the pancreas varying from 40 to 92 per cent. This was accompanied by a diminution of the acidophile granules of the pancreas cells. Large doses of thyroid were more effective than small, but the effects in different animals were variable. The diastase content of the intestinal juice was also decreased in some cases by the thyroid. In such positive cases the appetite was markedly depressed and the feces were soft; in extreme cases they contained considerable quantities of fat. Thyroid feeding frequently resulted also in marked enlargement of the pancreas. In such cases the pancreatic diastase was often decreased even when the amount of food consumed and the intestinal diastase were augmented. The decrease can not be ascribed to general metabolic perturbation since it frequently antedated any evidence of such. It is rather ascribed to stimulation of diastase discharge from the pancreas.

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THYROID DIABETES

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The relation of the thyroid to carbohydrate metabolism has often been commented upon, von Noorden having described, many years ago, what he termed thyroid diabetes. The more recent investigations initiated by Jacobsen (1), and more fully developed by others (2), have emphasized this relation still further. As is well known the work of Jacobsen and others has shown that the ingestion of considerable amounts of glucose is followed by a temporary hyperglycemia. It is generally accepted that when, in the course of this hyperglycemia, the concentration of the blood sugar rises above 185 mgm. per 100 c.c. of blood, in the majority of cases sugar appears in the urine. McCasky (3), who investigated this phase of metabolism in some thirty odd cases of exophthalmic goitre, was unable to demonstrate a specific curve of sugar tolerance in the blood during the disease, although, in common with others, he noted that there was a hyperglycemia even before the administration of glucose. Janney and Isaacson (4), found that the complete extirpation of the thyroid, in dogs, was followed by absence of hyperglycemia when large amounts of glucose were administered.

Theories attempting to explain the mechanism of sugar mobilization based on the data at present available are all unsafe, since no theory as yet advanced is sound enough to withstand the application of facts already demonstrated but disregarded in the formulation of any given theory. It may perhaps be permissible to state here that the question of glycemia and the glycemic reaction which follows either the ingestion of large amounts of glucose or the subcutaneous injection of a variety of organic and inorganic substances has a twofold significance: one directly concerned with metabolism, the other associated with the processes of immunity. These phases are considered in other publications (5).

The cases reported in the present article are of interest in that they apparently substantiate the current theory of the influence of the thyroid upon sugar metabolism, and for the suggestion they offer as to the possible etiology of the condition.

Case 1. While the following cases have been grouped as one, in reality four individuals were concerned. Two sisters with uneventful past and family histories developed what clinically appeared to be diabetes, one at the age of 45, the other at the age of 49. Both of these age periods corresponded with the actual cessation of menstruation in the respective individuals. The sister, Mrs. B., married a man who, at the age of fifty-six, developed diabetes. This couple had two sons. The first son was nondiabetic, and died at the age of twenty-three of a brain abscess following a mastoid infection. The second son developed diabetes at the age of eighteen years, and has been under observation for a period of seven years.

In order to present more concisely the salient facts in this interesting family, it may be stated that all examinations were negative, except for the positive facts that all the individuals were large and exceptionally well nourished, and that in each case the presence of sugar in the urine was associated with polyuria, at times itching of the skin, and excessive thirst. All four patients had been under observation for a period of about fourteen months, and had been placed on various restricted diets [the Allen treatment had not at that time (1909) been proposed], and had received various types of medication, i.e., codeine, atropine, etc. All of this was without appreciable effect, the urinary sugar varying between 2 and 4 per cent under restricted diet. For a period of approximately two years, several of the endocrine glands were administered per os. The changes in the urinary output of sugar under the influence of this type of medication were at times uncomfortably startling.

Chart 1 presents in graphic form the variations in percentages of urinary sugar under different regimes for all four cases. During this entire period the family were under dietary restrictions of a general type, but during the months indicated by "D" the restrictions were severe, the patients receiving only fat, proteins, and the broad group of vegetables growing above the

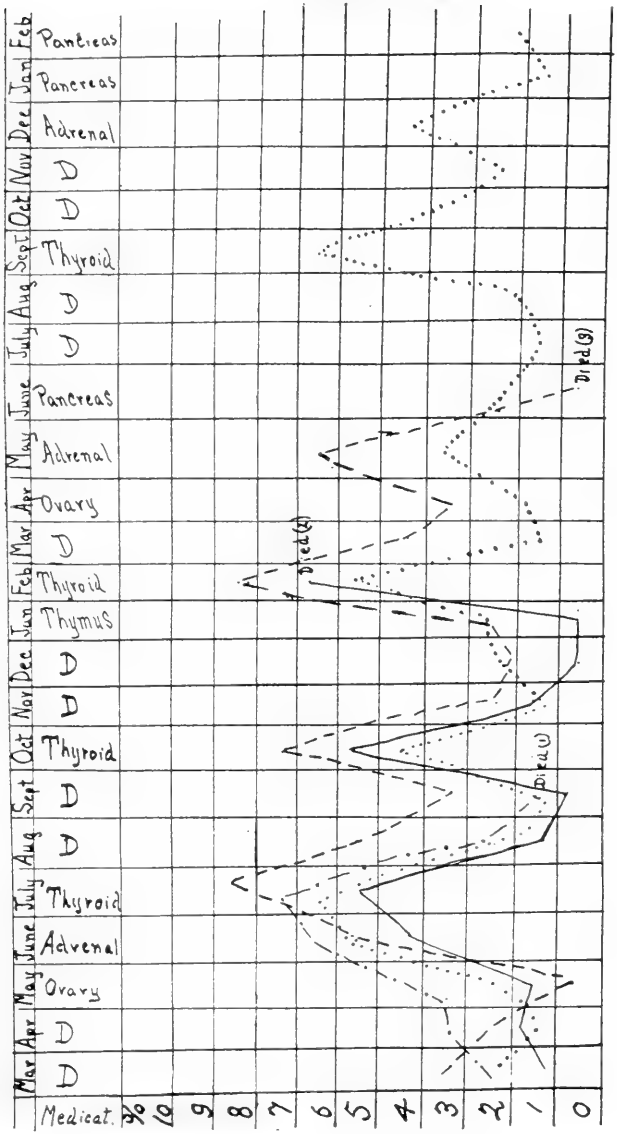
ground—peas, beans, and lentils excepted. During the months marked with one or another of the gland extracts, the desiccated gland was given in the dosage of three grains, three times a day. Urinary examinations were made weekly on twenty-four-hour specimens by the Fehling method, and the figures presented in the chart are the averages of the four examinations per month. The chart speaks for itself in that it shows in a striking manner the increased output of sugar when desiccated adrenal or thyroid gland was given, and the return to lower values when this medication was discontinued.

Interesting as these observations are, the subsequent course of events in each case is still more interesting. Mr. B. died in in a typical diabetic coma; autopsy was not obtained. Mrs. B., after some financial reverses, committed suicide by using illuminating gas. Mrs. A. died of sepsis following a typical diabetic carbuncle of the neck. Son B. passed from my observation temporarily some six months after the last month indicated on the chart. I saw him again five years later (1915), when he gave me the following history. About six months after seeing me for the last time, he had developed rapid heart action and considerable exophthalmos, and after four months in bed with no improvement, a portion of his thyroid was removed. This statement as to removal of the thyroid was borne out by physical examination. He had occasion to have his urine examined about six months after the operation and it was found to be sugar-free. The consumption of two pounds of grapes (Malaga) and three ice cream sodas within twelve hours at the time of his visit failed to produce sugar in the urine.

We have, then, in this family group a history of diabetes in one of the ancestors, the development of diabetes in two sisters at the time of the menopause, and the development of diabetes in one son at the time of puberty. We know that at these periods the thyroid is profoundly affected by the general changes in the organism. Again, the administration of thyroid gland repeatedly caused a marked increase in the sugar excretion; and, finally, the removal of part of the thyroid gland in one member of the family was followed by the disappearance of glycosuria.

Case 2. The second case is the reverse of the previously cited Son B., in that the development of Graves' disease oc-

Chart 1


Mar Apr May June July Aug Sept Oct Nov Dec Jan Feb Mar Apr May June July Aug Sept Oct Nov Dec Jan Feb
Medicat.
D D Ovary Adrenal Thyroid D D Thyroid D D Thymus Thyroid D Ovary Adrenal Pancreas D D Thyroid D D Adrenal Pancreas Pantreas
% 10 9 8 7 6 5 4 3 2 1 0
Died(2)
Died(3)
Mrs A - - - Mrs B —·—·— Mr B ····· Son B.
D = diet restricted. Sugar % based on average of 4 determinations made each month
(1)- Diabetic Coma (2) Sepsis, Carbuncle
(3)- Suicide

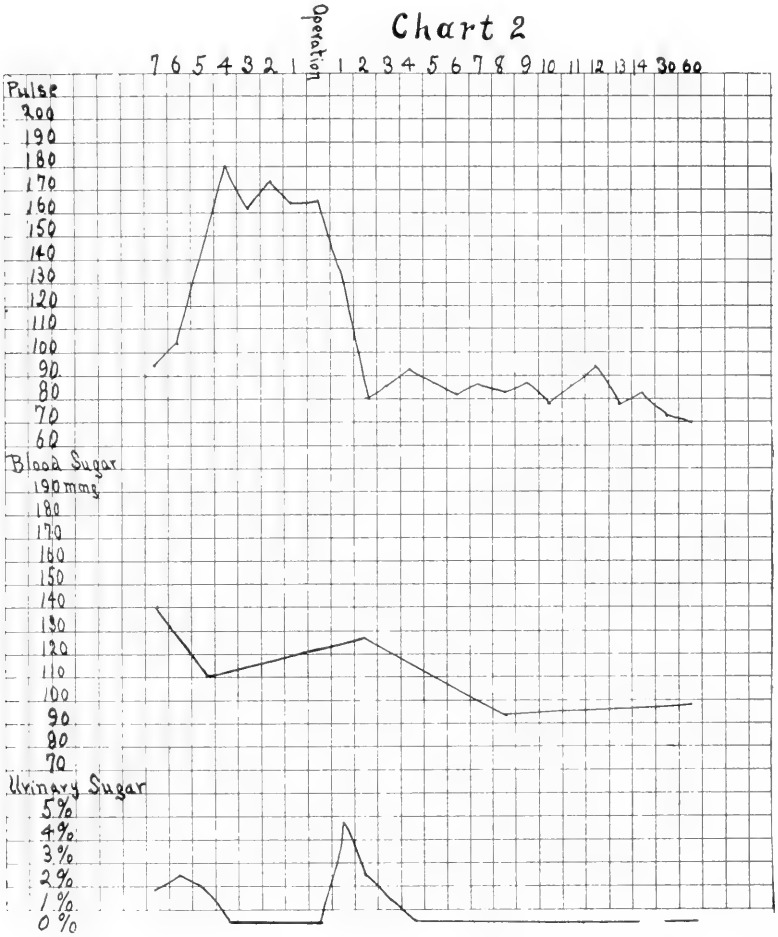
curred first and the development of diabetes second, and finally, a cure of both conditions followed removal of a large portion of the thyroid gland. In this case also we have more exact chemical details.

An American woman, married, aged fifty-three years, and a nullipara, gave the following history. Her family history was negative except that her father had died of diabetes. The other members of the family were of large frame and exceptionally well filled out, though she was small and would not be considered even plump. Her past life had been unusually strenuous, with many excessive demands upon both her physical and her mental energy. Her past history was without interest, except that in 1915 she had suffered from symptoms of excessive thyroid activity, with rapid pulse, loss of weight, and a typical tremor. Because of this condition one lobe of the thyroid was removed under local anesthesia by Dr. George H. Semken, to whom I am indebted for the case. The operation was followed by great improvement in her general condition, her weight increasing by fifteen pounds, and her pulse falling to 100. She was very definite in stating that for a number of years previous to her operation she had had a pulse ranging from 120 to 140.

Her present complaint was that during the past year she had noted a loss of thirty-five pounds in weight, polyuria, excessive thirst, and some itching of the skin. About six months ago she was told that she had diabetes; the percentage of sugar found was not stated. Physical examination at this time showed as the only abnormalities a systolic murmur at the base of the heart with roentgenographic evidence of a dilated aorta; pulse, 90 to 100; blood pressure, 95 d., 140 s.; and a subserous fibroid about the size of a lemon. No exophthalmos was noted. The Wassermann reaction was negative, and the blood count normal. The urine for four days on a full diet showed from 1.8 to 2.5 per cent sugar without evidence of acidosis; the blood sugar value was 140 mgm. per 100 c.c. The curve of sugar excretion and of pulse rate are shown in Chart 2.

A clinical diagnosis of diabetes having been made, the patient was starved. The urine voided after sixteen hours' starvation was sugar-free, but showed acetone and diacetic acid. After twenty-four hours' starvation the patient commenced to vomit,

and within a few hours was vomiting every three to ten minutes, bringing up mucus and bile. At the same time her pulse rose rapidly to 180 at the wrist (as nearly as could be determined). She was given a Murphy drip with a teaspoonful of sodium bi-



carbonate to the quart, in spite of the fact that the CO_2 combining power of the blood plasma was 55 volumes per 100 and sugar-free, broth was given per os. After twenty-four hours the vomiting ceased, the pulse remaining as rapid as before.

After five days of rapid pulse (160-180), the urine remaining sugar-free, Dr. Semken extirpated the other lobe of the thyroid under local anesthesia, leaving the isthmus in situ, the diagnosis of hyperthyroidism being evident. The day after the operation the urine showed 4.8 per cent of sugar; the next day, 2.4 per cent; the third day, 0.5 per cent, and on the fourth day was sugar-free. This sudden increase in urinary sugar was undoubtedly due to the sudden expression of thyroid secretion into the blood current due to operative manipulation. The pulse fell rapidly until, two days after the operation, it was 80 per minute. One month after the operation the patient had gained twenty-five pounds; her pulse was 72; and the ingestion of two ounces of cane sugar in twenty-four hours plus a diet consisting wholly of carbohydrates for two days previous and for the day of the test failed to produce any renal leakage of sugar. Three months after the operation she had gained an additional ten pounds, the pulse was 70, and on an unrestricted diet the urine was sugar-free.

The cases described above suggest some interesting trends of thought. The etiology of diabetes is most obscure. The disease may be induced in a variety of ways, ranging from injury to the nervous system, as shown by the classical piqure experiment of Claude Bernard, to extirpation of the pancreas or poisoning by phlorhizin. Still, even though extirpation of the pancreas does give rise to diabetes, it is the experience of every pathologist that carcinoma of the pancreas may destroy practically the entire organ and not give rise to glycosuria. The experiments of Janney and Isaacson, previously referred to, and the experiences in the cases cited here suggest that it may after all be possible that the condition is a manifestation of thyroid overactivity and not primarily of pancreas insufficiency, as is now commonly accepted. Personally, until the occasion of Case 2, we had lacked the courage to repeat thyroid feeding in cases of diabetes; but we now feel inclined, should the opportunity again present itself, to try the feeding of this gland; in the event of an increase in urinary sugar, after such feeding, a partial thyroidectomy could be rationally advocated.

SUMMARY

The author cites a family in which glycosuria was increased in intensity after the oral administration of either thyroid gland or adrenal. One member of this family was cured of his glycosuria after a partial thyroidectomy. In a second case the patient has previously had a portion of the thyroid removed for exophthalmic goitre, developing glycosuria several years later. The glycosuria in this case also disappeared after extirpation of more of the thyroid gland.

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THE BASAL METABOLIC RATE IN EXOPHTHALMIC GOITRE (1917 CASES) WITH A BRIEF DESCRIPTION OF THE TECHNIC USED AT THE MAYO CLINIC

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"In each mammal there is a basal metabolism" (19). By the term "basal metabolism" or better, "basal metabolic rate," of an organism is meant the minimal heat production of that organism, measured from twelve to eighteen hours after the ingestion of food and with the organism at complete muscular rest. This minimal heat production may be determined directly by actual measurement by means of a calorimeter, or indirectly, by calculating the heat production from an analysis of the end products which result from oxidation within the organism, or specifically, from the amount of oxygen used and the corresponding amount of carbon dioxid produced, together with the total nitrogen eliminated in the urine (although, for clinical work the urinary nitrogen may be neglected).

The experimental work of Lavoisier (17) marks the beginning of researches on metabolism, and to him belongs the conception that the life processes are those of oxidation with the elimination of heat. Technically, the problem was beset with many difficulties, for it was necessary not only to measure the amount of heat lost by radiation and conduction from the body (direct calorimetry), but also to collect accurately the various end products resulting from combustion within the body, from which data the heat production can be calculated (indirect calorimetry), in order to prove from a comparison of the results obtained from the two methods that the law of conservation of energy also holds for the living organism. Furthermore, before the method of indirect calorimetry could be employed the heat values of carbohydrate, fat, and protein had also to be determined in order to calculate the heat derived from their combustion in the body. The solution of these problems was greatly advanced by Carl Voit (23) and his pupils, the chief of whom

were Pettenkofer (22) and Rubner (27). The heat values of carbohydrate and fat were readily determined by Rubner (25) since these two substances are oxidized to the same end products (carbon dioxid and water) whether burning in the body or in a calorimeter. In the case of protein, however, the problem was somewhat more difficult, for a part of the end products of protein combustion in the body is eliminated in the urine and feces and the latent heat thereby lost had to be subtracted from the heat value of protein as determined in the calorimeter.

In 1894 Rubner (26) constructed the first successful respiration calorimeter designed for the measurement of the gaseous exchange between a living organism and the atmosphere which surrounds it and the simultaneous measurement of the quantity of heat produced by that organism. By means of this apparatus Rubner verified the method of Pettenkofer and Voit of calculating the heat production (indirect calorimetry) and he proved that the law of conservation of energy holds for the living organism.

It was not until 1905 that the respiration calorimeter was brought to a high degree of technical perfection by Atwater and Benedict (1). With their apparatus it was possible to determine simultaneously with the measurement of the heat elimination, not only the carbon dioxid production, but also the oxygen consumption of the subject. Studies made by Benedict and his associates, at the Carnegie Nutrition Laboratory, using the perfected calorimeter, have added greatly to the exactness of our knowledge with regard to the metabolism in prolonged fasting (4), the metabolism of normal persons (6), of infants (8), and of diabetics (7). They also confirmed the agreement between direct and indirect calorimetry. Lusk (18) and Du Bois and their co-workers have likewise demonstrated, in a large series of pathologic conditions, the close agreement between the two methods. As a result of these investigations the use of such a complicated apparatus as the respiration calorimeter has been shown to be unnecessary for clinical work and that in its place the comparatively simple method of indirect calorimetry may be used.

Krogh (16) of Copenhagen, and Carpenter (11) of the Carnegie Nutrition Laboratory, have described and compared in

great detail the various kinds of respiration apparatus used in indirect calorimetry. Carpenter has shown that for indirect determinations two types of apparatus are suitable, the closed circuit and the gasometer.

By far the best apparatus of the closed circuit type is the Benedict unit apparatus (2). By means of a mask, mouthpiece or nasal tubes, the subject rebreathes air from a closed system in which the carbon dioxid is absorbed by soda lime, and, as the oxygen is used up, it is replaced by oxygen in known amounts. The air within the apparatus is kept in constant circulation by means of a blower. A small spirometer is inserted in the circuit as an expansion chamber and volumetrically records the respiratory movements on a smoked drum. Knowing the weights of oxygen used and the carbon dioxid eliminated, one can readily calculate the heat production. As pointed out by Carpenter, this apparatus is very satisfactory and indeed the best for many purposes, especially when used in conjunction with a calorimeter or with the cot-chamber calorimeter described by Benedict and Tompkins (9). We have found, however, that for clinical work the unit apparatus is rather cumbersome. It requires constant checking to see that it is absolutely air tight, for a leak of 20 or 30 c.c. during a fifteen minute determination will appreciably affect the result, because such a leak in this type of apparatus will be equivalent to the loss of so much oxygen and not equivalent to the loss of so much air as is the case in the gasometer method. Furthermore, the accumulation errors of the apparatus fall on the oxygen and not on the carbon dioxid determination, thus causing an error in the calculation of the respiratory quotient and heat production. The absorbing chemicals must be changed frequently and with the repairing and constant checking of the apparatus it is on the whole difficult to use in clinical work, particularly if many determinations are to be made.

The portable respiration apparatus recently devised by Benedict (5) for clinical work is a modification of his unit apparatus described above. It is designed primarily to give a rapid and at the same time a comparatively accurate measurement of the oxygen consumption without involving analyses or weighing. We have not adopted it, as we prefer to determine not only the

oxygen consumption, but also the carbon dioxid elimination since the heat production can thereby be more accurately calculated. Moreover, the difficulties inherent in the closed circuit type of apparatus are still present in the portable apparatus.

For clinical work the gasometer method introduced by Tissot (29) in 1904 is considered by us the most satisfactory. Briefly, the determinations are made in the following manner: A mask is adjusted over the patient's mouth and nose and by means of expiratory and inspiratory valves the total volume of the patient's expired air is collected in a gasometer for a known period of approximately ten minutes. Duplicate determinations are made of the carbon dioxid and oxygen content of the expired air, the analyses being done in the Haldane gas analysis apparatus (14). Since the ventilation rate for each minute is known, as well as the amount of carbon dioxid produced and the oxygen absorbed, it is possible to calculate by means of calorie tables the total number of calories produced each hour.

The following points in the routine determination of the basal metabolic rate deserve further discussion: To obtain comparable results the patient must be in the postabsorptive condition, that is, he must fast for at least twelve hours preceding the test. It is very important that this rule should be observed, because all kinds of foods cause an increase in the heat production and this effect may not entirely disappear for twelve hours after their ingestion (28). Moreover, the patient must be at complete rest and the effects of previous muscular exertion eliminated by requiring him to rest in bed for twenty minutes before the test is started, for we have shown in a series of experiments that a rest period of this length of time is quite sufficient to obtain the basal metabolism (10). During the preliminary rest period an observer sits with the patient, noting at intervals the character and rate of the heart beat and the respiration; likewise, about the middle of the period, the blood pressures, both systolic and diastolic, are obtained. After twenty minutes' rest a mask is accurately adjusted over the nose and mouth of the patient and securely held in place by means of tapes so that there is no leakage of air around the mask (Fig. 1). A mask is preferable to either a mouthpiece or nasal tubes. With a little experience it is possible to adjust the mask

so that it is not only comfortable for the patient, but also air-tight. One of the chief advantages of the gasometer method is that should a very slight leak of a few cubic centimeters occur around the mask during the course of an experiment the end

Fig. 1. Mask and connections showing valves, intake pipe and towel with tapes.

result is not appreciably affected, while a leak of a similar volume in the closed circuit apparatus has a value at least five times as great, because in the latter case it is equivalent to the loss or gain of so much pure oxygen.

During the test proper the observer sits with the patient, recording his pulse and respiration rates and noting and recording on a special chart any movements. Care is taken to impress on the patients that even slight movements materially affect the

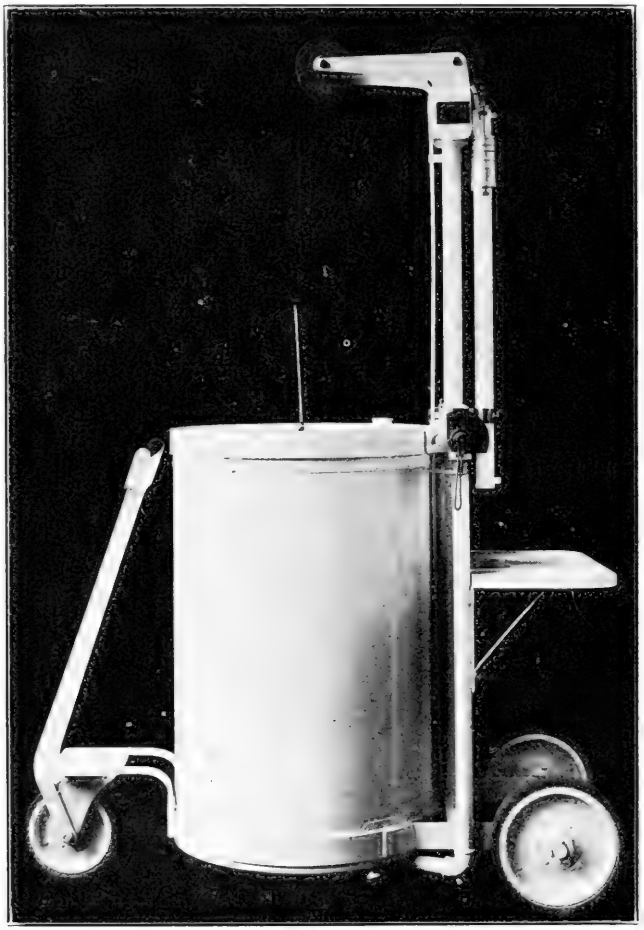

Fig. 2. Moveable gasometer.

test and it is almost always possible to obtain their complete co-operation. Sometimes, however, in an extremely nervous person, a basal rate cannot be obtained on the first test. Instead of repeating the determination the same day the patient is in-

structed to return the following morning for a second test. In such instances the rate will occasionally be ten points lower than that obtained the first time when the patient was unduly nervous and frightened about an unknown procedure.

The total volume of the expired air is collected in a gasometer (Fig. 2) over a known length of time. Unlike in the work with the closed circuit apparatus no appreciable error is introduced by failing either to start or stop the experimental period at exactly the end of a normal respiration, a difficult thing to do with accuracy in the case of patients who breathe irregularly. Samples of the expired air are then collected over mercury in sampling tubes and analyzed in duplicate for carbon dioxid and oxygen. Approximately 10 c.c. of expired air are transferred into the burette of the Haldane gas analysis apparatus (Fig. 3) and after adjusting certain levels the reading of the initial volume of the sample is made, reading to the nearest 0.001 c.c. The gas sample is then passed back and forth over a solution of dilute potash to absorb the carbon dioxid. The levels of the solution are again adjusted and a second reading of the volume of the remaining gas in the burette made. The contraction in volume of the gas, due to the absorption of the carbon dioxid by the potash solution, divided by the original volume, gives the percentage of carbon dioxid in the expired air. In like manner the percentage of oxygen is determined, potassium pyrogallate solution being used as the absorbent for oxygen.

The gasometer method is particularly suitable for clinical work because each step in the procedure can be checked by a second assistant, reducing to a minimum the chance of technical errors. Although the method requires care and accuracy in every part of the procedure, it is possible to teach the technic to laboratory workers who have had no preliminary scientific training other than that obtained in a high school. The most difficult step in the procedure is the analysis of the expired air. This, however, we have found to be inconsiderable. Our assistants can obtain routinely duplicate analyses agreeing within 0.04 per cent for carbon dioxid and 0.06 per cent for oxygen, and they are able also to take entire care of their gas analysis apparatus. The equipment necessary for this method is simple and inexpensive and when properly constructed

is rarely out of order and, except for cleaning, requires very little mechanical care. Furthermore, the apparatus is free from the many mechanical difficulties inevitably inherent in a closed circuit system in which the air current is driven by an electric

Fig. 3. Haldane gas analysis apparatus.

pump. In the metabolism laboratory at the Mayo Clinic we are averaging 30 cases a day and have developed a very definite and routine procedure which has decreased the chance of technical error to less than 1 per cent.*

* The details of the technic are described in a laboratory manual by Boothby and Sandiford (10). The apparatus may be obtained from H. N. Elmer, 1136 Monadnock Bldg., Chicago.

The calculation of the basal metabolic rate from the experimental data is very simple. Knowing the volume of air expired by the patient in a minute (the ventilation rate) and the percentage of carbon dioxid and oxygen in the expired air, it is possible to calculate the volume of oxygen absorbed by the patient in one hour, as well as the corresponding amount of carbon dioxid produced. Since the respiratory quotient, that is the ratio between the volume of carbon dioxid produced and the volume of oxygen absorbed, indicates the kind of food being burned at the time of the determination, and since by means of calorie tables the calorific value of one liter of oxygen absorbed by the body in the burning of these substances is known, the total heat production each hour can be calculated readily. The total number of calories must be divided by the surface area, a factor dependent on the patient's height and weight. The number of calories for each square meter of body surface each hour must then be compared with the normal standards of comparison which are dependent on the age and sex of the patient. For convenience, basal metabolic rates are expressed in percentages of the normal, and when the heat production is greater than the normal the percentage is plus, and when less than normal the percentage is minus.

A very important contribution was made by Du Bois (12, 13) in determining the heat production in normal controls. Rubner (24) had suggested that the heat production of an individual is proportional to his surface area. For the determination of the surface area Meeh (21) proposed the formula: Surface area in square centimeters=12.3 (a constant) $\times$ weight in grams$^{2/3}$. However, using the surface area obtained by this formula as a basis of comparison, the heat production of normal controls still showed quite wide variations, although not so great as when compared on the basis of weight alone. By exact measurements of the surface area of several bodies Du Bois demonstrated an error in the above formula due in greater part to the fact that the height of the subject was neglected. As a result of further studies Eugene F. Du Bois and Delafield Du Bois (12, 13) devised a formula based on height

and weight by means of which the surface area can be calculated with an average error of 1.7 per cent. This formula is:

$$A = W^{0.425} \times H^{0.725} \times 71.84$$

Where A is the surface area in square centimeters, W is the weight in kilograms and H is the height in centimeters, and 71.84 is a constant. On the basis of this formula they then constructed a height-weight chart by means of which the surface area can be estimated at a glance. Du Bois (12, 13), using this new height-weight chart for the determination of the surface area in conjunction with his standards of normal basal metabolism with regard to age and sex, further showed that the metabolism of normal persons can be predicted with an accuracy of ± 10 per cent. This fact has been confirmed both by Means (20) and by Boothby (19). Benedict (3) has severely criticized the method of predicting the heat production from the unit of surface area, maintaining "that the metabolism or heat output of the human body, even at rest does not depend on Newton's law of cooling, and therefore, is not proportional to the body surface." Harris and Benedict (15) in a very exhaustive treatise have reconsidered the entire problem of the prediction of the normal basal metabolic rate and show that by proper biometric formulas based on stature, body weight, and age (the same factors used by Du Bois), "results as good as or better than those obtainable from the constant of basal metabolism per square meter of body surface can be obtained by biometric formulas involving no assumption concerning the derivation of surface area, but based on direct physical measurements." Since their publication there has not been sufficient time to study in detail the fundamental accuracy of the two methods of prediction; we have, however, tabulated 404 determinations of the basal metabolic rate expressed in percentages above and below normal, using both the standards of Du Bois and of Harris and Benedict. The average rates of all the cases show that the rates obtained by Harris and Benedict's method are 6.5 points higher than those obtained by Du Bois' method. The parallelism between the results obtained by the two methods is strikingly shown by the fact that 195 of the 404 determinations are within ± 2.5 of the average variation. Only 52 of the entire 404 rates deviate

more than 7.5 from the average variation. The comparative agreement, therefore, of the two methods is very satisfactory, indicating as it does the similarity of both methods of comparison, and supporting in a high percentage of the cases the clinical conclusions based on the Du Bois and Du Bois height-weight chart and the Du Bois normal standards for comparison.

The metabolism laboratory at the Mayo Clinic was opened, in March, 1917 by Boothby and Sandiford, under the clinical direction of Dr. H. S. Plummer, and in that year 1143 metabolic rates were determined on 549 patients. At that time the number of cases that could be studied in the laboratory in proportion to the number of thyroid cases at the clinic was relatively small. In consequence, considerable care was taken by Dr. Plummer to select typical cases of the various groups of thyroid disorders and with his permission this analysis of the metabolic rates in the exophthalmic goitre cases studied during 1917 is presented.

The basal metabolic rate is of the greatest value in thyroid disorders because it gives a very accurate mathematical index of the degree of functional activity of the thyroid gland. For example, in exophthalmic goitre the metabolic rate may rise well over 100 per cent above normal while in myxedema, with apparently complete cessation of thyroid activity, the rate falls to the region of 40 per cent below normal. In the milder cases of both groups the metabolic rate variations from the normal are proportionately smaller. On the other hand, beside thyroid disorders, there are no diseases that have so far been shown to have a constant and distinct variation from the normal in the basal metabolic rate except disorders of the pituitary gland, conditions of profound inanition, and fevers. However, an occasional case is met with in which there is a variation in the basal metabolic rate that at present cannot be explained or properly classified. Such variations are more frequent in patients with considerable evidence of nephritis or anemia. No definite instance of an increased basal metabolic rate has been found in that group of cases known as neurasthenia or chronic nervous exhaustion. The basal metabolic rate has proved, therefore, to be of great value

in the differential diagnosis of neurosis simulating hyperthyroidism and true hyperthyroidism.

In 182 cases of exophthalmic goitre before any treatment was instituted the average metabolic rate was +51 per cent, with an average pulse rate of 115. In 13 patients whose average metabolic rate, as outpatients, was +59 per cent, with an average pulse rate of 115, the average metabolic rate fell to +46 per cent, and the average pulse rate to 108 as a result of approximately one week's complete rest in bed. In 5 patients whose average metabolic rate, determined within two to five days after they entered the hospital, was +59 per cent and the pulse 118, after a further rest in bed of approximately one week's duration there was a definite improvement in their condition, as shown by a fall in the metabolic rate to an average of +48 per cent and pulse to 104.

The effect of a single ligation was studied in 16 cases. The basal metabolic rate taken after the patient had had several days' rest in bed and within five days before the first ligation was +54 per cent and the pulse 116. One week after the single ligation the average metabolic rate had decreased to +44 per cent and the pulse to 112.

The immediate result of ligation or thyroidectomy in hyperthyroidism is to cause at first a rise in the metabolic rate for a few days, followed by a gradual fall to a distinctly lower level on the average than that obtained preceding the operation. The curve of the basal metabolic rate on the average roughly parallels the pulse rate curve. The former is, however, a far more accurate index of the degree of hyperthyroidism than is the pulse rate, as the latter shows more individual and extraneous variations, for example, the irregularities of auricular fibrillation.

The effect of the second ligation is likewise a general improvement in the patient's condition as evidenced by a decrease in the metabolic rate. An average figure of any value on the immediate result of the second ligation in the patients in the 1917 series cannot be given, as practically no rates were obtained in the same case immediately preceding and following the second ligation. There is a very marked improvement in these patients when they return for their thyroidectomy

two to four months after the second ligation. In 22 patients (Table 1) there was an average decrease in the basal metabolic rate from +46 per cent to + 39 per cent, and in the pulse from 115 to 107 with a gain in weight from 46.4 to 54.5 kilograms in the determinations made a few days after the second ligation as compared with the data obtained after three months' rest at home and just previous to thyroidectomy. From the clinical history it is probable that the basal metabolic rate determined at the time the patients returned for operation after having had two ligations and three months' rest at home may not necessarily represent in all cases the period of maximum improvement produced by the two ligations and rest. A definite improvement from thyroidectomy in those patients who had had two ligations and a three months' rest was shown two weeks following operation by a decrease in the basal metabolic rate from +39 per cent to +16 per cent, and in the pulse rate from 107 to 89.

In another group of 19 patients (Table 2) with exophthalmic goitre in whom the preliminary basal metabolic rate varied between +13 per cent and +50 per cent, giving an average of +31 per cent with an average pulse rate of 104, and in whom a primary thyroidectomy was done without any other preliminary treatment, except for a short rest in bed, the basal metabolic rate fell, about two weeks after operation, to +5 per cent and the pulse to 84.

The general effect of the treatment adopted at the Mayo Clinic for severe cases of exophthalmic goitre may be illustrated, then, by the following data: In a group of 22 patients (Table 1) the average basal metabolic rate, before any treatment was instituted, was +66 per cent, with a pulse rate of 123. As a result of rest in bed and two ligations the rate in these patients before they went home had decreased to +46 per cent and the pulse to 115. The further improvement that occurred from three months' rest at home reduced the average metabolic rate to +39 per cent and the pulse rate to 107 and finally, after thyroidectomy and just before the patients were discharged from the clinic, the rate was +16 per cent and the pulse 89.

As will be noted, following thyroidectomy there is almost always a marked decrease in the basal metabolic rate within

Table 1

THE EFFECT OF TWO LIGATIONS AND THYROIDECTOMY ON THE BASAL METABOLIC RATE IN EXOPHTHALMIC GOITRE

	Before treatment			Within five to nine days after second ligation			Three months after second ligation			Ten to thirty days after thyroidectomy		
Case	Wt. kg.	Pulse	B.M.R. Per cent	Wt. kg.	Pulse	B.M.R. Per cent.	Wt. kg.	Pulse	B.M.R. Per cent.	Wt. kg.	Pulse	B.M.R. Per cent.
208970	50.1	139	+101	38.1	118	+36	52.2	95	+50	56.8	69	+15
201022	48.5	175	+ 98	40.9	124	+49	51.5	114	+26	48.1	107	+ 6
196042	46.0	138	+ 93	45.6	126	+61	53.3	104	+43	51.9	91	+20
197894	46.7	128	+ 77	39.5	129	+46	58.4	113	+13	56.5	105	+ 1
192274	27.3	138	+ 76	40.1	120	+53	42.7	129	+58	40.9	92	+27
194824	42.4	127	+ 76	41.6	123	+58	51.9	110	+34	51.4	100	+13
210160	54.9	131	+ 75	57.7	124	+60	63.9	105	+55	63.0	82	+21
196845	49.7	129	+ 74	47.5	146	+78	55.3	129	+68	56.0	120	+58
215648	42.1	117	+ 73	43.4	115	+54	48.0	82	+12	53.7	74	— 6
202677	60.5	98	+ 65	58.4	96	+34	64.1	94	+55	61.9	86	+34
191713	49.0	87	+ 65	43.5	83	+45	50.5	90	+62	50.5	71	+49
187927	48.5	121	+ 63	45.0	117	+43	49.4	112	+53	48.6	70	+ 3
189311	60.7	141	+ 60	49.9	88	+27	58.3	105	+43	56.0	44	0
199039	43.1	121	+ 56	36.6	123	+50	48.2	100	+50	48.6	76	+14
200063	46.5	95	+ 55	45.9	110	+58	46.9	121	+54	46.6	97	+20
199909	46.0	134	+ 55	46.0	127	+42	52.8	132	+52	53.0	88	+13
136490	55.1	107	+ 55	44.2	104	+41	65.5	82	+11	65.3	85	0
194306	43.2	126	+ 53	42.0	124	+48	50.1	117	+21	49.5	105	+ 9
197356	58.5	99	+ 52	53.0	80	+13	60.0	77	+ 1	56.9	75	— 2
191257	60.5	130	+ 50	56.7	123	+45	61.2	110	+34	58.5	117	+16
209717	55.6	133	+ 47	54.0	141	+37	59.0	127	+39	57.0	88	+16
190576	53.0	86	+ 31	51.6	92	+31	55.6	106	+25	58.3	106	+19
Average	49.5	123	+ 66	46.4	115	+46	54.5	107	+ 39	54.0	89	+16

two weeks after the operation and, as a rule, there is still further improvement in the succeeding months, just as is seen to occur in the interval after the second ligation. Occasionally, a varying degree of hyperthyroidism may persist, as shown by

Table 2

THE EFFECT OF PRIMARY THYROIDECTOMY ON THE BASAL METABOLIC RATE IN EXOPHTHALMIC GOITRE

	Before treatment		About two weeks after operation	
Case	Pulse	B. M. R. Per cent	Pulse	B. M. R. Per cent
214581	88	+50	70	+19
196806	109	+45	93	+ 3
202992	107	+45	92	+ 5
200219	145	+42	115	+12
201229	102	+40	75	+14
202481	105	+39	68	+ 1
202527	112	+36	92	+15
194686	97	+35	75	+ 1
212298	108	+34	91	+ 5
202232	113	+32	118	+32
203326	127	+30	89	+10
3396	101	+29	83	+13
198725	99	+27	67	0
196664	79	+21	58	−11
203291	87	+18	73	− 6
199740	95	+18	69	− 7
217150	99	+16	85	− 5
215895	118	+16	98	− 9
208637	89	+13	84	+ 6
Average	104	+31	84	+ 5

an elevated basal metabolic rate. In these cases a second (and rarely a third) thyroidectomy is indicated.

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STRUCTURE OF THE THYROID AND ITS QUALITATIVE VARIATIONS: A REVIEW.

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A promising field for productive investigation is that of histochemistry. Although the tinctorial reactions by which cell structure is commonly studied amount, in effect, to qualitative chemical analyses, this fact has been little stressed. This possibly is due to the condition that investigators who utilize tissue stains are usually interested primarily in morphology. Accordingly, stains are chosen primarily for their ability to reveal structure and relative little attention has been paid to the fundamental chemistry involved.

There now are in use a large number of analytic procedures which depend upon qualitative color reactions for determining the composition of body products. Many of these would lend themselves to the analysis of cell components. Such microanalyses might well add much to our knowledge of conditions in the endocrine organs and their variations in health and disease.

An interesting series of studies in this field has been made by Prof. Buscaino of the San Salvi Clinic at Florence. (1)

Several mental diseases (epilepsy, paresis, etc.) in which a true condition of dysthyroidism exists, have not afforded conclusive histo-pathological findings in the thyroid, because, Buscaino remarks, the research was turned to the size of the acini, to the quantitative variation of the colloid, of the interalveolar connective tissue, to the proliferation of the epithelium and so on, instead of to qualitative variations of the colloid and of the elements apt to be found in it. Buscaino's object in this study has therefore been to look for such qualitative variations and see if it were possible to give an anatomical basis to the described conditions of dysthyroidism.

I. It was found that a first variation consists in real crystals (octahedral) in the mass of the colloid. They are not soluble in water, in alcohol, in acetone, in sulphuric ether, in mineral acids, in acetic acid or in alkali. They do not take the Sudan III stain. Therefore they are neither inorganic, nor fats, nor carbohydrates. With the xanthoproteic reaction, Millon's, Lieberman-Wurster's and Axenfeld's tests they appear to be of protein substance, and to contain, besides other groups, aromatic groups with oxyphenylic structure. These crystals vary in size

(1) Buscaino (V. M.) Rivista di Patologia nervoso e mentale (Firenze), 1914-15, **19**, fasc. 7-8; **20**, fasc. 2, 3, 4, 5, 10.

and are found in very few thyroids—usually in the normal, very seldom in the chromophil colloid.

II. There are also calcium oxalate crystals, which never appear in the octahedral form. They are to be found in the colloid, more or less close to the epithelium. They are not found in all thyroids and their number varies greatly.

III. Other crystals of organic nature have also been found in the colloid. It has only been determined that they are not amino-acid, uric acid, hippuric acid or xanthin. They have been found only once in a case of Basedow's disease.

IV. The colloid itself may vary; one of its modifications we call "chromophil colloid" on account of its reacting to several stains (Niblau, Mallory's reaction) in a different way than the normal colloid. It may fill the acini or appear only as an admixture with the normal colloid in a small amount. Characteristic is its way of never adhering to the epithelium, which is usually low and often degenerated.

V. The "Sudanophil" is another variation of the colloid. With the Sudan III and Delafield hemotoxylin the normal colloid is bluish and the chromophil intense blue, while the Sudanophil is reddish yellow. It hardly gives a positive xanthoproteic reaction and does not give the Millon's. It is found in enlarged acini and looks different from the normal and the chromophil colloid. It can be found in the interalveolar spaces,—very often where there are hemorrhages, which seem due to its toxic action on the walls of the blood vessels.

VI. The colloid may also appear in a degenerated form as broken in fragments more or less broad, with regular margins, mixed with detritus of epithelial cells.

VII. Granules of neutral fats and lipoids are also found which, stained with Sudan III, become intensely red-orange. They are believed to increase with the age of the subject. They are never found in the new born. They begin to show during early youth and their maximum is reached between 70 and 85. They are increased in senile dementia.

VIII. Abnormal fatty substances are also found as doubly refracting epithelial granules in the acinar epithelium; as ethers of cholestrol in the colloid and, finally, under conditions when the whole epithelial protoplasm takes the Sudan III, a reaction due to the presence of true lipoids, which are never found in the normal condition.

IX. Dark granules are also found in the alveolar epithelium which, by their reactions, are shown to belong to neither fats, proteins nor carbohydrates. It is believed that they are of melanotic pigment.

X. Granular inclusions are often found in the sudanophil colloid, not necessarily accompanied by hemorrhage; they ap-

pear when acini are lacking. These granules may be of three kinds, sometimes all together in one cell: (A) Sudanophil granules, mostly constituted of neutral fat and lipoids; (B) Black granules very similar to the "dark granules" (IX);

XI. (C) Thiophil granules (becoming violet-red with thionin) which are very likely protein.

XII. Other substances may appear in the interacinar spaces colored yellow-red with Sudan III, like the sudanophil colloid.

XIII. Finally, infiltration of lymphocytes has been found. This is supposed to be due to persistence of the thymus and status lymphaticus.

As regards lymphocytosis in connection with thyroid disorders, the author claims that the leukopenia observed in cases of Basedow's disease, with increase of the mononuclears, is not characteristic of this disease, but is found in almost all abnormal conditions of the thyroid. This condition seems to be due to a reaction on the part of the thymus and of the lymphatic system to any form of dysthyroidism; in other words, whenever an infectious toxemia can be excluded in cases of lymphocytosis it is to be considered as an expression of an endocrinic toxemia, i.e., a functional variation of thyroid, thymus and lymphatic systems.

In cases of simple goitre Buscaino found dilated acini, sudanophil colloid and hemorrhages. No protein crystals, no, or very little, chromophil colloid, and no calcium oxalate crystals were found.

In cases of Graves' disease, extreme diminution of the normal colloid, the presence of sudanophil and chromophil colloid, and absence of protein crystals and of calcium oxalate were noted.

From the post-mortem examination in cases of epilepsy, paresis, dementia precox, senile and arteriosclerotic dementia and amentia, the author came to the conclusion that all these forms (in which the patients showed more or less evidence of dysthyroidism while living) show the presence of chromophil colloid. Without being pathognomonic for any of these forms, such colloid seems to have a special importance in cases of paresis.

The crystals of calcium oxalate show only an active participation of the thyroid in calcium metabolism. They were found mostly in cases of dementia precox.

The octahedral protein crystals have a special significance in epilepsy. It was found that the cases of essential epilepsy showed signs of dysthyroidism; microscopic examination disclosed chromophil colloid and octahedral crystals of protein. In cases of symptomatic epilepsy the findings were negative.

To summarize: Chromophil colloid and sudanophil colloid were found in nearly all cases of mental disease which offered, during life, symptoms of dysthyroidism; the calcium crystals were seldom found and then, almost exclusively in dementia precox; the octahedral protein crystals were found in cases of epilepsy or other diseases with epileptic seizures.

In a study of the corpuscular variation of the blood in epilepsy and the psychoses the author could find variations of the formula in almost all forms. But the variations were not so constant as to afford any definite pathognomonic data. He found, though, that in epilepsy (in two-thirds of the cases) there was a very definite eosinophilia. Such condition of the blood seems always to be determined by disintegration and successive parenteral penetration of foreign or homologous proteins into the blood.

Owing to the frequency of eosinophilia in epilepsy, to the finding of crystals of protein in these cases and to the conclusions drawn by Schlecht, Schwenker, Ahl and Schittenhelm that the eosinophilia has a great importance in the phenomena of anaphylaxis, representing as it does the reaction of the organism against foreign or homologous protein, when it enters parenterally into the circulation, the author was brought to look for any possible analogy between epilepsy and anaphylactic shock, and to see if epileptic attacks could not be considered as an anaphylactic reaction of the organism against the penetration of abnormal protein from the thyroid. He therefore draws a parallel between the symptoms offered by these two conditions (epilepsy and anaphylaxis) which leads him to the conclusion that the "epileptic seizures offer the symptoms of an anaphylactic crisis, determined by intoxication of either peptones or substances resembling peptones in their protein genesis and in their toxic effects.

Of course not all the cases having epileptic attacks show protein crystals (as has been noted in a previous paragraph in regard to the difference between essential and symptomatic epilepsy) and not all the cases showing protein crystals have epileptic seizures. But in this case we must not forget that first, the eosinophilia, when present, can counteract the epileptic attack; second, that to obtain an anaphylactic condition there is required a certain amount of toxic substance which, besides, in its repeated action must enter the circulation at not too brief intervals in order to permit sensitization of the organism.

In studying paresis Buscaino found in every case the presence of chromophil colloid and came to the following conclusions:

1. Among the anatomo-pathological findings of dysthyroidism in paresis the chromophil colloid is the expression of a qualitative alteration of the thyroid function, leading to intoxication

of the organism and ultimately to hypofunction of the thyroid. 2. The chromophil colloid is not the cause of the disease, but an effect of it. 3. Its formation seems to be an effect of the lesions which determine the paralytic process and consequent formation of special cerebral toxic substances. 4. The chromophil colloid has been found in all cases of paresis studied. 5. The forming of the chromophil colloids is the starting point of the alteration of metabolism through alteration of other endocrine glands. There may be a predisposition to favor the incidence of thyroid complications. 6. Paresis is a cerebral spirochetosis which determines dysthyroidism which in its turn brings about organic decay. 7. Also, in paresis the epileptic seizures represent anaphylactic crises. In all these cases protein crystals have been found. 8. The association of thyroid treatment with specific antiluetic treatment helps to diminish the intensity of the Wassermann reaction (blood and spinal fluid).

Finally, a study was made of the possible alterations in the blood serum in connection with the presence in the thyroid, and probable introduction into the circulation, of the protein crystals and of the chromophil colloid, which both were proved to contain a substance with oxyphenylic structure (oxybenzoic).

Believing that the organism usually reacts against the presence of abnormal substances with the production of specific ferments, an attempt was made to determine if there were formation in normal serum of phenolysins for substances with cyclic groups with oxyphenylic structure; and if so, what kind of variation exists in cases where such substances were found in greater amount, as in epilepsy and paresis.

The ability of the blood serum to bring about oxidation of hydroquinon was investigated. Although the reaction was positive, the effect was not due to a real ferment, since this "phenolysin" kept its power after heating to 100° C. for a few minutes, and after precipitating the blood proteins with 96% alcohol filtering and boiling for ten minutes.

The conclusions were as follows: In normal conditions the human blood serum has in vitro a powerful oxydizing action on hydroquinon, due to a substance soluble in 96% alcohol and thermostable; this power increases a great deal in cases of paresis, and to a less extent in epilepsy—that is, the oxydizing power is more marked during the interaccessual periods, less before the seizure.

Owing to the fact that in these two diseases in which cyclic groups with oxybenzolic structure are found, the blood serum offers an increased oxydizing power toward such substances, the author asks if it might not be possible, with the above quoted reaction, to recognize in vivo the presence of these qualitative thyroid variations.

PATHOLOGICAL PHYSIOLOGY OF THE THYROID AND THE THYMUS IN RELATION TO INFECTIONS (FISIOPATOLOGIA DELLA TIROIDE E DEL TIMO NEI RAPPORTI CON LE INFEZIONI). Mario Barbara, R. Università di Palermo. Societa Editrice Libraria, Milano, 1918, pp. 260.

The book is based on an extensive consideration of the literature, a long bibliography of which is included, together with personal researches by the author. In the introduction are considered the relations which exist between the endocrine glands and infections and the relations of the thyroid and the thymus.

The first section of the thesis, proper, takes up a study of the thyroid in relation to infections. The gland has a defensive action against such. After thyroidectomy animals show a considerable degree of diminution of effectiveness of the immunizing mechanisms, as complement, bacteriolysins, opsonins and phagocytic power of the leucocytes. Through its relation with the liver and kidneys also the thyroid affects resistance. Histologic changes in these organs can be demonstrated after disturbances of thyroid function as in myxedema, cretinism and exophthalmic goitre, as well as after acute and chronic infections, which the author believes particularly influence the thyroid. In these conditions he has found either progressive thyroid metamorphosis (epithelial cell proliferation, increase of secretory granules and of colloid, accumulation of lymphocytes, etc.) or of regressive metamorphosis manifested as sclerosis, atrophy, alterations of the colloid and epithelial degeneration. These changes in turn lead to thyrogenic symptoms which vary more or less in accordance with the nature of the infection.

In the second part of the book the author summarizes a series of studies on thymectomised guinea pigs, as regards the phagocytic power of the leucocytes, and the complementary, opsonic and agglutinating power of the blood serum. It is concluded that in the thymus originate substances which stimulate phagocytosis; such substances can be demonstrated in extracts of the gland. It either forms complement or through its hormone influence on other structures stimulates complement formation. Similarly, it can be shown to form or augment the formation of opsonins, but apparently has no essential part in the formation of agglutinins. Neither does it play a significant role in the resistance to chloroform poisoning, as has been previously claimed. Thymectomy results in a loss of balance among the defensive mechanisms of the body but, later, compensatory changes take place in other structures to restore the balance. The opsonic power of the serum was found, however, to remain permanently lowered after thymectomy.

Anatomically, it was found that, following infections, the thymus reacts as do lymphoid organs and that ordinarily atrophy results. On this basis the question is raised whether primary thymus insufficiency may not be one of the conditions predisposing to infections. It is pointed out that in such conditions as pregnancy and starvation, when infection is more prone to occur, thymus atrophy is seen. As signs pointing to thymus insufficiency Barbara mentions trophic changes in the skin, cachexia, muscular atrophy and weakness, metabolic perturbations—especially of calcium metabolism in tuberculosis, etc. He describes the syndromes of "athymism," "hypothymism," status thymolymphaticus and the exudative diathesis of Czerny and then the corresponding opotherapy.

Thymic dysfunction is ascribed partially to infections in the parents. Such dysfunction leads to greater liability to some infections than to others. For instance, in Barbara's experience, tuberculosis is rare in individuals having thymus hyperplasia whereas, conversely, in cases of active tuberculosis, thymic atrophy is marked. Such atrophy, it is claimed, cannot in many cases be ascribed to the general wasting effect of the disease, being noted at a stage when time has not sufficed for such effect. It appears to the reviewer, however, that there is nothing so definite in the thymic changes recorded as to force upon us the conviction that they are specifically causal rather than a part of the general effect of disease in the organism.

Other objections to Barbara's conclusions might be offered. The inflammatory changes of the thyroid in acute infections, and sclerosis, atrophy and degeneration in chronic diseases would rather point to a non-specific reaction. In regard to the thymus, if we consider it as a lymphoid organ, it is evident that, in case of its suppression, there comes a greater strain on the lymphatic system; this may account for the lowered resistance of the organism as well as its subsequent recovery of balance after a certain length of time. Furthermore, even admitting that the thymus is not precisely a transitory organ, still its size and function undergo with age a remarkable diminution, but there is ordinarily no consequent impairment of organic resistance. The early disappearance of the thymus seems to be an occurrence common to all wasting diseases, rather than a peculiarity of tuberculosis and, as yet, we cannot state whether the disappearing thymus opens the door to the infection, or the infection makes the thymus disappear.

Notwithstanding the several points, which may be open to discussion, this work of Prof. Barbara shows a thorough knowledge of the literature and his diligent research opens new fields to the activity of investigators.

G. VERCELLINI.

ABSTRACTS

(ADRENAL) Sergent's "white line" in suprarenal insufficiency. Anon, Lancet (Lond.), 1918 (ii), 713-714.

An abstract of an article by Prof. Massalongo in which he describes the attempt to produce the white line in 400 cases of various diseases. The line was found in an unequivocal form in only 300 cases; the majority of these were typhoid or paratyphoid. Because of its rarity, inconstancy and transiency and because of its presence or absence in equal proportion in cases where changes in the suprarenal capsules are indisputable, he credits the white line with only a relative diagnostic importance and does not consider it as pathognomic. It has, however, some value from a prognostic point of view, since its maximum frequency is met with in cases of serious import with almost invariably a fatal issue. See Endocrin., 1917, **1**, 18-23.—L. G. K.

(ADRENALS) A case of Addison's disease with unusual onset. Anon., Guy's Hosp. Gaz. (Lond.), 1918, **32**, 286.

Report of sudden collapse and death of a patient three months after a radical mastoid operation. Previous to the collapse no particular abnormalities could be detected in any system. The collapse was accompanied by a fit, with twitchings of the limbs on the right side, and later, with rigidity on same side. This was followed by unconsciousness. Rupture of a cerebral abscess was thought of, but the cerebro-spinal fluid was clear. The patient died next day and at autopsy the only abnormality found was enlargement of the suprarenal bodies. These were 2½ inches long and ½ inch broad. On section no cortex was to be seen. In the medulla there were large caseating nodules; no normal suprarenal tissue was seen at all. The only pigmentation was a slight coloration on the internal aspect of the thigh.—F. S. H.

(ADRENALS) A case of Addison's disease from the surgical wards. Anon., Guy's Hosp. Gaz. (Lond.), 1918, **32**, 286-287.

A patient had a septic tarsus (tubercular), the X-ray showing well marked bone destruction and no bone formation. The previous history revealed broncho-pneumonia with slow

recovery, total alopecia and a feeling of lassitude during the past three years. Preliminary to amputation, phthisis was found in right lung. Though reacting unfavorably to the continued anesthetic he came out and did well for 18 hours, but suddenly collapsed and died of cardiac failure in about ten minutes. The autopsy demonstrated an extensive tubercular involvement of the whole body. Particularly to be noted were the enlarged adrenals filled with typically caseous tuberculous material.—F. S. H.

ADRENALS, Nervous control of the secretory function of the—(Die Innervation der Nebenniere durch den Splanchnicus). Asher (L.), Arch. f. d. ges. Physiol (Bonn), 1917, **166,** 372.

Asher points out, against the criticism made by Popielski, that in his experiments on the effect of splanchnic stimulation pressure upon the adrenals was carefully avoided. He, therefore, still maintains that the secretory function of the adrenals is controlled through the splanchnic nerve.—E. U.

(ADRENAL) The action of adrenalin on blood pressure (Die Blutdruckwirkung des Adrenalins). Bauer (J.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1217.

On page 955 of the same journal Dresel published an article in which he stated that the blood pressure reaction after adrenalin injection affords a good criterion to distinguish normal individuals from those having vagotonia and sympathicotonia. Bauer discusses Dresel's article and comes to the conclusion that the method indicated has no value. But we do not need a method for this purpose, as, also according to Bauer, the existence of "vagotonia" and "sympathicotonia" has never been proved and is extremely improbable.—J. K.

(ADRENALS GONADS) Tumor of the adrenals and destruction of the gonads in a man (Nebennierentumor und Geschlechtsdrüsenausfall beim Manne). Bittorf (A.), Berl. klin. Wchnschr., 1919, **56,** 776.

Description of a remarkable case. A man of 26 years noticed that his sexual desires had diminished. The testicles became atrophic and at the same time a tumor developed in the abdomen. The breasts hypertrophied, resembling the female type. The urine contained red and white blood cells, casts and large cells. The skin showed but little pigmentation. The diagnosis, hypernephroma, was confirmed by postmortem examination.—J. K.

(ADRENAL) Acute suprarenal disturbance in the course of hereditary syphilis with a polymorphic erythema (Surrénalite aiguë dans le cours d'une syphilis secondaire et á la suite d'un èrythème polymorphe). Blum, Bull. Soc. Méd. des Hôp. (Paris), 1916, **40**, 1767-1774.

A case report.—A. L. T.

(ADRENAL) Influenza as a cause of acute Addison's disease (Grippe als Auslösungsfaktor von akutem Addison). Brunecke, Therapeutische Monatshefte (Berlin), 1919, **33**, 354.

A remarkable case. A girl of 12 years with tuberculosis of the lungs and of the ulna gets influenza. Acute Addison's disease with pigmentation of the skin (not of the mucous membranes), enormous weakness, apathy and a blood pressure of 70 mm. develops. The child becomes so extremely weak that she cannot sit up alone in bed. Following treatment with "partial antigens" (Deyke-Sluck), the blood pressure rose, the child regained strength, the pigmentation began to disappear and after some time the child was able to play again in the garden.—J. K.

ADRENAL, enlargement of—in starvation. Byrne (C. H. C.) Brit. Med. J. (Lond.), 1919 (ii), 135.

The author noted that in a series of eight autopsies on soldiers who had died from underfeeding in a German prison camp, the adrenals were enlarged to almost one and a half times the normal size. The enlargement seemed, from naked-eye appearance, to be mostly in the cortex.

The suggestion is made that the adrenals had hypertrophied to counteract the low blood pressure produced through insufficient nourishment. The author is apparently unfamiliar with the more recent work on the subject of the effect of the adrenals on blood pressure.—L. G. K.

(ADRENAL) On the clinical evidence of involvement of the suprarenal glands in influenza and influenzal pneumonia. Cowie (D. M.) and Beaven (P. W.), Arch. Int. Med. (Chgo.), 1919, **24**, 78-88.

Necrospy reports indicate hypoplasia and evidence of suprarenal dysfunction following influenza. The occurrence of suprarenal dysfunction in influenza and influenzal pneumonia may be regarded as indicated by the cardinal symptoms—asthenia and low blood pressure—the characteristic rise in blood pressure following the prolonged administration of epine-

phrin, and the prolonged blood pressure curve following epinephrin injections. Further, the prolonged blood sugar curve after injection of epinephrin and the prolonged sugar curve after the ingestion of glucose also indicate an endocrinal disturbance in influenza. Hypoglycemia is not present in influenza or influenzal pneumonia as has been found to be the case in certain diseases of endocrinal origin. The administration of epinephrin is of no use in the treatment of influenzal cases. Possibly the proper method of administration has not been evolved; subcutaneous injections of epinephrin is valueless.

—H. W.

(ADRENAL PINEAL HYPOPHYSIS) The effects of some glandular extracts upon the contractile vacuoles of Paramecium caudatum. Flather (M. D.), Biol. Bull. (Woods Hole), 1919, **37**, 22.

This paper describes a series of experiments to determine the influence of some glandular extracts upon the contractile vacuole of Paramecium caudatum. An exhilaration of pulse frequency was produced by solutions of pituitary substance, adrenalin and pineal extract, the extent and duration being dependent upon the concentration of the solution. The greatest exhilaration was produced by pituitary substance, the least by pineal extracts. The author believes that the stimulation is produced, not by the direct effect of the autacoid principles upon the vacuole itself, but by the indirect effect of heightened metabolism in the entire organism. The vacuoles become more active in compensation for this increase in metabolism. A review of the literature giving the nature and function of the contractile vacuole is given. (Author's abstract.)

Shumway had previously shown that thyreoid substance placed in cultures of Paramecium also will hasten metabolism, but he called the activating principle of the thyreoid a "dissimilatory" hormone. The idea expressed by the present writer is probably more accurate than that of Shumway.

—E. R. H.

(ADRENAL) Da asthenia suprarenal. de Fonseca (J. M.), Arch. Brasil. de Méd., 1919, **9**, 149-163; Physiol. Abst., **4**, 340.

The author by means of electric stimuli exhausted the gastroenemius muscles of frogs and determined that by the injection of adrenin into the tissue mass the muscle could be immediately restored. Curare injected simultaneously with adrenin at once loses much of its effect. From these results and those of other investigators de Fonseca accepts the theory

that adrenin neutralizes the products of muscular activity, preventing their curare-like effects. Similarly, the asthenia observed in certain pathologic conditions is regarded as due to a failure of the adrenal glands to secrete adequately.

—R. G. H.

(ADRENALS) Syndrome of incipient or abnormal Addison's disease with presence of "white line of Sergent" (Syndrome d'addison fruste avec présence de la ligne blanche). Mussio Fournier (J. C.) and Sergent (E.) Bull. Soc. Méd. des Hôp. (Paris), 1919, **43**, 207.

An atypical case of Addison's disease, characterized by acute abdominal pains, pigmentation on skin areas normally subjected to pressure and in the sclera and buccal mucosa. A history of scrofulous glands existed. There was a high degree of sugar tolerance, failure of appearance of glycosuria after ingestion of 200 gm. of glucose, or after injection of 3 mg. of epinephrine.

Treatment: 40 gtt. adrenalin per day was followed by disappearance of vomiting, diarrhoea, and for the most part pain and fall of heart rate from 120 to 80. However, the heart continued to be very unstable as, under effort, the rate would rise to 130 to 140, yet without serious fatigue or feeling of weakness. The "white line" of Sergent no longer appeared.

—A. L. T.

(ADRENAL) The relation between central nervous system, adrenals and carbohydrate metabolism. A discussion of the problem: Sugar puncture and adrenals (Über die nach zentraler Reizung zur Störung des Kohlehydratstoffwechsels führenden Vorgänge. Eine kritische Studie zur Frage: Zuckerstich und Nebennieren). Kahn (R. H.), Arch. f. d. ges. Physiol. (Bonn), 1917, **168**, 326.

A discussion of experiments relating to the role of the adrenals in the glycogen mobilization occurring after sugar puncture. It was concluded that both the glycolytic ability of the liver cells and the adrenalin excretion by the adrenals are controlled, through the splanchnic nerve, by the central nervous system. Sugar puncture makes the liver cells more sensitive to the action of adrenalin and increases adrenalin secretion. Therefore a slight increase of the glycogen mobilization may take place after sugar puncture also in the absence of the adrenals, while in their presence glycogen mobilization after sugar puncture is far more marked. The mobilization of sugar after sugar puncture demonstrates one of the physiological

activities of the adrenals, the function of which is probably to regulate carbohydrate metabolism under the control of the central nervous system.—E. U.

ADRENAL glands, The effects of a scorbutic diet on the—. McCarrison (R.), Brit. Med. J. (Lond.), 1919, (ii), 200.

The effects of a scorbutic diet on the adrenal glands were studied in guinea-pigs fed on crushed oats and autoclaved milk. The naked-eye changes consist in enlargement of the adrenals with increase in their weight and in congestion. The weight of the adrenal glands of animals dying in consequence of the scorbutic diet is approximately double that of health. The increase in weight is even more marked when the weight of the glands is calculated per kilo of original and final body weights.

Microscopically hemorrhagic infiltration and disintegration of the cellular elements of the cortex and medulla are seen. The areas of hemorrhagic infiltration are situated around the periphery of the cortex. These changes are regarded as pre-scorbutic, since they occur in animals exhibiting no clinical evidences of scurvy during life.

The adrenalin content of the glands (estimated by the method of Folin, Cannon and Dennis) is less than half that present in healthy guinea-pigs, in spite of the greater weight of the organs.

It is pointed out that normally the total adrenalin per gram of gland in pigeons is approximately ten times greater than in guinea-pigs. The author has previously shown that a great increase in the adrenalin content of the adrenals occurs in pigeons deprived of accessory food factors of all classes (Endocrin. 1919, **3**, 201-2). He now finds that when vitamines of the "A" class in the form of fresh butter are added to the diet, an increase of adrenalin does not as a rule occur. He therefore concludes that lack of accessory food factors of the "A" class causes excessive production of adrenalin associated with oedema in aves, and that in guinea-pigs the lack of factors of the "C" class causes diminished adrenalin production associated with hemorrhage into the body tissues.

L. G. K.

The ADRENAL glands and toxi-infections. Marie (A.), Ann. inst. Pasteur (Paris), 1918, **32**, 97-110.

Tetanus toxin can be rendered innocuous for mice by mixture and incubation with adrenalin. Simultaneous injection of adrenalin with the toxin does not, however, prevent the onset

of symptoms. Mixture and incubation must precede injection. Such mixtures retain the power of producing specific antitoxin on injection into rabbits. Tetanus toxin, non-diffusible in the pure state, dialyzes after contact with adrenalin, the dialysate being capable, on injection, of producing specific antibody, but not of causing tetanus.—Chem. Abst. **13**, 3233.

(ADRENAL) A study of hyper-adrenalism; its influence in producing congenital pyloric hypertrophy and subsequent obstruction. Pirie (G. R.), Lancet (London), 1919, (ii), 513-515.

The author suggests that congenital pyloric hypertrophy is the result of spasm primarily due to hyper-adrenalism before birth, and that other subsidiary post-natal causes determine the persistence or recurrence of the spasm. This condition is supposed to be due to a lack of balance between the secretions of the various endocrinic organs in the process of their development and involution, which may result either in a relative or an absolute hyper-adrenalism.

Phimosis is mentioned as one cause contributory to the pyloric hypertrophy and the phimosis is supposed to be due to a precocious sexual development resulting from slow involution of the suprarenals. Hyper-adrenalism is also suggested as a cause of pancreatic insufficiency. The consequent absence or reduction of the alkaline pancreatic secretion, which normally neutralizes the acid chyme in the duodenum, allows the pylorus to remain closed longer than usually. This again tends to produce hypertrophy of the sphincter muscle.

The hypothesis is entirely speculative and no real evidence is offered in its support. The author evidently forgets that in fetal life the cortex rather than the medulla is hypertrophied when he advances the large size of the fetal adrenal gland as a possible cause of hyper-adrenalism.—L. G. K.

(ADRENAL) Adrenin and Adrenals. 1. The Presence of adrenin in the venous blood of the adrenals the result of pressure exerted upon the adrenals. (Adrenalin und Nebennieren. 1. Komprimierung der Nebennieren und Adrenalin.) Popielski (L.), Arch. f. d. ges. Physiol. (Bonn), 1916, **165**, 565.

The fact that adrenalin is found in the venous blood of the adrenals is no proof of the adrenalin being the product of a secretory activity of these glands. First, it seems that adrenalin occurs, not as free secretion, but enclosed in the parenchyma cells of the adrenals. Second, these cells can be pressed through the walls of the vessels by means of the

slightest pressure exerted upon the adrenals, and such a pressure cannot be avoided in handling the glands. P.'s experiments show that compression and even the slightest touch upon the adrenals is sufficient to make adrenalin appear in the circulation. In dogs, after cutting the spinal cord in the region of the medulla oblongata, the splanchnic and the sympathetic nerves, pressure exerted upon the adrenals resulted in a considerable increase of the blood pressure, which was the higher the more pressure there was exerted and the longer it lasted. Defibrinated blood obtained from the circulation of the dog after the pressure experiment increases the blood pressure of the rabbit injected with the blood, and, added to Tyrode's solution, it abolishes tonus and contractions of the isolated intestine. The possibility that the increased blood pressure was the result of a stimulation of the peritoneal membrane was excluded by cutting the medulla oblongata and the splanchnic. P. finds that stimulation of the sympathetic, even in the absence of adrenalin, causes a rise of the blood pressure similar to that resulting from compression of the adrenals; the action of the sympathetic is independent of adrenalin. Yet, in the above described experiments the rise of the blood pressure was actually due to compression of the adrenals and not to stimulation of the splanchnic nerve; this was made sure by especially careful experimentation. If the aorta is compressed for one minute, the pressure in the carotid artery rises very high; sudden removal of the clamp from the aorta results in the production of a rapid flow of blood through the adrenals, which would carry adrenalin accumulated in the vein of the adrenals into the general circulation and make the blood pressure rise. No rise, however, took place in this experiment. It was concluded that adrenalin is not an internal secretion of the adrenals, since it is not excreted by the adrenals and is found in the circulation only when pressed out of the parenchyma by compression of the glands. The function of the adrenals is to detoxicate the blood by removing adrenalin and storing it in the parenchyma of the glands in the form of an unstable compound. If the cells containing this compound are pressed through the walls of the vein of the adrenals, the adrenalin can be broken away from this compound by the CO_2 of the venous blood.—E. U.

(ADRENAL) Adrenin and the Adrenals. II. Normal blood, nervi splanchnici and adrenin (Adrenalin und Nebennieren. II. Normales Blut, Nn. splanchnici und Adrenalin). Popielski (L.), Arch. f. d. ges. Physiol. (Bonn), 1616, **165**, 581.

Blood, taken from the vena cava inferior by means of a

device which secured blood coming from the adrenals only and yet did not permit of compression of the adrenals, was carefully defibrinated and injected through the vena jugularis of the animal from which it was taken. It did not raise the blood pressure, but on the contrary, like defibrinated blood of all organs, decreased it. The adrenals, therefore, do not excrete the adrenalin into the circulation. In order to determine whether or not the sympathetic nerve controls secretion of adrenalin, the sympathetic was stimulated under conditions which avoided any compression of the adrenals. Such stimulation caused no excretion of adrenalin; blood taken from the animal during stimulation of the nerve did not increase blood pressure if injected into circulation. P. criticizes severely Cybulsky's experiment, according to which adrenalin acts upon the central nervous system, and claims that its action is purely peripheral. But, since under normal conditions the tonus of the vessels is actually controlled by the central nervous system, P. thinks that adrenalin has nothing to do with normal maintenance of the tonus of the blood vessels.—E. U.

(ADRENAL) The excretory innervation of the adrenals. A critique of the work of Asher, Elliot, Cannon and de la Paz, Anrep, Tscheboksareff, and Kahn and Eiger (Über die sekretorische Innervation der Nebennieren. Kritische Bemerkungen über die Arbeiten von, Asher, etc.). Popielski (L.), Arch. f. d. ges. Physiol. (Bonn), 1918, **170**, 245.

A criticism of various papers, maintaining the standpoint that adrenalin found in the blood during stimulation of the splanchnic nerve entered the circulation, not because of the stimulating effect of the splanchnic upon adrenalin excretion, but because it had been forced from the adrenals into the circulation by pressure exerted upon the glands in the course of the experiment.—E. U.

(ADRENAL) Addison's disease of war (L'addisonisme de guerre). Ramond (F.) and François (R.), Bull. Soc. Méd. des Hôp. (Paris), 1917, **41**, 1001.

From a series of studies the authors conclude that it is extremely probable that Addison's disease as observed in, and initiated by, stress of war is in all cases ultimately tubercular in origin. This tuberculosis may be secondary to any other latent or active focus, and is but rarely primary.—A. L. T.

(ADRENAL) A case of hypoadrenia simulating intestinal obstruction. Rashbrook (H. M.) and Carter (F. W.), Lancet (Lond.), 1918, (ii), 240.

A case is described of tuberculous destruction of the suprarenal glands, the symptoms of which were repeated attacks of epigastric pain and vomiting, accompanied by constipation. The patient was weak and had a temperature of 95° F. and a pulse of 110. There was no pigmentation. At autopsy the suprarenal glands were found to be almost completely replaced by caseous masses, and the few remaining cortical cells showed cloudy swelling.—L. G. K.

(ADRENAL) A case of coexisting suprarenal and renal disease of uncertain origin. Sparrow (H. G.) and Soden (W. S.), Brit. Med. J. (Lond.), 1919, (ii), 461-462.

The patient, a British soldier in Palestine, was admitted to hospital with weakness, vomiting and night blindness. He appeared very weak and anemic. Blood films were negative for malaria. He had occasional attacks of pyrexia. The blood pressure was low. The urine contained albumin. Some two weeks after admission a blotchy purpuric eruption appeared on the chest, abdomen and extremities. Acetone was then detected in the breath, and the patient vomited a large ascaris worm. The acetone odor then gradually disappeared. The deep reflexes were gradually lost and abnormal skin pigment became evident. There was slight leucocytosis, with a relative increase in polymorphonuclears. The patient was treated with quinine through the greater part of the illness. He died about two months after admission.

The autopsy showed a narrow, atrophied suprarenal cortex and no trace of medullary substance unless represented by some fatty spaces. The kidneys showed a certain amount of degeneration. The intestine showed numerous purpuric patches, with evidence of recent bleeding. No worms were present.—L. G. K.

ADRENIN, Action of—on the spleen (Milzwirkung des Adrenalins). Schenk, Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1037.

In cases of haemolytic icterus the author injected adrenalin. Twenty minutes after an injection the enlarged spleen returned temporarily to its normal size. The injection of adrenalin is quite useful to distinguish an enlargened spleen from other tumours (tumours of left adrenals or left kidney). —J. K.

(ADRENIN HYPOPHYSIS PANCREAS) Action of organ extracts on induced hyperglycemia (Action des extraits d'organs sur l'hyperglycémie provoquee). Achard (Ch.), Ribot (A.) and Binet (Leon), C. R. Soc. de Biol. (Paris), 1919, **82,** 788; Abst. Presse Méd. (Paris), 1919, **27,** 401.

The authors produced hyperglycemia in dogs by intravenous injections of glucose. They conclude that the rate and duration of the hyperglycemia depends on the quantity of glucose injected. It is particularly clear in regard to duration. If 0.50 gm. of glucose per kilo. body weight is given, the hyperglycemia lasts 20 minutes; if 1 gm. per kilo. is given, the duration is 40 minutes. Having determined this, they tried the effect of injecting the active principle of various organs.

Adrenalin. They first injected 3.5 gm. glucose; two days later, 1 mgm. adrenalin; two days later still, 3.5 gm. glucose plus 1 mgm. adrenalin. The figures show that the addition of adrenalin causes an increase in the blood sugar greater than the sum of the increases obtained with glucose alone or adrenalin alone. The duration of the hyperglycemia was also prolonged, as if under the influence of adrenalin the organism was incapable of fixing or burning the sugar.

Extract of Hypophysis. Injection alone causes a slight hyperglycemia. Sugar plus hypophysis increases the hyperglycemia, but not to the same extent as in the case of adrenalin; the rate more than the duration is affected.

Pancreas. Commercial extracts alone, or associated with glucose, have no effect. Extracts of fresh pancreas added to the glucose injected causes a diminished hyperglycemia, both in amount and duration.

Added to the glucose-adrenalin mixture, pancreas extract inhibits the action of adrenalin. The same is true when hypophysis is used instead of adrenalin.—T. C. B.

(ADRENIN) Hemorrhage and adrenalin. Remarks on the vascular reaction to infinitesimal doses (Hémorrhagie et Adrénaline. Remarques sur la réaction vasculaire aux doses infinitésimales). Bardier (E.), C. R. Soc. de Biol. (Paris), 1919, **82,** 758.

The observations of Rous and Wilson (see Endocrin. 1919, 3, 188) are confirmed in all points. Hemorrhage causes a diminished pressor response to minute doses of adrenalin. (Does this mean augmentation of the depressor component of the reaction?—Ed.)—T. C. B.

(ADRENIN) Hemorrhage and adrenalin. Remarks on the cardio-vascular reaction to large doses (Hémorrhagie et

[illegible] sur la réaction cardio-vasculaire aux [illegible] Soc. de Biol. Paris, 1919. [illegible]

[illegible] of the [illegible] the respiratory [illegible] and with premature [illegible] by injecting 0.03 mgm. of [illegible] an energetic cardio- [illegible] the heart action, favors [illegible] and augments the [illegible] same time we give [illegible]. The conclusion is [illegible] system to large [illegible] with the magnitude of [illegible] until the [illegible] may be of prof[illegible] [illegible]—[illegible] B.

ADRENIN [illegible]phenamine and Neoarsphenamine plus— [illegible] 3. 124.

[illegible] the use of adre- [illegible] and "serous [illegible] which tends [illegible] largely in an [illegible] which this conception [illegible] symptoms in these con- [illegible] 2 the destructive [illegible] proven experimen- [illegible] autopsy findings of [illegible] and 3 adrenalin has [illegible] these conditions. [illegible] factors which may play a part [illegible] and "encephalitis hemor- [illegible] of adrenal insuf- [illegible] adrenin 1 mil of a 1:1000 [illegible] ten minutes before the [illegible] agent adrenalin will [illegible] use is as a pr[illegible]ctic. The [illegible] index to the [illegible]drenalin [illegible] it produces. [illegible] [illegible] is well mark[illegible] it is an indica[illegible] [illegible]—[illegible] F.

ADRENIN, Le action of [illegible] [illegible]-vas[illegible] apparatus (l'action de [illegible]

vasculaire). Binet (L. . Presse. Méd. Paris'. 19[illegible] 25. [illegible]

An historical review of the literature of the p[illegible] namic actions of epinephrine on heart, systemic, co[illegible] pulmonary blood vessels. No original data are [illegible] A. L. T.

ADRENALIN, desiccated **THYROID** and cert[illegible] salts; **Effect of, on catalase production.** Burge W[illegible] J. Physiol. (Balt.), 1919, **50**, 165.

The injection of adrenalin into the portal vei[illegible] the liver to an increased production of catalase. [illegible] that adrenalin is increased during combat, this w[illegible] the increased oxidations. Desiccated thyroid intro[illegible] the alimentary tract also produces an increased [illegible] catalase from the liver. The same is true for large [illegible] of water, urea, sodium chloride, etc.—T. C. B.

(ADRENIN) Effect of epinephrin on the electr[illegible] of patients with "irritable heart." Clough H. [illegible] Int. Med. Chgo.', 1919, **24**, 284-294.

Patients with "irritable heart" who were s[illegible] epinephrin (Goetsch test) gave the following devia[illegible] the normal electrocardiographic records: Changes [illegible] tion, delayed conduction, partial heart block (at [illegible] duction of ventricular extrasystoles. Other find[illegible] about the same as in normal individuals.—B. T. S.

(ADRENIN) The changes of blood pressure afte[illegible] of adrenalin as a measure of the tonus of the inv[illegible] nervous system (Die Blutdruckveränderung nach [illegible] injektionen als Gradmesser für den Tonus im [illegible] und sympatischen Nervensystem). Dresel K. [illegible] med. Wchnschr. (Berlin), 1919, **45**, 955.

The author injected adrenalin subcutaneously a[illegible] ured blood pressure every five minutes. Thus he ob[illegible] curve. In normal individuals this curve is a par[illegible] vagotonia it has the form of the letter S in serious [illegible] blood pressure is first largely diminished. In sym[illegible] tonia the curve rises and falls very steeply.—J. K.

ADRENALIN in annelids. Gaskell (J. F. . J. Physiol. [illegible] 1919, **53**, Proc., xxviii.

Certain annelids, including the Hirudineae, posse[illegible] cells in their central ganglia which give the chrom[illegible]

adrénalin. Remarques sur la réaction cardio-vasculaire aux fortes doses). Bardier (E.), C. R. Soc. de Biol. (Paris), 1919, 82, 760.

In the dog, after bleeding to the extent of 6-7% of the body weight, the pressure being nearly zero, the respiratory movements having nearly disappeared, and with premortal cardiac retardation, it is possible, by injecting 0.03 mgm. of adrenalin per kilo body weight, to observe an energetic cardio-vascular action. This, in strengthening the heart action, favors the resumption of the respiratory rhythm and augments the chances of survival of the animal, if at the same time we give either an artificial serum or transfusion. The conclusion is that the irritability of the cardio-vascular system to large doses of adrenalin in the dog decreases with the magnitude of the hemorrhage, but does not disappear until the "periode ultime." The persistence of this irritability may be of profit in the treatment of hemorrhage.—T. C. B.

ADRENIN, Arsphenamine and Neoarsphenamine plus— Beeson (B. B.), Am. J. Syphilis, 1919, **3**, 129.

It is the author's purpose to emphasize the use of adrenalin in the treatment of the "nitroid crisis" and "serous apoplexy" of Milan. The literature is collected which tends to place the etiology of these two conditions largely in an adrenal insufficiency. The evidence upon which this conception rests is: (1) there is a similarity of symptoms in these conditions and in acute adrenal insufficiency, (2) the destructive action of arsenic upon the adrenals has been proven experimentally and repeatedly demonstrated in the autopsy findings of cases dying after salvarsan injections, and (3) adrenalin has therapeutic value in treatment of both these conditions.

The author discusses other factors which may play a part in the production of "nitroid crisis" and "encephalitis hemorrhagica" only to emphasize the importance of adrenal insufficiency, and recommends that 1 mg. adrenin (1 mil of a 1:1000 solution) be given intramuscularly ten minutes before the intravenous injection. As a curative agent, adrenalin will shorten a crisis, but its chief use is as a prophylactic. The author suggests that the best index to the action of adrenalin is the marked pallor which it produces. When this "leuco reaction," as it is termed, is well marked about the site of injection and on the face, it is an indication that the dosage has been sufficient.—J. F.

(ADRENIN) The action of epinephrine on the cardio-vascular apparatus (L'action de l'adrenaline sur l'appareil cardio-

vasculaire). Binet (L.), Presse. Méd. (Paris), 1917, **25,** 191.

An historical review of the literature of the pharmacodynamic actions of epinephrine on heart, systemic, coronary and pulmonary blood vessels. No original data are presented.—A. L. T.

ADRENALIN, desiccated THYROID and certain inorganic salts; Effect of, on catalase production. Burge (W. E.), Am. J. Physiol. (Balt.), 1919, **50,** 165.

The injection of adrenalin into the portal vein stimulates the liver to an increased production of catalase. Assuming that adrenalin is increased during combat, this will explain the increased oxidations. Desiccated thyroid introduced into the alimentary tract also produces an increased output of catalase from the liver. The same is true for large quantities of water, urea, sodium chloride, etc.—T. C. B.

(ADRENIN) Effect of epinephrin on the electrocardiograms of patients with "irritable heart." Clough (H. D.), Arch. Int. Med. (Chgo.), 1919, **24,** 284-294.

Patients with "irritable heart" who were sensitive to epinephrin (Goetsch test) gave the following deviations from the normal electrocardiographic records: Changes in conduction (delayed conduction, partial heart block) and the production of ventricular extrasystoles. Other findings were about the same as in normal individuals.—B. T. S.

(ADRENIN) The changes of blood pressure after injection of adrenalin as a measure of the tonus of the involuntary nervous system (Die Blutdruckveränderung nach Adrenalin injektionen als Gradmesser für den Tonus in autonomen und sympatischen Nervensystem). Dresel (K.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 955.

The author injected adrenalin subcutaneously and measured blood pressure every five minutes. Thus he obtained a curve. In normal individuals this curve is a parabola, in vagotonia it has the form of the letter S (in serious cases the blood pressure is first largely diminished). In sympathicotonia the curve rises and falls very steeply.—J. K.

ADRENALIN in annelids. Gaskell (J. F.), J. Physiol. (Lond.), 1919, **53,** Proc., xxviii.

Certain annelids, including the Hirudineae, possess nerve cells in their central ganglia which give the chromaffine reac-

influence on the biological action of the extract on the eye of the frog or the blood pressure in dogs.—J. K.

(ADRENIN PANCREAS) The supposed antagonism between internal pancreatic secretion and adrenaline on smooth muscular fibres of vessels. Polettini (B. D.), Atti ist. Veneto, 1916, **16**, 503-508.

Surviving vessels, in Ringer's solution, modified specially after Meyer and Müller for these tissues, were treated with (1) an adrenaline-pancreatic solution, the two being left in contact for 48 hours; (2) Ringer's solution and adrenaline. Graphs show no appreciable difference in the two cases. Vessels and adrenaline from cattle were used.—Physiol. Abst., **4**, 340.

ADRENIN, Influence of—and physostigmine upon the blood picture in malaria. Pulay (E.), Ztschr. f. exp. Med., 1917, **7**, 108-118.

Adrenaline causes an increase in the relative lymphocytosis but still below the normal; physostigmine causes a decrease. Both produce an increase in the polymorphonuclear leucocytes. —Chem. Abst., **13**, 2925.

ADRENALIN in blackwater fever. Robertson (J. A.), Brit. Med. J. (Lond.), 1919, (ii), 272.

Adrenalin chloride is given in a dose of 20 minims every four hours. After the first three or four doses the urine clears up remarkably. No quinine is given. Iron tonics without quinine are prescribed during convalescence. The author suggests that the adrenalin balances a suprarenal insufficiency, which is perhaps the cause of the hemoglobinuria in some cases of malarial infection. No evidence is submitted that such is the case.—L. G. K.

(ADRENIN) Neglect of the internal secretions as a cause of high mortality in many diseases. Sajous (C. E. de M.), J. Med. Soc. New Jersey (Orange), 1918, **15**, 109-116.

The author holds that the persistent high mortality of many diseases is due to the fact that the physio-pathological role of the ductless glands in these diseases is virtually disregarded. He cites among other diseases the mortality of which has not been reduced by modern knowledge, pneumonia, characterized by Osler: "Almost the natural death of old people,"

in which death sometimes occurs unexpectedly, in the midst of the patient's daily occupation. Sajous does not regard this senile form—the cause of a large proportion of the deaths attributed to the disease—as a true pneumonia, but as the result of a more or less sudden failure of the adrenals. The symptoms in most of these cases, in fact, include but few of those peculiar to pneumonia: the fever is slight, there is a moderate rise of blood pressure, but little if any cough or expectoration, no pain in the chest, soon followed by rapid lowering of the arterial tension, marked lividity, pulmonary edema and extreme asthenia—all typical signs of adrenal failure. A suggestive fact in this connection is that dilatation of the right heart sometimes precedes infection, thus indicatng that the latter is secondary to the adrenal failure. An illustration shows the steady loss of vascularity of the adrenals as age advances, a condition which leads these to fail readily under varying degrees of stress in the aged, primarily in some cases or a slight pneumococcic infection due to exposure, fatigue, etc., in others. Sajous states many of these cases would be saved were the role of the adrenals in the process recognized and the patient carried safely through the stage of acute adrenal failure. Injections of 10 minim doses of epinephrin 1:1000 solution in a syringeful of saline solution, are administered slowly, avoiding a vein, every two hours, three times, then, when the cardiac action improves sufficiently, four times daily. Antistreptococcus serum is indicated, rather than vaccines, the latter serving only to excite adrenals that are unable to respond, while the serum contributes to the systemic asset in antibodies. Sustaining food in small quantities, creosote carbonate to prevent tympanites and avoidance of depressants, particularly the opiates and coal tars, are important therapeutic aids.

Another phase of adrenal failure connected with infections which the author has termed "terminal hypoadrenia" may occur at all ages. As its name suggests, this condition occurs late in the history of the disease, owing mainly to exhaustion of the adrenals during an exceptionally severe and prolonged febrile process. Hence its frequent occurrence in typhoid fever, broncho-pneumonia, diphtheria, scarlatina, erysipelas, septicemia, mumps, severe measles and peritonitis. The signs differ but little from those observed in senile pneumonia, and if the failure of the adrenals is overlooked in these cases, death often occurs from exhaustion, notwithstanding the so-called "supporting" treatment. Conversely, the use of epinephrin as above described, in addition to these measures, often turns the tide with surprising promptness.—Author's Abst.

ADRENIN, The action of—on the muscular coat of digestive organs. Spadolini (I.), Arch. di Fisiol. (Firenze), 1918, **16,** 135-150.

Both adrenalin and sympathetic nerve fibres may provoke inhibitory as well as motor reactions on the part of the muscular coat of the stomach and small intestine. These antagonistic reactions are in relation with the quantity of adrenalin injected into the blood-stream; the inhibition is provoked by solutions more dilute than those necessary to produce motor phenomena. These results are explained by Spadolini having recourse to Langley's doctrine of receptive substances. Small quantities of adrenalin would become bound by the inhibitory receptive substances, whereas larger quantities could combine also with the motor ones; inhibitory receptors would have a greater affinity for adrenalin than the motor ones, which could combine with adrenalin only after the inhibitory receptors have been fully bound by it. For that, of course, both inhibitory and motor receptors must be present in the same sets of cells.—Physiol. Abst., **4,** 340.

(ADRENIN) The effects of epinephrin on the basal metabolism in soldiers with "irritable heart," in hyperthyroidism and in normal men. Tompkins (Edna H.), Sturgies (C. C.) and Wearn (J. T.), Arch. Int. Med. (Chgo.), 1919, **24,** 269-283.

The same technique was employed as in the preceding experiments.

Conclusions: Intramuscular injections of epinephrin cause an increase of total metabolism in normal men and patients with "irritable heart" and in hyperthyroidism. Increase in metabolism is greater in cases showing a positive "Goetsch" reaction to epinephrin. The increase in metabolism is due to some other factor than excitement or stimulation of heart by the injection of epinephrin; it may be due to increased muscular tonus or hyperglycemia.—B. T. S.

ADRENIN treatment of serious lung diseases in infants (Adrenalinbehandlung schwerer Lungenerkrankungen bei Säuglingen). Vogel, Wiener klin. Wchnschr., 1919, **32,** 850; Berl. klin. Wchnschr., 1919, **56,** 503.

The author saw good results from subcutaneous injections of 2-5 cc. of adrenalin (1:1000 solution) in serious capillary bronchitis and bronchopneumonia of infants.—J. K.

(ADRENIN) Effects of the injection of epinephrin in soldiers with "irritable heart." Wearn (J. T.) and Sturgis (C. C.), Arch. Int. Med. (Chgo.), 1919, **24,** 247-268.

Studies were begun to determine the relation of the thyroid gland to the symptom complex of "irritable heart of soldiers." From this study it was concluded that hyperthyroidism does not play a significant role in the condition. In these studies of the basal metabolism it was decided to employ at the same time the "Goetsch" epinephrin test. It was soon observed that some cases with normal basal metabolism showed definite hypersensitiveness to epinephrin.

Studies were made on both normal soldiers and soldiers with irritable hearts, who had been in training for a number of months. The technic was the same as that followed by Goetsch. After an hour's absolute rest in bed, control readings of blood pressure, pulse and respiratory rates are made; also a note is made of objective symptoms. After satisfactory control readings are made, 0.5 cc. 1:1000 solution of freshly prepared epinephrin is injected deep into the deltoid muscle. Readings as above are made at five minute intervals for one hour. A positive reaction manifests itself in about twelve minutes as a rise in systolic blood-pressure, increased pulse rate, tremor, precordial pain, nervousness, etc.

The results of the studies were as follows: Of twenty-six normal soldiers (controls) who had had severe army training for fourteen months, not one gave a positive reaction; of seventy-three patients with symptoms of "irritable heart" sixty per cent gave a reaction which definitely indicated a hypersensitiveness to epinephrin.—B. T. S.

(AUTONOMIC N. S.) Treatment of vagotony and sympathetic-cotony. Noronha (H.), Arch. Brasil. de Med. (Rio de Janeiro), 1919, **9,** 92-100.

Noronha warns that the main thing in treatment of either condition is to aim to restore tone to the unstable nervous system as a whole; atropin can then be given for vagotony and epinephrin for sympatheticotony, but the doses should be small and cautiously given.—J. Am. M. Ass., **73,** 650.

(BLOOD SUGAR ADRENIN DIABETES) Permeability of erythrocytes to sugars in hyperglycemia. Kozawa (S.), Tokyo Igak. Zasshi, 1916, **30,** 9-18; Jap. Med. Lit., 1917, **2,** 2.

In vitro the hexoses and the pentoses readily penetrate the erythrocytes of man and the monkey, and penetrate those of the

dog to a certain extent, but do not at all penetrate those of the puppy, goat, pig, cat, or cattle. In a diabetic patient the sugar content of the corpuscles was definitely increased, and approached, but never exceeded, that of the serum; the cells were swollen; and the hematocrit reading was twice the normal value for the same number of cells. Adrenaline hyperglycemia in puppies did not alter the sugar content of the red cells; in dogs it produced a definite increase in the sugar content of these cells, though not to such a degree as occurred in the experiments in vitro.—Physiol. Abst., **3**, 504.

Cataract and INTERNAL SECRETION. Schioetz (C.), Norsk mag. f. laegevid. (Christiania), 1913, nr. 9.

Cataracta centralis congenita is fairly frequent in cretinous calves, which has first been demonstrated by the Norwegian veterinary surgeon Loeken. This fact brings the author to discuss the occurrence of cataract in various endocrine disorders. Cataract is observed after extirpation of the parathyroids and diabetic cataract may possibly be referred to the pancreas; Langfeldt (Norway) has seen cataract in dogs after pancreatectomy. Senile cataract is hypothetically referred to hypofunction of the sexual glands. Cataract is further discussed in relation to diseases of the thyroid, pituitary and suprarenals.

—K. M.

(CORPUS LUTEUM) Double ovariectomy because of bilateral ovarian cysts, at the end of the fourth month of pregnancy. Suppression of the corpus luteum. Delivery at term. (Ovariotomie double pour kyste ovariques bilateraux, a la fin du quatrième mois dela grossesse. Suppression du corps jaune. Accouchement terme). Grosse (A.), Ann. de Gyn. et d'Obst. (Paris), 1919, **13**, 464-473.

A report of a case of bilateral ovarian cysts necessitating removal by laparotomy in the fourth month of pregnancy, followed by delivery after a normal and uneventful course. The milk secretion was marked and the child breast fed. References are given to the literature of similar cases from which, and in consideration of his own results, the author concludes that it does not appear as if the corpus luteum is indispensible for embryonic and foetal development at the beginning of pregnancy and that its suppression is not sure to cause abortion.—F. S. H.

CORPUS LUTEUM, The use of—in pregnancy. Welz (W. E.), J. Michigan State M. Soc. (Grand Rapids), 1919, **18,** 373-376.

The toxemia of early pregnancy is equivalent to corpus luteum deficiency. Extracts of the corpus luteum relieve such symptoms and may control habitual abortion. The latter is considered the result of deficient corpus luteum development in early pregnancy.—H. W.

(CORPUS LUTEUM) Corpus luteum extracts in the vomiting of pregnancy, with report of cases. Quigley (J. K.), Am. J. Obst. (N. Y.), 1919, **80,** 183-185.

Of seventeen cases of vomiting of pregnancy, twelve were benefited permanently by the use of corpus luteum extracts, four were benefited but relapsed, and one was a complete failure.—H. W.

DIABETES innocens. Solomon (H.), Wiener klin Wchnschr. 1919, **32,** 871.

An important article. The author saw cases of diabetes innocens during five years, not becoming more serious. The blood sugar is on the empty stomach mostly normal; in a few cases it was slightly increased. There are cases who have a carbohydrate tolerance, but in other cases, even after the smallest amount of ingested carbohydrates, a trace of sugar comes in urine. If more carbohydrates are given the amount of sugar in the urine is not increased. In rare cases larger amounts of sugar are excreted (up to 40 grams) daily. In these cases blood sugar estimations are necessary to distinguish them from ordinary diabetes.—J. K.

DIABETES and complication with surgical diseases (Glykosurie und Diabetes bei chirurgischen Erkrankungen). Weiland (W.), Berl. klin. Wchnschr., 1919, **56,** 887; same article but more detailed, in Mitt. a. d. Grenzgeb. Med. u. Chir. (Jena), 1919, **31,** 473.

Traumatic diabetes is very rare; the author has seen only one case. Traumatic glycosuria is, however, very frequent. Surgical diseases caused by diabetes do not exist. The gangrene as it is frequently seen in diabetes is of arteriosclerotic origin.—J. K.

DUCTLESS GLANDS in military practice. Sajous (C. E. de M.), Penn. Med. J. (Athens), 1919, **22**, 215-220; N. Y. M. J., 1919, **109**, 569.

The author calls attention to the large number of hyperthyroid soldiers detected in army practice. The asthenia of excessive strain, the sudden deaths of adrenal failure, the soldier's irritable heart, warfare shock, the terminal hypoadrenia of infections, the collapse following antityphoid vaccination are examples of disorders in which the adrenals take a prominent part, and in which appropriate therapy can accomplish considerable good, and even save life. Sajous ventures the belief that the irritable heart of the soldier is frequently due to exhaustion of the adrenals, while in others an overactive thyroid is responsible. In the latter group adrenalin, nitrites and digitalis are ineffective and prolonged mental, physical and emotional rest are necessary for recovery.—H. L.

DYSTROPHIA musculorum progressiva. Schmidjell (F.), Wiener klin. Wchnschr., 1919, **32**, 867.

Of no direct endocrine interest.—J. K.

ENDOCRINE DISEASE, Progressive muscular dystrophy as an—. Timme (W.), Arch. Int. Med. (Chgo.), 1917, **19**, 79-104.

Exhaustive search of the literature, by the writer, impressed him with the fact that accompanying the muscular dystrophies, endocrine disturbances of one form or another were present. He reports a somewhat atypical form of muscular dystrophy resembling the familial infantile form. This disease occurred in four generations. Four out of five individuals having this condition, showed distinct changes in the region of the pineal gland. Three of the four patients were under twenty-four years of age.—J. H. L.

(ENDOCRINE EXTRACTS) Treatment of shock by complex artificial serum (A propos du traitement du shock. Essais d'un sérum artificial complexe). Descomps and Clermonthe, Bull. Soc. de Chir. (Paris), 1918,—,—, (July 18).

The "serum" referred to is a modified Ringer-Locke solution plus strychnine, digitalin and extracts of endocrine organs (thyroid, spleen, pituitary, adrenal and testis).—Physiol. Abst., **4**, 346.

ENDOCRINE GLANDS, Affections of—in acquired syphilis. Hazen (H. H.), Am. J. Syphilis, 1919, **3**, 205.

This paper does not lend itself readily to abstracting inasmuch as it is a resumé of the literature. Syphilis is discussed in its relation to hyperthyroidism and hypothyroidism. Emphasis is placed upon the suggestion of Mendel that many of the so-called cases of thyroid syphilis might be merely examples of iodine thyroiditis. The literature of syphilis of the parathyroids, thymus, pineal gland, adrenals, and pituitary is treated.

—J. F.

(ENDOCRINE GLANDS) The climacteric of life. Rankin (G.), Brit. Med. J. (Lond.), 1919, (i), 63-67.

The author claims that for men as well as for women there is a climacteric period, which coincides with life's full maturity. It occurs from seven to ten years later in men than in women, and in both is a time of special liability to the development of disease, especially of such as may be regarded as the expression of hereditary tendencies that have down to this period remained dormant. The immediate counterpart in man of the ovarian changes in woman is to be found in the structural alterations which become established in the prostate gland. Acute illnesses occurring during this period are attended with more than average risk, and the frequency of malignant growths at this age is well known. Besides these conditions arteriosclerosis, interstitial nephritis and diabetes are common ailments in men between 55 and 63, while in women colitis, rheumatoid arthritis and hyperthyroidism are common accompaniments of the change of life.

The author claims that at this age the starvation treatment for diabetes is such a tax upon the nervous control of the patient that it imperils his "serenity of temper and happiness of life." And besides, the author minimizes the importance of sugar in the urine of elderly men, claiming that it does not interfere with their life or work to an appreciable extent.

—L. G. K.

ENDOCRINE influence of the pylorus. Frumson (L. G.), Med. Fortnight. (St. Louis), 1919, **51**, 157-158.

A most facetious attack upon all known facts and theories relative to gastrointestinal disturbances and upon investigators generally. However, Frumson claims for himself great results in the treatment of achylia by the administration of watery extracts of the pylorus of cattle.—H. W.

ENDOCRINE manifestations. Strauss (S. G.), U. S. Nav. Med. Bull. (Washington, D. C.), 1918, **12,** 609-615.

An appeal for the study of subjective as well as objective symptoms and for a consideration of the patient as a whole, instead of the complainant part alone. The article is accompanied by a description of two cases presenting no laboratory proofs of adrenal derangement but which, being studied from a general knowledge of the possibilities of such disorder and treated accordingly, gave favorable response and substantiated the value of the method advocated.—F. S. H.

(ENDOCRINE ORGANS) Cerebral localization from the point of view of biologic psychology (Las localizaciones cerebrales bajo el punto de vista de la Psicología Biológica). Enrique Mouchet, Prensa Med. Argentina, 1919,—,—, (No. 2.)

The totality of intelligence is derived not through the senses alone. The cerebrum receives an inner stimulus through the blood as well as internal secretions proper which contribute to the formation of instincts and, to a notable extent, of the psychic qualities.—B. A. H.

(ENDOCRINE ORGANS) The differentiation of mankind into racial types. Gallwey (T. J.), Lancet (Lond.), 1919, (ii), 666.

Gallwey criticises the view of Keith (see abstract in this issue) that the differentiation of the races of mankind has been due to varying degrees of endocrine activity. He claims that environment alone is responsible for the various types, although he does not show why environment could not modify the type through modifications in the ductless glandular system .

—L. G. K.

(ENDOCRINE ORGANS) Dystrophie myotonica. Kastan, Berl. klin. Wchnschr., 1919, **56,** 837.

A case of dystrophia myotonica (myotonia atrophica). The thyroid was only half the size of a normal organ; both testicles were atrophic. The X-rays showed no changes in the hypophysis.—J. K.

(ENDOCRINE ORGANS) The differentiation of mankind into racial types. Keith (A.), Lancet (Lond.), 1919, (ii), 553-556.

This paper has attracted a good deal of attention in the lay press as evidenced by the number of newspaper articles which have lately appeared on this subject. The author sets

forth the view that the distinguishing characteristics of the races of mankind have been produced by the varying degrees of activity manifested by the ductless glands in the different races. For instance, he explains the sharp and pronounced nasalisation of the face, the tendency to strong eyebrow ridges, the prominent chin, the tendency to bulk of body and height of stature in Europeans as a result of a greater activity of the pituitary gland in them than in the Negro or Mongol races. Similarly the beardless face and almost hairless body of the Negro and Mongol are attributed to a lesser degree of activity on the part of the interstitial cells of the gonads. The suprarenals, because of the darkening of the skin in Addison's disease, are said to regulate the amount of pigmentation of the skin. A reduced activity of the thyroid is supposed to account for the characteristic aspect of the Mongolian face. The hypothesis thus attributes to the Caucasian a slight degree of acromegaly while it declares that the salient characteristics of the Mongolian and Negro races are due to a tendency toward eunuchism, Addison's disease and cretinism. Achondroplastic dwarfs and Mongoloid idiots are regarded as the results of defects in the growth regulating mechanism of the thyroid, and since, in the opinion of the author, both these types resemble the Mongolian, this is advanced as an added piece of evidence that hypothyroidism has been partly responsible for the Mongolian type of man.

(The hypothesis is unsupported by experimental evidence, and the author has apparently taken advantage of the unsettled condition of our knowledge of the ductless glands to put forth a theory which explains the unsolved in terms of the unknown.)—L. G. K.

(ENDOCRINE ORGANS) Endocrine glands and fever. (Glandes endocrines et fiévre). Leopold-Levi, C. R. Soc. Biol. (Paris), 1919, **82,** 410-412.

The author is of the opinion that endocrine activity and the production of fever are very closely related. He believes that the thyroid, ovary, suprarenal and anterior lobe of the pituitary can all produce fever or increase the fever of autoinfection, the premenstrual period and particularly the fever of tuberculosis.—L. G. K.

(ENDOCRINE ORGANS) Bradykardie mit Hypotonie. Lommel, Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1096.

The author observed many cases of slow action of the heart combined with a low blood pressure. Often the temper-

ature was low, there were oedemas and eosinophilia. Perhaps an abnormal function of the endocrine organs plays a part in the disease, but treatment with adrenalin, with thyroidin, with pituglandol and with extract of gonads had no effect whatever.—J. K.

ENDOCRINE organs, Diseases of the—. Poulten (E. P.), Guy's Hosp. Gaz. (Lond.), 1918, **32,** 234-241.

This is an abstract of two clinical lectures by the author and contains but a brief survey of the outstanding features of the clinical significance of adrenal, pituitary, thyroid and parathyroid syndromes.—F. S. H.

(ENDOCRINE ORGANS) Changes in the weights of the various parts, systems and organs in albino rats kept at birth weight by underfeeding for various periods. Stewart (C. A.), Am. J. Physiol. (Balt.), 1919, **48,** 67-78.

The weights of the various organs, systems and parts of the body were studied in eight newborn controls and 15 test rats kept at birth weight by underfeeding for period ending at 11 to 22 days of age. In the test animals the individual endocrine glands showed the following percentage increase in weights when compared to the corresponding organs of newborn rats: Testes 374, spleen 33, hypophysis 29, pineal gland 21. The thyroid, ovaries and suprarenals showed practically no change, while the thymus decreased in weight 49 per cent.—L. G. K.

(ENDOCRINE ORGANS) Diet in chronic arthritis. Thomson (F. G.), Practitioner (Lond.), 1919, **103,** 10-121.

In discussing the importance of vitamines in feeding cases of chronic arthritis the author states that lack of these food constituents results in ill-balanced function of the endocrine glands, which he considers a constant feature of arthritis. "Whereas in rheumatoid arthritis, hyperthyroidism due to toxic thyroiditis occurs with great frequency, in osteo-arthritis, fibrositis, and chronic gout, the balance swings in the other direction, with thyroid inertia and hyperactivity of the suprarenal system. — — — — Modern investigation has shown that uncooked food is an essential element in diet, owing to the action of vitamines in promoting normal digestive and assimilative processes and maintaining the balance of endocrine activity."—H. L.

ENDOCRINOPATHIES, Clinical manifestations and basis for treatment of some—. Timme (W.), J. Nerv. and Ment. Dis. (N. Y.), 1918, **47**, 446-449.

Timme points out the inadequacy of some of the present-day endocrine terminology in that such names as exophthalmic goitre do not cover the entire or even the fundamental pathology. He distinguishes between the abnormal glandular manifestations which dominate the clinical picture and the disturbed gland which is the key to the whole syndrome. The two are not always identical and certainly difficult to determine because of such complicated inter-relations between the various glands. The problem then lies in selecting the crucial symptom or the crucial gland on which to base the therapy.—A. R. T.

(GONADS) A case of hypernephroma (Ein Fall von Hypernephrom). Bittorf, Deutsche med. Wchnschr. (Berlin), 1919, **45**, 981.

A very short description of a man with hypernephroma, atrophy of the testes and development of female breasts.
—J. K.

(GONADS) Steinach's treatment of homosexuality (De behandeling van homosexualiteit volgens Steinach). de Boer (S.), Geneeskundige Bladen (Haarlem), 1919, **21**, 175.

Gives a very good review on the work of Steinach and the literature on this point. No new facts.—J. K.

(GONADS) Masculine tubular hermaphrodism. Abdominal hysterectomy in the course of a radical cure for inguinal hernia in a man of 31 (Hermaphrodism tubulaire masculin. Hysterectomie abdominable au cours d' une cure radicale de hernie inguinale chez un homme de 31 ans). Couvelaire (A.) and Duelaux (H.), Ann. de. Gyn. et d'Obst. (Paris), 1919, **13**, 474-478.

An interesting case of masculine tubular hermaphrodism of the internal variety consisting in the heterologous development of the Müllerian ducts to a normal degree, in contradistinction to the usual condition observed in the female organs when found in the male, which are usually rudimentary in character. The external appearance was thoroughly masculine without any secondary sexual characteristics of the female. He was married and his wife had given birth to two children since that time. The testicle that was removed contained spermatazoa as did his semen on ejaculation. On operation for in-

guinal hernia, scrotal variety, there was discovered in the scrotum a well developed uterus 10 cm. in length and 4 cm. in breadth at its maximum.—F. S. H.

GONADS, Structure of—. (Bauplan der Keimdrüsen). Kohn (A.), Wiener klin Wchnschr. (Vienna), 1919, **32,** 50; Berliner klin. Wchnschr., 1919, **56,** 70.

A general review.—J. K.

(GONADS) Influence of the interstitial gland upon body temperature (Über die Abhängigkeit der Körpertemperatur von der Pubertätsdrüse). Lipschütz (A.), Arch. f. d. ges. Physiol. (Bonn), 1917, **168,** 177.

The rectal temperatures of normal male and female, of castrated male and female guinea pigs without grafts and of castrated male and female guinea pigs into which ovaries and testes, respectively, had been grafted, were measured. Result: The interstitial gland of the male sex gland has no influence upon the body temperature of the male and probably no influence upon the temperature of the castrated female when it is grafted into the latter. The interstitial gland of the female gonad increases the temperature from 0.4 to 0.5° C., as indicated by the fact that in castrated females the body temperature is 0.4° C. lower than in normal females, while in castrated males into which ovaries were grafted, it is 0.5° C. higher than in castrated males into which no ovaries had been grafted.
—E. U.

GONADS, The formation of sexual characters by the—. (Die Gestaltung der Geschlechsmerkmale durch die Pubertätsdrüsen). Lipschütz (A.), Arch. f. Entw. (Berlin), 1918, **44,** 396.

A review of the work on the influence of the removal and transplantation of the gonads on sexual characters. No new data.—M. M. H.

(GONADS) Transformation of the clitoris into a penis-like organ through experimental masculinization. (Umwandlung der Clitoris in ein penisartiges Organ bei der experimentellen Maskulierung.) Lipschütz (A.), Arch. f. Entw. (Berlin), 1918, **44,** 198.

After implantation of a testis in a spayed female guinea pig, the clitoris develops into an organ somewhat like the penis of a normal male. The foreskin and the corpora cavernosa

penis are well developed, and "piercing" organs are present, though abnormally placed. The organ is shorter than a normal penis and the growth of the corpus cavernosum urethrae is not stimulated by the operation.—M. M. H.

GONADS, Fundamentals of knowledge about the—. (Prinzipielles zur Lehre von der Pubertätsdrüse). Lipschütz (A.), Arch. f. Entw. (Berlin), 1918, **44**, 207.

Further discussion of the reasons why different parts of an organ (e. g. the clitoris) react differently to transplantation of the gonads. No new data.—M. M. H.

(GONADS) Die spermatogenesis des Grottenolmes. Stieve (H.), Anat. Anz. (Jena), 1918, **51**, 321.

A cytological study of the germ cells of the amphibian Proteus anguineus. Not of endocrine interest.—E. R. H.

(GONADS) Hermaphroditism in men (Ueber Zwitterbildung bein Menschen). Polano. Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1231.

Report of a remarkable case. The clitoris was developed like a penis, but the urethra ended at the base of the organ. By an operation the end of the urethra was transplanted to the glans. When the patient was 18, she menstruated regularly from this artificial orifice. The secondary sexual characteristics were mixed, but more female than male. At operation for an abdominal tumor a normal uterus was found. In one of the ovaries normal testicular tissue was seen. To this ovary was attached a vas deferens with a normal epididymis. —J. K.

(GONADS) Männlicher Pseudohermaphroditismus. Schmalfuss. Berl. klin. Wchnschr., 1919, **56**, 789.

A girl with female external genitals underwent a "herniotomy." One normal and one atrophic testicle were found. Six months later the patient died of sepsis. Though during the operation two testicles were removed, at the postmortem examination living spermatozoa were found in the vesiculi seminalis.—J. K.

(HORMONES) An hypothesis of "hormone hunger." Harrower (Henry R.), Med. Rec. (N. Y.), 1919, **96**, 276-278.

Harrower notes that in his experience with organotherapy

brilliant results are obtained in some cases of endocrine disturbance and no results whatever in clinically similar cases. This has led him to formulate "an hypothesis of hormone hunger." He believes that each organ in the body has a selective capacity to pick up and utilize certain hormones that are circulating in the blood stream, and that the more urgent its requirement for a specific hormone, the more "hungry" it is, the more readily it picks up and utilizes this hormone. The interrelationship of the ductless glands, with the result that abnormal secretion of one produces alterations in the activity of the others, justifies pluriglandular therapy, in Harrower's opinion, and removes from it the odium of "shotgun" therapy. In giving pluriglandular products, Harrower thinks the opportunity is given the body to do its own selecting. "We can trust the organism to pick out from the menu we offer it those hormones that it needs most, and, too, in the degree it needs them." (If this hypothesis be true, why should patients with the same clinical signs and symptoms, and therefore the same "hormone hunger," respond differently to the same ductless gland diet? The author has not proved his point, and the encouragement of unintelligent, indiscriminate pluriglandular therapy, usually in totally inadequate dosage, is most unwise; Osler has recently given a timely warning and deserved criticism of this latest therapeutic "fad.")—H. L.

HORMONES and phosphatides. Fraenkel (S.) and Herrmann (E.), U. S. Patent No. 1,314,321, Aug. 26, 1919.

A preparation suitable for treatment of disorders produced by failure of the ovarian functions is prepared in the following manner: 50 pieces of human placenta are carefully dried in vacuo and pulverized and the resulting material, about 5000 g. of dry substance, is extracted with ether. After evaporation of the ether, the phosphatides are precipitated from the residue by adding a 4-fold amount of acetone. The acetone-containing mother liquid is freed from solvent in vacuo. The residue is then taken up in cold alcohol, by which treatment a great part of cholesterol and cholesterol esters (less soluble in the cold solvents) is separated out. After evaporation of the alcohol, the residue is purified by fractional distillation in the highest vacuum possible. Under a pressure of 0.06 mm. Hg a mixture of hormones with cholesterol distils over as the principal fraction. By treating this distillate with cold alcohol, the hormones are dissolved, while cholesterol and saturated esters of cholesterol crystallize out. For a further purification of the desired product, a second fractionation in a high vacuum can

be utilized after evaporation of the alcohol. The product is a thickly flowing oily liquid showing the typical reactions of cholesterol. Various modifications of the procedure are described.—Chem. Abst. **13,** 2736.

HORMONES, Hypothesis concerning—. (Hypothèse sur les hormones). Ide, C. R. Soc. de Biol. (Paris), 1919, **82,** 944.

The role of the "glandes sanguines" can be explained by their embryologic origin. They produce substances useful to themselves and to their sister cells. This hypothesis is suggested by a number of facts.

Adrenalin is a specific excitant of the dorso-lumbar sympathetic. Embryologically, there are two elements in the suprarenals, nervous ganglia coming from the dorsal region of the cord and going to meet the coelomic islets. These two elements intermingle and unite intimately, the nervous part forming the medulla of the suprarenals. These chromophile cells are nervous cells that have become secretory, and their secretion is a special excitant to their group. They work for their cell-sisters. The other glands are considered from the same point of view.

If we some day find a "vagotonin" analogous to adrenalin, but exciting the terminations of the vagus or parasympathetic, it will spring from a parasympathetic nervous element originating in the cervical or cranial portion of the medullary canal. It is useless to look for it in the lymphatics or the marrow of the bones. It will be necessary to look for it in the head about the pharynx, or at the surface of the midbrain.—T. C. B.

(HYPOPHYSIS) Hypophysaire Polydipsie. Arnstein (A.), Wiener klin. Wchnschr., 1919, **32,** 928.

The author demonstrated a woman of 47 with polydipsia. Four years before a stomach cancer had been removed. Perhaps the polydipsia was due to a metastasis of the first tumor into the hypophysis. Injections of pituglandol was followed by improvement.—J. K.

(HYPOPHYSIS) Hypophysispolydipsie und—polyurie. Arnstein (A.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1176.

A woman of 47, three years after an amputation of a breast for cancer, developed diuresis of 5 liters daily. The urine had a specific gravity of 1003-1007. She drank over 5 liters of water in 24 hours. Injection of pituglandol diminished

the quantity of urine to about 2 liters. The quantity of ingested water diminished also in the same proportion.—J. K.

HYPOPHYSIS, Tumor of the—(Hypophysisgezwel). Beukers (A. C. M.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (II), 1312.

A patient had adiposity but no polyuria of acromegaly. There were also present bilateral atrophy of the optic nerve and headaches. The roentgenogram disclosed no abnormality. Other endocrine organs than the hypophysis were apparently normal. At operation a hypophyseal tumor was removed. The microscopic diagnosis was cancer. After the operation the patient saw much better, but her adiposity increased. The headaches disappeared and the psyche was much improved.—J. K.

(HYPOPHYSIS) Posterior pituitary secretion in the treatment of mitral regurgitation. Bate (R. A.), Ky. Med. J. (Bowling Green), 1919, **17**, 419-422.

Cases of "rheumatic" endocarditis may be supported to compensation by posterior pituitary extracts.—H. W.

(HYPOPHYSIS) The infundibular syndrome in a case of tumor of the third ventricle (Le syndrome infundibulaire dans un cas de tumeur du troisième ventricule). Claude (H.) and Lhermitte (J.), Presse méd. (Paris), 1917, **25**, 417.

The well-known syndrome consisting of narcoleptic attacks, of cardiovascular irregularities (tachycardia, irregularity of the pulse, extra-systoles, embryocardia and increased blood pressure) and polyuria with polydipsia are not, as it is frequently claimed, due to lesions of the hypophysis, but to lesions of the infundibulum. The authors had occasion to observe a patient in whom, at autopsy, a tumor of the third ventricle was found. Examination revealed an epithelial cystic tumor formed from the ventral wall of the third ventricle and distinctly confined to the infundibulum; the hypophysis, however, was completely normal. This patient had shown the following symptoms: Bitemporal hemianopsia, attacks of dysarthria, amnesia and delirium, attacks of narcolepsy, tachycardia, irregularity of the heart beat, extra systoles, embryocardia and increased blood pressure, polyuria and polydipsia. The first two symptoms proved to be due to pressure exerted by the tumor upon the optic region and upon the pedunculi cerebrales, respectively. The disturbances of the mental condition are not due to the lesions of any specific region of the

brain, since they are caused very frequently by all sorts of brain tumors; it may be that they are the result of circulatory disturbances caused by these tumors.

In contradiction to A. Salmon's hypothesis of a hypophyseal origin of narcoleptic attacks, the case in question demonstrates that a disturbance of the excretory function of the pituitary gland is not the cause of this phenomenon, since the hypophysis was entirely normal. The same is true for the cardio-vascular disturbances, and in this respect clinical experience fully confirms the experimental results obtained by several observers, and particularly by Aschner, which show that it is the excitation of the tuber cinereum and the infundibulum, and not of the hypophysis, which produce the phenomena in question. Finally the experimental data obtained by J. Camus and G. Roussy proving that experimental lesions of the tuber cinereum and infundibulum cause polyuria seem to be well in accordance with the clinical data observed here; polyuria accompanied by polydipsia is due to lesions of the basis of the third ventricle, but not to lesions of the hypophysis. The most important result of this clinical observation seems to be that the secretion of the pituitary gland does not play any role in the cardio-vascular phenomena in question, nor in the regulation of the metabolic processes of water excretion.

—E. U.

(HYPOPHYSIS) Pituitary treatment in gynecology. Dalché (P.), Rev. Mens. de Gynéc. et d'Obstét. (Paris), 1919, **14**, 165-182.

Dalché gives pituitary by the mouth, preferring the dry extract of the whole gland, giving from two to four cachets a day of 0.10 gm. each. This treatment can be applied in every case of metrorrhagia, and it often will give good results. But success depends on its being kept up perseveringly for weeks and months with bleeding fibromas, diffuse fibromatosis and sclerosis of the uterus, retrodisplacement with congestion, virginal metrorrhagia, intermenstrual dysmenorrhea—whenever, in short, the aim is to modify a condition of long standing. For example, a young girl with too frequent and too profuse menstruation should take the pituitary extract every day for a month, then for two weeks each month, beginning the week before the anticipated menses and continuing till the close. The other two weeks he orders 10 drops of tincture of hamamelis in a little water before the two principal meals. In case of a fibroma he alternates the two pituitary weeks with other organotherapy, and may conclude with roentgen treatment. Congestions and excessive functioning of the ovaries or

thyroid may likewise benefit by pituitary treatment, as also certain types of headache, even those suggesting false brain tumors, with exacerbations at the menstrual periods. It seems in these cases as if the endocrine upset had induced congestion in the pituitary body and that this congestion was what causes the headache. The action of pituitary treatment is not restricted to the genital organs; it may attenuate and suppress the hot flashes and sudden sweats of the menopause and other symptoms of ovarian insufficiency. It seems to promote sleep, appetite and diuresis, and combat asthenia.—J. Am. M. Ass.

(HYPOPHYSIS) A case of dystrophia adiposogenitalis in a man after trauma of the skull (Ein Fall von Dystrophia adiposo-genitalis bei einem Manne nach Schädeltrauma). Goldsteig. Berl. klin. Wchnschr., 1919, **56,** 958; Münchner med. Wchnschr., 1919, **66,** 1009.

A short note on a case. The temperature showed an inclination to rise. From time to time temperatures up to 42.3° C. (107.6 F.) were observed; the pulse stayed at 70. Probably the centre for heat regulation was disturbed.—J. K.

(HYPOPHYSIS) Conditions in "hyperhypophysized" animals. (Ueber Befunde bei hyperhypophysierten Tieren). Hofstätter (R.), Monatsschr. f. Geburtsh. u. Gynäk. (Berlin) 1919, **19,** 387.

Results from transplantation and from feeding were negative. Injections of "pituitin" were given to 70 rabbits. The doses (1 cc. each) were given every two days, until from ten to forty had been given. The results were as follows: 1, Hypertrophy of the heart, with hyperemia of all the organs; 2, Diuresis not influenced; 3, No effect on growth or on skeleton; 4, Decrease of the colloids of the thyreoid; 5, Hypertrophy of the adrenals; 6, Slight hypertrophy of the hypophysis; 7, Hastening of ovulation and spermatogenesis in young, but no such effects on full-grown animals; 8, No effect on the atrophy of the uterus after castration; 9, Development of mammary glands stimulated; 10, Sexual stimulation. The author concludes that the hypophysis aids embryonic development, "protects" the sex glands and their functions, as well as the milk glands, and inhibits the thyreoid. Hypophysis medication is indicated for general hypoplasia, amenorrhea and Graves' disease.

—E. R. H.

(HYPOPHYSIS) Epilepsy combined with endogenous adiposity [Epilepsie kombiniert mit endogener (hypophysärer?)

Fettsucht]. Ibrahim. Münchener med. Wchnschr., 1919, **66**, 1069.

A girl of twelve years suffered from epilepsy. After the first fit adiposity began. The Wassermann reaction was negative; there was no increased brain-pressure; blood-pressure was low. The skin showed abnormal pigmentation. Adrenalin injection did not produce glucosuria. After 100 grams of glucose a trace of sugar was found in the urine. The sella turcica was not enlarged, but showed the form of a rhombus. The patient was mentally deficient. The blood serum gave a positive Abderhalden reaction with hypophysis, ovary and thyroid and a negative reaction with adrenals and kidney.

—J. K.

(HYPOPHYSIS) An experimental investigation of the pharmacologic properties of the active principle of commercial pituitary extracts, and the comparative action of histamine. Jackson (D. E.) and Mills (C. A.), J. Lab. & Clin. Med. (St. Louis), 1919, **5**, 1-27.

The active principle of the posterior portion of the pituitary gland is a simple body of the sympatho-mimetic amine type which, in the dog, produces contraction of the uterus but fails to contract the bronchi. This is probably due to action of the substance on certain nervous elements and not a direct muscular action. Certain commercial preparations of pituitary gland contain small, variable proportions of histamine which might exert some therapeutic action, but it is not a necessary constituent of first-class preparations of posterior portion of the pituitary. It is probable that the action of histamine on the bronchioles of spinal dogs can be used as a commercial test for the presence of small amounts of this substance in ordinary commercial extracts. For obstetrical uses pituitary extracts have obvious clinical advantages over the broncho-constricting and blood pressure lowering histamine.—B. T. S.

HYPOPHYSIS, The relation of—to glycogenolysis. Keeton (R. W.) and Becht (F. C.), Am. J. Physiol. (Balt.), 1919, **49**, 248-253.

The authors show that stimulation of the hypophysis in dogs causes hyperglycemia independently of the ether used for anesthesia. This hyperglycemia is absent after transection of the cord at the level of the second thoracic vertebra and after section of the splanchnics, but persists after section of the nerves in the hepatic pedicle, i.e. where the nerve supply to the adrenals is not interfered with. Consequently, if a hormone

is liberated by stimulation of the hypophysis, it must have a central action. Following hypophysectomy a transitory hyperglycemia, persisting three to five hours, occurs. After this the sugar level remains normal until death. The authors favor the view that the pathway is a nervous one mediated through the splanchnic nerves to their terminations in the adrenals and liver. Also, they are of the opinion that the hypophysis does not affect glycogenolysis but is concerned with the utilization of sugar by the organism.—L. G. K.

(HYPOPHYSIS) Hypophysaire diabetes. Koopman (J.), Ned. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (II), 1071.

A short abstract of an article published in Endocrinology, **3**, 485.—J. K.

(HYPOPHYSIS-PANCREAS) Acromégalie et diabète. Labbé (M.) and Langlois (S.), Bull. Soc. Méd. des Hôp. (Paris), 1919, **43**, 229-234.

Observations are herein reported of a typical case of acromegaly, in a miner of 48, but superimposed upon this were polyuria and glycosuria. Neither polyuria nor glycosuria were in any definite way influenced by hypophysis medication, either by whole gland or by extracts of posterior lobe. On the other hand, reduction of the carbohydrate intake or fasting for three days cured the glycosuria without affecting the polyuria. Furthermore this particular patient did not lose weight nor become emaciated and had in effect a high tolerance for sugar.

The polyuria was thought to be due, following the ideas of Loeb, to irritation of the centers at the base of the brain by the enlarged hypophysis. The glycosuria was thought to be due in part to irritation to this region and in part was thought to be alimentary glycosuria in the ordinary sense.—A. L. T.

(HYPOPHYSIS) Antipituitary serum. In arteriosclerosis and diabetes mellitus. (Preliminary communication.) Laura (C. L.) N. Y. Med. J. (N. Y.), 1919, **110**, 713.

A preliminary report of the action of serum obtained from the horse following immunization with extracts of posterior and infundibular pituitary, upon blood pressure and sugar metabolism. This "antipituitary serum" was used on about 40 patients who received several intramuscular injections, in doses of from one to three cc., at intervals of from two to five days. The larger number of patients were diabetics, some were suffering from arteriosclerosis, some from various diseases and

two were normal. In all of the patients except two, and after every injection, the blood pressure was affected with small as well as large doses. Within thirty minutes following the injection, the blood pressure became reduced by 15 to 20 mm. and gradually reached a maximum depression in one or two hours and remained down for several hours. Of 30 patients suffering with diabetes mellitus treated with the serum, eight did not respond, fourteen had a complete disappearance of sugar from the urine, while the intake of carbohydrates was notably increased, and eight had a diminution of glycosuria. Polyuria commonly disappears with rapidity, even in the most unfavorable cases.—H. W.

(HYPOPHYSIS) An explanation of acromegaly (Ein Streiflicht auf die Akromegalie). Lentz (F.), Münchener med. Wchnschr., 1919, **66**, 992.

The author tried to answer the question why in acromegaly do the hands, feet, nose, ears and chin grow. He tries to find a relation with the experiments of Schultz, who experimented on Russian rabbits with white hair, except on the ears, where it is black. If a part of this white hair is removed and the animal is kept in the cold, the new hairs on this spot are black. Because of these experiments Lentz believes that hands, feet, nose, ears and chin grow in acromegaly because they are the coldest parts of the body.

(The experiments of Schultz are interesting, but the conclusion of Lentz is at least unproved, not to use another word).—J. K.

(HYPOPHYSIS) A method of tissue analysis: Applied to the lobes of cattle pituitaries. MacArthur (C. G.), J. Am. Chem. Soc., 1919, **41**, 1225-1241.

The method of separation into proteins, lipins, and extractives is based upon the method of W. Koch (J. Am. C. S. **31**, 1329). The original method has been simplified and made available for amounts of material extending from 10 gms. to as low as 2 gms. Methods are given for the determination of Ca, Mg, total N, ammonia N, urea N, amino N, creatinine, creatin, uric acid, total S, S as sulfate, neutral S, extractive S, neutral P, lipin residue N and P, cholin N, absorbed iodine, sugar, cholesterol, humin-N, in the three fractions. Complete analyses of the anterior and posterior lobes are given.

The anterior lobe has 2.4% more solids, 4% more protein, 0.9% less lipins, 0.9% less extractives than the posterior lobe. The distribution of the various elements and compounds in the

protein fraction indicates a close similarity in nature of the proteins of the two lobes. Except for the small amount of sulfatides in the hypophysis the distribution and amounts of the various lipins are similar to those of the cortical gray matter. The extractives predominate in the posterior lobe. This predominance consists mainly in the non-phosphate P, amino N, and undetermined N fractions. The two latter may be present in the pressor compound.

The chemical composition of the hypophysis resembles the gray matter of the brain or young nervous tissue in most respects. There are points of resemblance to the thyroid and spleen, quite a few to the liver, but practically none to the connective tissues, muscle, or white matter of the brain.

In those respects in which the two lobes differ the posterior is more like the gray matter than the anterior. Both lobes resemble each other more closely, than either resembles any other tissue. It cannot be stated that the pituitary is more like unmedullated nervous tissue than it is like undifferentiated pus cells. It can be assumed as an hypothesis that the partly differentiated embryological materials, after union of the two parts, develop together, resulting in a similarity of composition.—V. K. L.

(HYPOPHYSIS) The effect of feeding pars tuberalis and pars anterior proprior of bovine pituitary glands upon the early development of the white rat. Marinus (C. J.), Am. J. Physiol. (Balt.), 1919, **49**, 238-247.

A group of 53 rats was fed upon pars anterior proprior of the pituitary gland, a second group of 37 animals upon pars tuberalis, while a control group of ten received beef muscle. During the 12 weeks of feeding the rats of the first group exhibited an increased growth rate accompanied by a more rapid development of the reproductive system, evidenced by gross and microscopic hypertrophy of the organs and by the earlier birth of young. In the pars tuberalis-fed rats there was no change in the sexual development as compared with that of the control group. The growth rate was slightly slower in the second group, due perhaps to the smaller amount of meat received. The author concludes that his study does not show that any of the functions ascribed to the anterior lobe as a whole are due to the pars tuberalis.—L. G. K.

(HYPOPHYSIS). Report on the use of tethelin. Mayo (Helen M.), Med. J. Australia (Sydney), 1918, **5**, 413.

This is a report of the treatment of an electrical burn on the leg of a long-standing diabetic, with combined injections

and applications of "tethelin." The burn had been complicated by the application by the patient of carbolic solution. The tethelin was administered in 100 milligram doses divided between the two methods of procedure for ten days, when healing was practically complete. No further trouble was experienced with the leg, but the patient died four months later, insane, and in coma.—F. S. H.

(HYPOPHYSIS) The possible cause of hereditary optic atrophy. Pancoast (H. K.), Am. J. Roentgenology, 1919, **6,** 17.

Fisher has advanced the theory that this disease might be due to a transient disorder of the pituitary body with enlargement occurring at definite epochs of the sexual life. With the idea that the roentgen examination would seem to be the most certain means of proving this point, provided the enlargements were sufficient and of a necessary prolongation to produce a sellar deformity, the author presents his studies of the affected members of two families. These studies tend to lend weight to Fisher's theory of the etiology of this disease, but cannot be regarded as proof positive.—J. F.

(HYPOPHYSIS) Operation der Hypophysistumoren. Piffl. Berl. klin Wchnschr., 1919, **56,** 863; Wiener klin. Wchnschr., 1919, **32,** 870.

Only of technical surgical interest.—J. K.

(HYPOPHYSIS) Action of endo-hypophysin and infundibulin on the pregnant uterus (L'azione dell' endo-ipofisina e dell' infundibulina sull' utero gravido). Pugliese (A.) Terapia, 1916, No. 22 (Reprint, p. 16.)

The former preparation is an extract of the whole pituitary; the latter of the infundibulum with a portion of the pars intermedia. Although the non-pregnant uterus of the guinea-pig and rabbit reacts well enough when isolated in a bath of Ringer's solution it does not respond readily in situ to a hypodermic injection. For this purpose a pregnant uterus is necessary, and since the therapeutic method of administration is a hypodermic one, the author considers this method also necessary for laboratory testing. Hence he employs pregnant guinea-pigs or rabbits, removes the fetuses and allows a uterine horn to protrude through a small opening in the abdominal wall into a myograph chamber jacketed with warm water.—Physiol. Abst., **3,** 386.

HYPOPHYSIS, On an uncommon disease caused by an adenoma of the— (Über ein ungewöhnliches Krankheitsbild bei Hypophysenadenom). Reichmann (V.), Deutsches Archiv. f. klin. Med. (Leipzig), 1919, **130,** 133; Münchener med. Wchnschr., 1919, **66,** 1103.

Two cases are described with the same symptoms: red swollen face, protusion of the eyes without other symptoms of Graves' disease; no goitre, bradycardia, myasthenia, general cachexia, edema of the legs; slight glycosuria, no albuminuria, arteriosclerosis, high blood pressure (without Bright's disease), osteoporosis of the vertebral column. One patient died. The post-mortem examination showed an eosinophil adenoma of the hypophysis. The second patient showed an abnormal shadow in the place of the sella turcica on the roentgenogram. Probably the disease may be considered as a hyperfunction of hypophysis and adrenals and a hypofunction of the thyroid.

—J. K.

(HYPOPHYSIS) Hypophysäre Kachexie. Reye. Berl. klin. Wchnschr., 1919, **56,** 790.

A woman with general cachexia and oedema was treated with hypophysis with good success. Her treatment was not continued and in four months the patient became seriously ill with cachexia, oedema and a blood pressure of 80 mm. Again treatment with hypophyses gave splendid result, but, though the oedema disappeared, the patient gained enormously in weight.—J. K.

(HYPOPHYSIS) Signs and symptoms of hypopituitarism. Roberts (Stewart R.), Proc. Southern Med. Assn., J. Am. M. Assn. (Chgo.), 1919, **73,** 1795.

Undergrowth, dwarfism, dysgenitalism, feminine hirsuties, feminine type of skeleton, lack of secondary sexual characteristics, genital atrophy and impotence, headaches, languor and weakness may appear in varying degrees in different cases at different periods. The classic signs and symptoms of hypopituitarism are subnormal temperature, dry skin, adiposity, low blood pressure, slow pulse, constipation, amenorrhea, drowsiness and inactivity. Lack of attention, impairment of memory, actual dulness, and mild psychoses to actual convulsive seizures with epileptic attacks may occur. The cause may be glandular deficiency of one or both lobes, a pituitary tumor with damage

of the gland, or a neighborhood tumor or hydrocephalus with pituitary pressure. The symptoms of intracranial tumor may be more prominent than those of pituitary deficiency. Infantilism, dysgenitalism and obesity, and symptoms of intracranial tumor, warrant pituitary study.—Quoted.

(HYPOPHYSIS) A metabolism study in a case of diabetes insipidus. Rosenbloom (J.) and Price (H. T.), Am. J. Dis. Child. (Chgo.), 1916, **12**, 53-60.

The writers recognize two types of diabetes insipidus in children: (1) primary or idiopathic cases, including those in which there is no evident organic basis for the disease; (2) symptomatic, including those cases in which some organic disease is present in the brain or elsewhere. According to them, there are three theories as to the etiology of this condition, as follows: (1) that it is due to a lack of ability of the kidneys to concentrate the urine; (2) that primary polydipsia exists with normal kidney function; (3) that it is a polyuria, purely symptomatic in origin, produced by stimulation of the kidneys by many causes, but in some cases by a hypersecretion of the hypophysis. They give a brief review of the literature on the relationship between the hypophysis and diabetes insipidus.

—M. B. G.

(HYPOPHYSIS) Pituitary standardization. The relative value of infundibular extracts made from different species of animals and a comparison of their physiological activity with that of certain commercial preparations. Roth (George B.), U. S. Pub. Health, Hygienic Lab. Bull. No. 109 (Washington), 1916.

The determination of the activity of infundibular extracts made from the pituitary body obtained from various species of mammals—namely, cattle, sheep, horses, hogs, rabbits, cats, and dogs—was made by both the blood pressure and the isolated uterus methods, and it was found that the infundibular extracts made from cats or dogs were more active than similar extracts made from the other species of mammals. An individual variation was shown in extracts made from the same species of mammals. Commercial infundibular extracts examined in the same way showed a variation of 800 per cent by the blood pressure method and of 1,000 per cent by the isolated uterus method. A commercial preparation of infundibular extract which contained chlorbutanol as a preservative was shown to depress the motility of the isolated intestine of the rabbit when used in concentrated solution.

It was concluded that the activity of infundibular extracts on the isolated uterus of the virgin guinea-pig should not be taken as an index of their activity on the blood pressure. Infundibular extracts made from the pituitary bodies obtained from cattle, horses, hogs, cats, dogs, and rabbits differ quantitatively in their activity. The infundibular lobe of the pituitary body of cats, dogs, and hogs contains a greater amount of active materials than from cattle, sheep, horses, or rabbits. Commercial infundibular extracts vary widely in their physiological activity. The motor depression of the isolated intestine which is caused by certain commercial infundibular extracts is due in certain instances to the depressing effect of the preservative chlorbutanol.—Author's Summary.

HYPOPHYSIS, Development of the form of the human—. (Formentwickelung der menschlichen Hypophysis cerebri). Rudel (E.), Anat. Heft. (Weisbaden), 1918, **55,** 187.

Technical description of the hypophysis, as indicated by the title.—E. R. H.

(HYPOPHYSIS) Hypophysentumoren. Saenger. Berl. klin. Wchnschr., 1919, **56,** 789.

Demonstration of two patients in whom tumors of the hypophysis were extirpated. In the first case neither the amaurosis nor the dystrophia adiposo-genitalis were beneficially influenced, but the patient felt better. In the second case the eye symptoms became first better after the operation, but returned later on and acromegaly developed.—J. K.

HYPOPHYSIS, X-ray treatment of tumors of the—and acromegaly with temporal hemianopsia (Zur Röntgenbehandlung der Hypophysistumoren und der Akromegalie mit temporaler Hemianopsie). Schäfer (F.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 981; Berl. klin. Wchnschr., 1919, **56,** 886.

A short note. Of eight cases treated with X-rays, six were largely improved. It is most important to place the head in a way that the hypophysis is situated in the focus of the X-rays.—J. K.

HYPOPHYSIS. Operation der Hypophysistumoren. Schloffer, Berl. klin Wchnschr., 1919, **56,** 863.

Only of surgical interest.—J. K.

(HYPOPHYSIS) The action, use, and abuse of pituitrin. Schulze (A. G.), Jour.—Lancet (Minn.), 1919, **39**, 584-589.

Nothing new—H. W.

(HYPOPHYSIS) Post-mortem examination of a dwarf. (Sektionsergebnis bei einem Zwerg). Simmonds. Berl. klin. Wchnschr., 1919, **56**, 790.

The post-mortem examination showed atrophy of the testicles; the anterior lobe of the hypophysis was nearly completely destroyed by cysts. The posterior lobe was normal.
—J. K.

(HYPOPHYSIS) Case of acromegaly. Soner. Med. J. S. Africa (Johannesburg), 1918, **13**, 102-104.

A clinical presentation and discussion of a case presenting a syndrome indicative of myxoedema, but which on X-ray analysis showed undoubted acromegalic characteristics, though with some accompanying thyroid derangement.—F. S. H.

(HYPOPHYSIS) On the use of very small doses of pituitrin in inducing labor at term in combination with nitrous oxide anaesthesia to alleviate the labor pains. Stein (A.). Trans. Am. Gyn. Soc., Am. J. Obst. (N. Y.), 1919, **80**, 471.

No new data.—H. W.

(HYPOPHYSIS) Dyspituitarism, with limitation of the visual fields. Symptoms disappearing under the use of internal glandular therapy, with a return of the visual fields to normal. Timme (Walter), Arch. Opth., 1917, **46**, 151-153.

This patient came under observation after suffering six years from constant headaches and diminished vision. On examination contracted visual fields were found. A diagnosis of pituitary enlargement was made with dyspituitary symptoms. Treatment was with extracts of thyroid and pituitary and, because of the low blood pressure manifested, whole suprarenal gland was administered with excellent results.—J. H. L.

(HYPOPHYSIS) A case of pituitary tumor treated by operation. Whale (H. L.), Lancet (Lond.), 1919 (ii), 11-12.

Sellar decompression and removal of endotheliomatous tissue from the anterior lobe of the pituitary gland was followed by great improvement in the previous pressure symptoms.—L. G. K.

(INTERNAL SECRETION) Phenomena of transformation of larval tissues into reserve tissues, observed during the metamorphosis of some metabolan insects. (Phénomènes de transformation de tissus larvaires en tissus a réserves observés pendant les métamorphoses des insects metaboles. Bordage (E.), C. r. Acad. d. Sci. (Paris), 1917, **165**, 477.

Bordage observed that in insects, the developmental cycle of which includes a chrysalis stage, the larval tissues during the chrysalis stage undergo a direct (without the action of phagocytes) and complete histolysis (lyolysis of Anglas) in the course of which they are entirely dissolved. It seems that this histolysis is exactly equivalent to the histolytic processes known to take place during the metamorphosis of amphibians. (In the latter case we are fairly certain that the histolysis of the larval tissues is caused by the thyroid hormone. Bordage's suggestion that in insects a histolytic secretion may be excreted into the body fluids by some organ, seems, therefore, to have some already well established facts in favor and it would be of greatest importance to look for those organs or tissues which might excrete such substances in insects. Possibly we will find here the predecessors of the vertebrate thyroid gland.) —E. U.

INTERNAL SECRETIONS, Progress in the knowledge of— (Fortschritte in der Lehre von der inneren Sekretion). Pütter (A.), Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1008.

A general review of some well known facts of endocrinology.—J. K.

(INTERNAL SECRETIONS) Exophthalmos in leukemia. Schioetz (C.), Tidsskr. f. d. norske laegeforen., 1916, —, —.

Details are given of two cases of acute lymphatic leukemia, where exophthalmos was a prominent symptom. This is demonstrated anatomically to be due to edema of the fatty tissue in the orbits. The various toxic and endocrine causes of exophthalmos are discussed; the explanation is offered that certain toxic substances, especially aromatic amino-compounds, have an elective effect on the orbital fat.—K. M.

LIPODYSTROPHIA progressiva, A new case of—. Weber (F. P.) and Gunewardene (T. H.), Brit. J. Child. Dis. (Lond.), 1919, **16**, 89.

Weber reports another case of this rare condition. The

patient was a girl of 12½ years of age, who since the age of 7½ years, has been losing the subcutaneous fat over her face, neck, upper extremities and trunk as far down as the pelvis, being emaciated in these parts, but normal below the hips. The change occurred following attacks of measles, pertussis and pneumonia, in rapid succession. The previous case of this condition which was reported by Weber was abstracted in Endocrin. 1917, **1**, 481.—M. B. G.

MYOTONIA ATROPHICA. Slecht. Berliner klin. Wchnschr., 1919, **56**, 405.

Three typical cases. All three showed cataract, loss of hair, atrophy of skin and atrophy of the thyroid and testes.
—J. K.

OSTEOMALACIA, A case of infantile—(Ein Fall von kindlichem Osteomalazie). Blencke, Münch. med. Wchnschr., 1919, **66**, 948.

Of no direct endocrine interest.—J. K.

OSTEOMALACIA, An epidemic of— (Ueber gehauftes Auftreten von Osteomalazie). Partsch (F.), Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1130.

The same epidemic that has been observed in Vienna has been seen in Dresden. The description is of no direct endocrine interest.—J. K.

(OSTEOMALACIA) Familial starvation-osteomalacia (Familäire Hungerosteomalazie). Schlesinger (H.), Wiener klin. Wchnschr., 1919, **32**, 929.

The author demonstrated two sisters and a mother and a daughter with osteomalacia. The latter two patients had large goitres.—J. K.

(OVARY) On the origin of the corpus luteum of the sow from both granulosa and theca interna. Corner (G. W.), Am. J. Anat. (Phila.), 1919, **26**, 117.

The ovary of the sow possesses certain advantages for the solution of this problem. The paper is based upon a large series in which the stage of the reproductive cycle was determined by observation of the living animals and their ova. The results may be summarized as follows: In swine the membrana

granulosa is retained intact after the rupture of the Graafian follicle. Its cells increase in size without division, the cytoplasm becomes laden with lipoid substances, and they become the larger elements commonly called "lutein cells" in the fully formed corpus luteum. The membrana granulosa is invaded by blood capillaries from the theca interna which ramify to form an extensive vascular plexus throughout the new structure. The lipoid-laden cells of the theca interna are increased in number by mitotic division, lose many or all of their fatty inclusions, and pass into the corpus luteum to become lodged between the granulosa cells throughout the whole structure. There is no evidence that cells of the theca interna are ever converted into fibroblasts of the usual spindle-cell type or that they lay down the fibrils of the close-meshed reticulum which is present in the corpus luteum. There appears to be good evidence that some of the theca interna cells persist throughout pregnancy as distinct elements of the corpus luteum, but the exact fate of all of them cannot be learned by present methods because of the confusing resemblance between some of the theca and some of the granulosa derivatives. (Author's abstract.)

(OVARY) Uterine haemorrhages and their relation to internal secretion (Über Gebärmutterblutungen und ihre Beziehung zur inneren Sekretion). Flatau, Münch. med. Wchnschr., 1919, **66**, 1069.

Gynecologists too often forget that many uterine haemorrhages find their origin in the ovary. In these cases treatment with the curette is a failure. Treatment with corpus luteum preparations may give good success in these cases.—J. K.

(OVARY) Two cases of hypernephroma of the ovary. Gordon (A. K.), Brit. Med. J. (Lond.), 1919 (ii), 495.

Not of endocrine interest.—L. G. K.

(OVARY) Are the operative procedures done for dysmenorrhea and sterility justifiable in the light of developmental study? Holden (F. C.), Am. Jour. Obst. (N. Y.), 1919, **80**, 415-420.

Report of beneficial results following endocrine therapy in cases of sterility and dysmenorrhea.—H. W.

(OVARY) Preliminary report on the influence of alcohol and nicotine upon the ovary. Ogata (S.), J. Med. Res. (Boston), 1919, **40**, 123-127.

No apparent changes were found in the ovaries following repeated injections of ethyl alcohol into the ear vein of rabbits, though in some cases there were fewer developing Graafian follicles than in the normal, in addition to inhibition of growth of the ovary. Similar experiments with extract of cigar tobacco resulted in no apparent changes in the ovary either macroscopically or microscopically.—Chem. Abst., **13**, 2924.

(OVARY) Absence of uterus, fallopian tubes, one ovary and vagina, with one large central kidney. Parakh (F. R.), Brit. Med. J. (Lond.), 1919, (ii), 496.

The condition found during an exploratory coeliotomy is indicated in the title. The woman was perfectly healthy, except that she had never menstruated.—L. G. K.

(OVARY) Ovulation, conception and abitrary impregnation. (Ovulation, Konzeption, und willkürliche Geschlechtsbestimung). Ruge (C.), Verhand. der Gesall. f. Geburtsh. u. Gynäk zu Berlin, Ztschr. f. Geburtsh. u. Gynäk (Berlin), 1919, **81**, 256.

An extended series of clinical observations, the number of which is not recorded, has led the author to the conclusion that ovulation follows the first half of the menstrual cycle. It can begin as soon as the progressing corpus luteum, which during its growth inhibits the complete development of other follicles, begins to retrogress, and is dependent as much upon internal factors still unknown to us as upon external, among which, apparently, the sexual stimulus plays a significant part. The optimum conception time is after menstruation.—F. S. H.

(OVARY) Osteomalacia in an antelope. Schumann (E. A.), Trans. Obst. Soc. Philadelphia, Am. Jour. Obst. (N. Y.), 1919, **80**, 223.

A pregnant antelope was so weak that it could not stand. It miscarried and later regained health and at the end of six months again became pregnant. Weakness became marked and the animal finally died. An autopsy revealed cystic ovaries and a partly developed embryo in the uterus. The skull was typical of osteomalacia, the pelvis was distorted and the bones throughout were flexible. Osteomalacia appears to be common in wild animals held in captivity. The author is inclined to believe that the condition is essentially the result of improper metabolism. However, the occurrence of the symptoms of

osteomalacia with pregnancy seem to indicate that the disease is in some way associated with pathological states of the primary reproductive organs.—H. W.

OVARY, Experimental degeneration in the—of the fowl, caused by altered surroundings. [Ueber experimentelle durch veränderte äussere Bedingungen hervorgerufene Ruckbildungsvorgänge am Eierstock des Haushuhnes (Galeus domesticus)]. Stieve (H.), Arch. f. Entw. (Berlin), 1918, **44**, 530.

Actual anatomical changes (degeneration of follicles) take place in the ovary of a fowl kept in close confinement. The author concludes that this is not due to absence of sexual stimulation, though this possibility is not absolutely excluded. Too much food and too little exercise caused fatty degeneration in some cases, but in the majority of instances no other cause than psychic disturbance can be assigned.—M. M. H.

(PANCREAS) Diabetic lipoidemia. Bang (Ivar), Biochem. Ztschr., 1919, **94**, 359-391.

From an extended study of a number of cases B. concludes that there is not necessarily a relationship between carbohydrate tolerance and lipemia. Experiments also indicate that diabetic lipemia is of alimentary origin. Coma is an exception. Hyperlipemia is not of pure alimentary origin. That the diabetic organism cannot take care of the resorbed fat is probably due to the liver. Since this liver insufficiency cannot be associated with acidosis or with hyperglycemia, it stands rather alone and B. questions the significance of lipemia. Is it a good or bad prognostic symptom?—Chem. Abst., **13**, 3239.

(PANCREAS) The dietetics of diabetes and glycosuria. Brown (W. Langdon), Practitioner (London), 1919, **103**, 88-99.

The author, in addition to an interesting review of modern methods of treating diabetes calls attention to "non-diabetic glycosuria." Overaction of either the thyroid or the pituitary lowers carbohydrate tolerance, and may excite frank glycosuria. He considers the glycosuria of pregnancy (as distinct from lactosuria) probably due to its stimulating effect on the thyroid and pituitary.—H. L.

(PANCREAS DIABETES) Glycosuria in pregnancy. Cameron (M. H. V.), Can. Med. Assn. J. (Toronto), 1919, **9**, 717-722.

In 468 cases of pregnancy, five cases of glycosuria were found. In four of these the sugar was identified as glucose and in the other, as the patient died of diabetes, the sugar supposedly also was glucose. Consequently finding of sugar in the urine during pregnancy must be regarded seriously and not lightly dismissed as a probable lactosuria. Where glycosuria exists, true diabetes may be about to manifest itself or may be already in existence. Regulation of the diet keeps the symptom in abeyance. A careful selection of anesthetic and any means possible to lessen the shock of delivery helps to prevent the onset of such changes in the endocrine system, already strained beyond the normal, as indicated by the glycosuria and which might result in diabetes. Should the glycosuria be controllable by diet regulation, frequent examination of the urine may be sufficient to protect the patient during gestation. This does not, however, decide whether her diabetes is under control because of the possibility of foetal hormones, functioning in the maternal economy, nor does it differentiate a glycosuria due to hyperalimentation or secretion of inverted lactose. The only means of arriving at definite conclusions is by estimation of the sugar in the blood.—L. G. K.

(PANCREAS) Diabetes, The fasting treatment of—. Cammidge (P. J.), Brit. Med. J. (Lond.), 1916, (ii), 160-161, 243.

Contains a table showing the carbohydrate content of various foods to be used in the fasting treatment of diabetes. Excellent results from this method are reported.—L. G. K.

(PANCREAS DIABETES) Glycosuria in elderly persons. Cammidge (P. J.), Brit. Med. J. (Lond.), 1919, (i), 112-113.

Cammidge criticizes the view of Rankin (see abstract in this number), that a moderate amount of sugar in the urine of elderly persons need not cause alarm. In the author's experience there are two types of such persons, and the difference depends largely upon the sugar content of the blood. Even a moderate excretion of sugar associated with hyperglycemia leads in the course of time to complications, whether the patient be young or old, whereas glycosuria unattended by an excess of sugar in the blood is not likely to give rise to trouble or shorten life, especially if, as often happens in elderly persons, the reducing substance in the urine is not really a sugar but the ketonic acid previously described by the author under the name of "pseudo-laevulose."

The success of the Allen treatment of diabetes in elderly persons depends upon individualization of the treatment and

education of the patient, so that he may follow his diet intelligently. Such persons do not stand starvation well, but as a rule, actual fasting is not necessary to secure a normal blood sugar and a sugar-free urine if a carefully arranged system of dieting is followed.—L. G. K.

(PANCREAS) Dehydration of blood and organs in diabetic coma. (La déshydratation du sang et des organes dans le coma diabétique). Chauffard (A.), Le Conte, Darie. Presse Méd. (Paris), 1917, **25**, 185.

A careful study was made of two instances of diabetes mellitus in which there was found definite evidence of dehydration in various tissues. The blood was characterized by a polycythemia and increase in density. In other tissues an increase in density or decreased water content of kidneys, liver and pancreas was found. The most marked changes in tissue density were in the pancreas.—A. L. T.

(PANCREAS) Disappearance of glycosuria in diabetics during intercurrent infectious diseases. (De la disparition de la glycosuria chez les diabetiques ou cours des malades infectieuses intercurrents.) Cottin (E.) and Saloz (M. C.), Arch. d. mal. de l'appar. digest (Paris), 1916-1918, **9**, 371-383.

The authors report that in four diabetics with glycosuria the occurrence of an intercurrent infection with fever was accompanied by a cessation of the urinary sugar excretion. This they consider may be due to an abnormal destruction of protein; an alteration in the glyco-regulating mechanism by virtue of the septic process; an activation of combustion by the increased temperature; or, as seems more plausible, consumption of the glucose by the infectious agent.—F. S. H.

(PANCREAS) Diabetes mellitus of four years standing followed by pulmonary tuberculosis with apparent cure of both as told by patient. Cram (E. A.), Ky. Med. J. (Bowling Green), 1919, **17**, 408-409.

Content indicated by caption.—H. W.

(PANCREAS) Diabetes mellitus. Densten (J. C.), N. Y. Med. J. (N. Y.), 1919, **110**, 613-615.

There is little or no interference within the animal economy of a diabetic with the ingestion and metabolism of animal nitrogenous foods and some vegetable proteins. The major

metabolic fault lies in the noncleavage of sugar into alcohol or its radicles. Hence, alcohol is indicated in amounts sufficient fully to account to the system the lack of nourishment which the sugar should furnish if split further by a normally constituted system. The withdrawal of carbohydrates from a diabetic of any age is not advisable. Starvation only causes the body to utilize its own fat. Moreover, such procedures only tend to result in inanition. Diabetes should not be considered a disease per se, but rather a symptom of some existing constitutional organic abnormality or disease. It may be a sequel of syphilis, or it may be traced to some viscus as the pancreas, liver, spleen, appendix, etc., or to a deranged function of the pituitary body. Hence, the etiology of diabetes should be sought and treated.—H. W.

(PANCREAS) Diabetes mellitus. Edgar (T. W.), N. Y. Med. J. (N. Y.), 1919, **110**, 612-613.

Starvation of diabetics is not applicable in all cases and should not be used empirically. Emaciation and lowered bodily resistance contraindicate starvation. The emaciated or cachetic diabetic who has resorted time and again to starvation with ever decreasing tolerance does better if carried along on his last assimilation limit for a short time. The intermittent starvation of animals first results in an increased ability to assimilate sugar, but is later followed by a decrease as time advances, that is, after body weight has been sacrificed, hence a decreased resistance has a direct bearing on the carbolytic action of the sugar enzyme or enzymes. The diabetic patient, although rendered aglycosuric by starvation, will require a longer period of time to attain his previous point of tolerance than if granted a short reprisal and allowed to continue his last diet in spite of the urine showing sugar.

Specific serum therapy (Edgar serum) is highly recommended in the treatment of diabetic cases. No discussion appears relative to this serum.—H. W.

(PANCREAS) Edgar serum treatment of diabetes mellitus. Edgar (T. W.), West. Med. Times (Denver), 1919, **39**, 172-174.

Treated elsewhere.—H. W.

PANCREAS, Relation of the—to the diabetic state. Ervin (D. M.), J. Lab. & Clin. Med. (St. Louis), 1919, **4**, 711.

The pancreatic diabetic state is characterized by several pathological changes—absence of glycogen, hyperglycemia,

fatty changes, acetone bodies and glucose in the urine and a lower respiratory quotient. Experiments were performed to test the glucose consumption in the diabetic animal. The latter was produced by the removal of the pancreas. The results showed that, while after depancreatization, the blood sugar increased in amount, the actual oxidation by the tissues is practically the same as before the operation. The hyperglycemia is readily explained by assuming a glycogenetic function for the pancreas through an internal secretion of the islands of Langerhans.

The internal secretion contains an enzyme which resembles that of the external secretion. It is assumed that the enzyme acts by stimulating a reversible chemical reaction. The external secretion reduces the starch in the intestine to glucose while the internal secretion poured into the portal circulation reverses the action upon the absorbed glucose, synthesizing it into glycogen which is stored by the liver. By clamping the pancreatic vein and injecting glucose solution in the small intestine, a marked hyperglycemia was produced. A controlling experiment did not show this rise. The same results occurred with the removal of the pancreas.—B. T. S.

(PANCREAS) Diabetes with pancreatic insufficiency. Treatment by glandular extracts; selective therapeusis of the external secretory function of the pancreas (Diabète avec insuffisance pancréatique. Traitment opothérapique; disjonction thérapeutique des secretions externe du pancréas). Faroy (G.), Bull. Soc. méd. des Hôp. (Paris), 1917, **41**, 235.

A case of diabetes is described running a typical course until there appeared, in addition to endocrine deficiency, a deficiency of the external secretion of the pancreas. The exocrine dysfunction of the pancreas was alleviated by the administration of pancreatic extract. The true diabetes, however, was not in the least affected by this therapy. The case is illustrative of the independence of the endocrine functions of the pancreas, and of the fact that the exocrine function may be replaced, or secretion stimulated by exhibition of pancreatic extracts without any diminution of the glycosuria, polyuria and other signs of true diabetes mellitus.—A. L. T.

(PANCREAS) Notes on the starvation treatment of a young diabetic. Fenwick (P. C. C.) Lancet (Lond.), 1919 (i), 299.

Record of a case of diabetes in a boy of 16 who recovered under the starvation treatment.—L. G. K.

(PANCREAS DIABETES) Hyperglycaemia and glycosuria. Hamburger (H. J.), Brit. Med. J. (Lond.), 1919 (i), 267-271.

This paper is a summary of a number of articles appearing in other journals, and is indirectly of interest to endocrinologists. The research was primarily undertaken to determine whether it is necessary to assume the existence of a combined sugar of colloidal form in the blood in order to explain the complete impermeability of the normal kidney to glucose. By means of perfusion experiments with frogs in which the renal portal system was tied off so that only the glomeruli could function, it was found that the glomerular membrane has the power of retaining free glucose. This power is governed by the influence of the chemical composition of the perfusion fluid upon the glomerular epithelium. When Ringer's solution of the usual composition containing 1% glucose is used then 0.3% is excreted and 0.7% is retained. In the perfusion liquid the quantities of potassium and calcium can be altered with respect to each other in such a way that the retentive power need not be changed, and the potassium can be replaced by radium or uranium, the amount required being proportional to their radioactivity rather than to their atomic weights. However, when the concentration of the sodium bicarbonate in the Ringer's solution is raised from 0.2% to 0.285%, the quantity which is present in frog's serum, all the glucose in the perfusion fluid is retained, the artificial urine being sugar-free. It is, therefore, unnecessary to postulate a combined sugar in the blood.

However, when the amount of glucose in the perfusing fluid is increased some of the sugar is not retained, and the greater the degree of hyperglycæmia produced the stronger the permeability becomes. Once the kidney has become permeable, it cannot again be rendered impermeable by reducing the amount of sugar, at least not during the several hours taken by the experiment.

The retention of glucose is not due to the size of the molecule since sucrose, maltose, lactose and raffinose are not retained. It is probably due to the configuration of the molecule since the isomeric fructose, the stereo-isomeric mannose and galactose and even the lævo-rotatory glucose pass through the glomerular membrane. If a mixture of glucose and another sugar is present the glucose only is retained.

The following provisional hypothesis is submitted. As long as the concentration of sodium bicarbonate in the blood plasma is normal, even a moderate hyperglycæmia will cause no glycosuria. If, however, the sodium bicarbonate concentration is diminished, the glomerular epithelium becomes sen-

sitive to the proportions of calcium and potassium in the blood plasma. A deficiency in the potassium must be met artificially, but the excretion of sugar can be prevented also to a large extent by increasing the concentration of $NaHCO_3$.—L. G. K.

(PANCREAS). Notes on two cases of diabetes melltius. Horsburgh (P.) and Nicol (W. D.), St. Barth. Hosp. J. (Lond.), 1917-18, **25,** 43-45.

A detailed clinical report of two cases of diabetes mellitus, the first of whom, a young boy, responded favorably at first to the hunger and vegetable diet, but failed a fortnight later and improved on having 25 gms. of carbohydrate added to the diet. The second case had 40 grams added suddenly to the diet and showed a tolerance for the same.—F. S. H.

(PANCREAS) Diabetes, The fasting treatment of—. Hume (John), Brit. Med. J. (Lond.), 1916 (ii), 160.

See previous abstract.—L. G. K.

(PANCREAS) Pancreatic diabetes. (Le diabete pancreatique). Labbé (M.), Ann. de Med. (Paris), 1919, **6,** 204-217.

After giving an historical resume of the evolution of the ideas concerning pancreatic diabetes, Labbé presents six cases with the clinical picture of a double syndrome: insufficiency of of the glyco-regulating mechanism through the abolition of the internal secretion of the pancreas, and digestive insufficiency through suppression of the external secretion. The glycoregulative mechanism presents various degrees of disturbance ranging from a small and passing glycosuria to a complete and continuous glycosuria accompanied by hyperglycemia, polydypsia, polyuria and other symptoms. In the most typical cases there frequently occurs protein denutrition and acidosis. The author considers that the moderate cases without a negative nitrogen balance can be regulated by dietary regime. The digestive syndrome is characterized chiefly by the type of stools voided; these are abundant, fatty, soft and have a butyric odor. Opotherapy with pancreatic products has proven beneficial in Labbé's hands in some cases of the digestive type, but not in all.—F. S. H.

(PANCREAS) Gas metabolism in diabetes (Gaswechsel beim Diabetes.) Löffler. Ztschr. f. klin. Med. (Berlin), 1919, **87,** 309.

In not too serious cases of diabetes the effect of the administration of a dose of casein on the respiratory quotient is

just the same as in normal individuals. If in these cases a dose of glucose is given, about as high as the tolerance for carbohydrates, no influence on the respiratory quotient is observed. A second dose of glucose raises the excretion of CO_2, but less than would be expected, theoretically. Probably the first dose of glucose fills the glycogen depots. The author concludes that in diabetes there are only quantitative changes in carbohydrate metabolism.—J. K.

(PANCREAS) The cause of the increased heat production following pancreatectomy in the dog. Murlin (J. R.), Am. J. Physiol. (Balt.), 1917, **42**, 584-585.

In three experiments on dogs the heat production was determined before and after pancreatectomy; and immediately following each respiration blood was drawn and examined for blood fat. In one case, also, the CO_2 carrying power of the whole blood was determined by the Haldane method. Thus it was possible to compare the heat production with the intensity of the protein metabolism (N output in urine), with the concentration of blood fat and with the actual acidosis.

Two dogs were fed before and after pancreatectomy and on the second day the heat production rose 31 and 42 per cent respectively. In a third dog which fasted throughout it rose only 7 per cent, and the increased protein metabolism alone was sufficient to account for the heat production, but not in the dogs that were fed.

In none of these cases did the maximum heat production coincide with the maximum concentration of blood fat, while normally after an injection or meal of fat the increased heat production runs parallel to the blood fat concentration. Since the CO_2 carrying capacity of the blood rose after pancreatectomy in the one case studied, acidosis was not considered to be the cause. Nor could any combination of the protein and fat factors be made to account for it in the two fed animals.

—L. G. K.

(PANCREAS) Blood sugar in diabetes (Blutzuckeruntersuchungen bei Diabetes Mellitus). Roth (N.), Berl. klin. Wchnschr., 1918, **55**, 589-592.

The blood sugar rises after meals in the early stages of diabetes, but in later stages falls; it is thus no parallel to the glycosuria.—Chem. Abst., **13**, 2399.

(PANCREAS) The control of acidosis in the treatment of diabetes. Stillman (E.), Arch. Int. Med. (Chgo.), 1919, **24**, 445-457.

A description of the methods employed at the hospital of the Rockefeller Institute in the detection and prevention of acidosis in diabetic patients. Typical cases are discussed.
—H. W.

(PANCREAS) Diabetes mellitus, The etiology of—and the diet and condition of life during the war. Williamson (R. T.), Brit. Med. J. (Lond.), 1918 (i), 139-141.

The histories of 300 cases of diabetes show the following as predisposing causes: (1) prolonged great excess of sugar, sweet food or sweet drinks (alone or combined with other predisposing causes) in 31 per cent; (2) prolonged and intense mental anxiety, worry, overstrain or sudden mental shock (alone or combined with other predisposing causes) in 40 per cent; (3) family history of diabetes (alone or combined) in 25 per cent. No definite predisposing factor was discovered in 19 per cent. In the author's opinion war time food restrictions should lessen the number of cases caused by an excessively sweet diet, while worry and shock would become greater predisposing factors.—L. G. K.

(PARATHYROIDS) Chondrodystrophie. Dietrich, Münch. med. Wchnschr., 1919, **66**, 945.

The author found at the post-mortem examination of a chondrodystrophic dwarf of 35 years a hypoplasia of the parathyroids.—J. K.

PARATHYROIDS, Tetany and the functions of the—. Paton (D. N.) and Findlay (L.), Brit. Med. J. (Lond.), 1917, (i), 575-577.

Data published elsewhere. See Endocrin., 1917, **1**, 476-480.
—L. G. K.

(PARATHYROIDS) On glandulae parathyroidea. Vermulen (H. A.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (II), 1448.

An anatomical description of the parathyroid in different animals. See also Endocrinology, **1**, 333.—J. K.

PITUITRIN in labor. Agnew (A. P.), Brit. Med. J. (Lond.), 1916 (ii), 871.

Advocates the use of pituitrin to hasten the late first stage of labor. The pains are more severe but of shorter duration following its use.—L. G. K.

(PITUITRIN) Sieben Jahre, etc. Hofbauer, Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1918, 325.

Correction Endocrin. **3**, 402: For "Holfauer" read "Hofbauer."

(PINEAL) On the pineal region in human embryos. Warren (J.), Anat. Rec. (Phila.), 1917, **11**, 428. (Abstract).

A description of the primary arches in the roof of the forebrain of human embryos of 10 mm. and 15 mm., the paraphysis in embryos of 15 mm. to 44 mm. and the post-velar arch in embryos of 23 mm. to 44 mm. Full paper published later. See Endocrinol. 1918, **2**, 67.—E. R. H.

POLYGLANDULAR disease, Case of —. Climenko (H.), J. Nerv. & Ment. Dis. (N. Y.), 1918, **47**, 276.

Report of a case showing menstrual disorder, rapid gain of weight followed by loss, polyuria, weakness and mental derangement in which treatment had produced no change.

—A. R. T.

(REPRODUCTION) Yellow pigmentation and fecundity. Palmer (L. S.) and Kempter (H. L.), J. Biol. Chem. (N. Y.), 1919, **39**, 313-331.

The authors have shown in a preceding paper that the natural yellow pigment of fowls is derived from the xanthophyll of the food and that it bears no important relation to growth or to the functions of fecundity and reproduction, at least for one generation. The fading of the yellow pigment from the ear lobes, beak, shanks, etc., of hens during fecundity is due to the fact that fecundity deflects the normal path of excretion of the xanthophyll from these parts of the skin to the egg yolk. This fading as the result of egg production is an index of continued fecundity only, and not of heavy laying.

—V. K. L.

SCLERODERMA in infants (Sklerodermie im Saüglingsalter). Kraus (A.), Wiener. klin. Wchnschr., 1919, **32**, 830.

Of no direct endocrine interest.—J. K.

(SECRETIN) Chemical stimulation of the glands of the mucous membrane of the stomach. I. The influence of organ extracts upon the excretion of the gastric juice. (Über die chemischen Erreger der Magendrüsen. 1. Der Einfluss von Organextrak-

ten auf die Sekretion des Magensaftes.) Tomaszewski (Z.), Arch. f. d. ges Physiol. (Bonn), 1918, **170,** 260.

The experiments reported in this paper do not support Edkin's hypothesis of the existence of a specific substance (gastric secretin) contained in the mucosa of the pylorus and causing gastric secretion. Intravenous injection of pylorus extract, like that of other organ extracts, does not produce gastric secretion; subcutaneous injections of extracts of the mucosa of the pylorus and fundus, of the muscularis of the stomach, of the pancreas and of the small and large intestine all cause outpouring of large amounts of gastric juice. This proves that the substance in question is not only contained in the mucosa of the pylorus but in many other organs also. Since only subcutaneous injection of these extracts is effective, it is likely that the effective substance is produced by chemical reactions occurring in the subcutaneous tissue. Attempts to isolate the effective principle were not successful, but revealed a number of its characteristics.—E. U.

SEX, The control of—. Bey (L.), Urol. and Cutan. Rev. (St. Louis), 1918, **22,** 642.

A purely theoretical discussion adding but another theory to the long list of sex-control or determination theories. Not of endocrine importance.—A. R. T.

(SEX?) Uroleptus mobilis Engelm. II. Renewal of vitality through conjugation. Calkins (G. M.), J. Exp. Zool. (Phila.), 1919, **29,** 121.

Experiments proving that conjugation in protozoa rejuvenates. The usual isolation culture method was employed; a standard food medium was used throughout, and all series were kept under the same conditions. A single ex-conjugant of Uroleptus mobilis, kept from conjugating and from endomixis, goes through approximately 300 generations by divisions, the division rate steadily declining until the protoplasm dies from old age in from seven to nine months. Closely related individuals from such a series will conjugate. Such ex-conjugants invariably give an optimum division rate regardless of the vitality of the parent race at the times of conjugation. The first sixty-day period of all ex-conjugants shows a uniform vitality measured by approximately 17.4 divisions in ten days. If vitality of the parent series is high (e.g. 15 divisions in 10 days) the increase of vitality in the filial series is low (2.4). If vitality of the parent series is low (e.g. 0.2 division in 10 days) the increase of vitality is high

(e.g. J series ex-conjugant from A311 showed an increase in vitality 17.6 divisions in 10 days). Fourteen such series were studied, the conjugations giving rise to them occurring in all phases of vitality of parent series. In all cases the results were the same—high initial vitality, declining division rate, and ultimate death. A sexual reorganization (parthenogenesis or "endomixis") occurs during encystment. Individuals recovered from cysts have the same high rate of division and length of life as individuals after conjugation. Parthenogenesis, therefore, as well as conjugation, rejuvenates. (Author's abstract.)

SEX, Studies on—in the hermaphrodite mollusc Crepidula plana. III. Transference of the male producing stimulus through sea water. Gould (H. M.), J. Exp. Zool. (Phila.), 1919, **29**, 113.

The gastropod mollusc, Crepidula plana, passes through a male phase, a transitional phase and a female phase during its life. The male phase is unstable and occurs only as the result of a stimulus furnished by an individual of the same species larger than the one stimulated. Complete isolation of small sexually undeveloped specimens over long periods shows that no development of male characters takes place under such conditions further than the formation of a few spermatogonia. In time female characters appear. Small sexually undeveloped individuals confined at fixed distances of from 4 to 7 mm. from large females where contact is prevented will in the majority of cases develop male characters of various degrees of maturity. Fewer and less well-developed males are produced under such conditions than when the small animals are nearer the source of stimulus. Large individuals of Crepidula fornicata, a species related to Crepidula plana, have not been found to induce male development in small Crepidula plana except in a few doubtful cases. The stimulus to male development acts in such a manner as to indicate that it is a substance given off from the bodies of the large Crepidula plana diffusible through sea water, but very unstable. (Author's abstract.)

(SEX) Studies on inbreeding. IV. A further study of the effects of inbreeding on the growth and variability of the body weight of the albino rat. King (H. D.), J. Exp. Zool. (Phila.), 1919, **29**, 71.

The data given show that the growth and variability of the body weights of over 600 albino rats along in the sixteenth to the twenty-fifth generations of the strain inbred brother and

sister from the same litter only. The chief points of interest are as follows: 1. Continued inbreeding does not produce any deterioration in the original albino stock as regards rate and extent of growth and body weight, and neither has it altered the form of the growth graphs for the two sexes. 2. Normal body weight relations of the sexes have not been changed by twenty-five generations of inbreeding. 3. The variability of the body weights of these animals is relatively high at all age periods, and did not decrease as inbreeding advanced. 4. A comparison of the variability of the body weights in different series of stock albinos with that for inbred rats indicates that the increased variability in the inbred animals was due to an environmental and nutritive action, not to inbreeding. (Author's abstract.)

(SYMPATHETIC N. S.) The irritable heart in general practice. A comparison between it and the irritable heart of soldiers. Neuhof (S.), Arch. Int. Med. (Chgo.), 1919, **24,** 51-64.

The irritable heart as observed in general practice is similar to that found in soldiers save for the fact that vasomotor symptoms are more pronounced in the former. The etiological factors are similar, but because of severe training and war conditions, dormant and latent neuroses are more readily evoked in the soldier. Hence, the cardiac syndrome is more violent and lasts longer. Infection is a factor only in so far as it induces and produces nerve or muscular fatigue and psychasthenia. No pathologic changes occur in the cardiovascular system. The fundamental cause of the cardiac neurosis with its various manifestations, appears to be due to hyperexcitation of the sympathetic nervous system. Such cases are best treated with mixed bromides and suprarenal gland extracts. The latter seems to stabilize and decrease vasomotor instability by its action on the vasomotor centers, thus counteracting the cause of many of the symptoms.—H. W.

TESTES, A study of the seasonal changes in avian—. Watson (Alex.), J. Physiol. (Lond.), 1919, **53,** 86.

Histological. The interstitial cells show their most marked development in the non-oestrus period, and decrease in number as spermatogenesis advances.—T. C. B.

TESTES, A case of—in a "girl." Cooke (G.), and Smuts (Ph. A.), West London M. J., 1918, **23,** 21-24.

A description with pictures of an individual presenting the normal secondary sexual characteristics of the female, as well as a clitoris and partial vaginal chamber, but devoid of uterus. She possessed two oval bodies in the inguinal region which, on removal by surgical interference, were found to be immature testes.—F. S. H.

(TESTIS) Detection of protective enzymes in very small quantities of serum—micro-Abderhalden reaction. Pregl (Fritz) and de Crinis (Max), Fermentforschung, 1917, **2**, 58-73.

The authors describe a technique whereby Abderhalden reactions can be determined with 2-3 cc. of serum. They investigated among other things the effect of serum from cases of dementia precox upon dried testicular material. The reaction was positive. Numerous other data on technique, etc., included in the article will be of interest to those undertaking studies of the Abderhalden reaction. (Further details in Chem. Abst., **13**, 3230.)—R. G. H.

(TESTES) The form of the tubules in the embryonal testicle of the mouse (Over den vorom van de zaadkanaaltjes in den embryonalen testikel van de muis). de Ruiter (H. T.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (II), 1503.

Of no endocrine interest.—J. K.

(TESTES) Muskelatrophie. Schmidt. Berl. klin. Wchnschr., 1919, **56**, 667.

A case of dystrophia musculosum of the masseter and the temporal muscle and of myotonia (so-called atrophic myotonia), with formation of cataract and atrophy of the testicle. —J. K.

(TETANY) Endemic rickets in adults (Endemisches Auftreten von Spätrachitis). Bittorf (A.), Berliner klin. Wchnschr., 1919, **56**, 652.

In Breslau many cases of rachitis were observed in men of 15-18 years. In all cases symptoms of tetany were seen. In one case there was a goitre with slight symptoms of Graves' disease. Treatment consists in rest, good and abundant feeding and calcium preparations.—J. K.

(TETANY) Endemic disease of the bones (Endemisch auftretende Erkrankungen des Knochensystems). Fromme. Berl. klin Wchnschr., 1919, **56**, 667.

In Göttingen many cases of a rickets-like disease were observed in male individuals of 11-18 years. The bones contained less calcium than normal. In many cases symptoms of latent tetany were observed. The cause is probably an abnormal function of the endocrine organs, caused by poor nutrition.
—J. K.

(TETANY) Ueber sensible und sensorische Tetanie. Curschmann (H.), Münch. med. Wchnschr., 1919, **66,** 983.

The author describes two new symptoms of tetany. One patient had attacks in which "she felt her own body," an abnormal sense perception. Another patient had attacks of spasms in the tongue. During these attacks her taste and her smell were changed: bitter substances tasted sour, etc.—J. K.

(TETANY) Hemi-tetany and lesions of the cerebrum (Hemitetanie bei Grosshirnlaesion). Spiegel (E.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 928.

After removal of a goiter paralysis of the left side was observed, with tetany in the paralyzed muscles. The author thinks that during the operation an embolus caused a disturbance in the function of the right side of the brain.

Perhaps during the operation the parathyroids were partly removed; this would not be enough to cause tetany in a normal muscle, but the lesion of the brain had increased the irritability of the muscles of the left side. Therefore one-sided tetany was seen.—J. K.

(THYMUS) A review of the recent literature bearing on the function of the thymus gland. Blatz (W. E.), J. Lab. and Clin. Med. (St. Louis), 1919, **5,** 50-54.

The content is sufficiently indicated in the caption.
—B. T. S.

(THYMUS, PARATHYROID) Fragile skeleton and blue sclerae (Het. broze skelet en de blauwe sklerae). Bolten (G. C.), Medisch Weekblad (Amsterdam), 1919, **26,** 289, 301.

This disease is due, according to Bolten, to insufficiency of the thymus and the parathyroids and a beginning hyptonia of the sympathic system. The X-rays show that the bones are poor in calcium. It was reported by Klose, Vogt and Erdheim that thymectomy or parathyroidectomy are followed by fragility of the bones. In experiments on animals after thymectomy symp-

toms of tetany have been reported. Bolten saw in all his cases symptoms of latent tetany. (Recent detailed experiments in Japan and in the United States show that thymectomy causes none of the effects postulated.—Ed.)—J. K.

THYMUS, A recent thesis upon the biology of the— (A propos d'une thèse récente sur la biologie du thymus). Dustin (A. P.), Arch. Zool. Exper. et Gen. Notes et Revue (Paris), 1916, **55**, 95-109.

The author reviews briefly a recent article by Salkind on the thymus of mammals, birds, reptiles and amphibians. The author regards the small thymic cells as epithelial in origin. He states that in amphibian larvae on a thymus diet (rich in nucleins) the epithelial pouches of the pharynx that give origin to the thymus become very large, forming large thymus glands which contain a relatively large number of small thymic cells, but not of the other cellular elements, and the reverse is true in starving larvae. Thymus feeding also causes an increase in the number of small thymic cells, and thyroid feeding a destruction of the small thymic cells of adult frogs.

Dustin states that the small thymic cells are the only fundamental, constant, specific elements in the organ, and that all other elements are inconstant and variable, are produced by metaplasia, and are simply episodes in the degeneration of the thymus. It is concluded that the thymus is not a true gland, but is rather the center of nuclein metabolism acting as a reserve for nucleins which are liberated by hormones from other organs such as the liver and pancreas. (The author's conclusion finds some support in the rapid loss of thymic substance in inanition and wasting diseases.)—E. R. H.

(THYMUS) A few words on the human thymus gland (Quelques mots a propos du thymus humain). Dustin (A. P.), Ann. et Bull. Soc. Royale Sci. Med. et. Nat. (Bruxelles), 1919, —, 30.

Sections through the thymus glands of individuals who succumbed suddenly to accidents demonstrated that the thymus remains functionally active to a relatively high age. In individuals of 40 years the thymus is still rich in small lymphocytes and consequently in chromatin. In persons who died from diseases of longer duration, typical thymus involution was observed, similar to that in fasting vertebrates. The thymus reacts in a most sensitive way to nutritive disturbances. Dustin also calls attention to the work of Delezenne who recently found that the thymus is among the organs very rich in zinc,

this being closely associated with the nucleolytic ferments. D. thinks that this is another fact supporting his theory, according to which, the thymus plays a very important role in regulating the nuclein metabolism of the body.—E. U.

THYMUS and THYROID (Thymus et corps thyroide). Dustin (A. P.) and Zunz (E.), Bull. Soc. R. Sc. Méd. et Nat. Bruxelles, 1919, —, 27-28 (Mch. 3)

The thymus is rarely atrophic in men of 19 to 34 years of age who have succumbed rapidly to war wounds. Large thymuses were found associated with small thyroids and vice versa, which fact seems to indicate that there is a balance between the two organs.—Physiol. Abst., **4,** 339.

(THYMUS) Infantile eczema and status lymphaticus. Lindsay (L. M.), Can. Med. Assn. J. (Toronto), 1917, **7,** 135-136.

A case of sudden death in a child suffering from infantile eczema is recorded. At autopsy an abnormally large thymus gland was found. The diagnosis of status lymphaticus was made. The case is presented because of the existence of a difference of opinion as to the cause of sudden death in infants with eczema.—L. G. K.

(THYMUS) Malignant neoplasms of the thymus gland. Strauss (S. G.), N. Y. Med. J. (N. Y.), 1919, **110,** 646-648.

The thymus is an endodermal epithelial structure remnants of which surely persist to forty, probably longer. Malignant neoplasms arising from the gland may be divided into sarcomata and carcinomata, and a diagnosis of such may be made in spite of the absence of Hassal corpuscles in the growth. Sarcoma is more common than carcinoma in the young, carcinoma more frequent in the aged.—H. W.

(THYMUS, THYROID) Operation upon the thymus in Graves' disease (Thymusoperation bei Basedow). Melchior, Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1061.

When, during operation for Graves' disease, the thymus is removed, exacerbations may just as well be observed as in cases where the thymus is left in its place. Removal of the thymus has sometimes a fatal influence on the symptoms of Graves' disease.—J. K.

(THYMUS) Studies on the reputed endocrin function of the thymus gland (Albino rat). Takenouchi (M.), J. Exp. Zool. (Phila.), 1919, **29,** 311.

The serum obtained from rabbits immunized with the thymus substance of the albino rat shows a positive precipitin reaction with thymus extract, but this is not strictly specific. The anti-thymus rabbit serum does not show any positive hemolytic action against rat corpuscles when guinea-pig normal complement or rat normal serum is used as complement. The anti-thymus sera injected into rats do not cause symptoms of "primary antiphylaxis," neither are the rats affected in their growth. No modifications of the viscera were observed. Nearly the same results were observed with anti-testis serum from rabbits injected with rat-testis emulsion. Hemolysin production in rabbits by injection of washed rat blood corpuscles was attempted, but the normal rat serum with its complement cannot activate the hemolysin against the rat corpuscle, owing to the presence of some inhibiting substance. The chicken is not suitable for the production of the hemolysin acting on the rat corpuscles. Our attempt to produce strong anti-thymus serum from the rabbit by the injection of rat thymus failed probably because of anti-body production in the rabbit and because the thymus cells of the rat are protected. We cannot yet admit that any endocrin function of the thymus gland has been established. (Author's abstract.)

Persistent THYMUS in exopthalmic goitre. Tebbutt (A. H.), Med. J. Australia (Sydney), 1918, **5**, 430-431.

A report of a case of exitus after removal of the right lobe of the thyroid gland and the finding at autopsy of a persistent thymus. This, however, is not considered to be the cause of death through pressure and cardiac inhibition since the terminal phases did not present a picture leading to such conclusion.—F. S. H.

(THYMUS?) Clinical notes of a case of myasthenia gravis. Thomson (J.), Brit. J. Child. Dis. (Lond.), 1919, **16**, 92.

The author gives a good clinical report of this rare condition in children in a girl of 11½ years of age. The child died five and a half months after he had seen her. He does not make any mention of any treatment employed.—M. B. G.

(THYMUS) Sudden death by acute dilatation of the heart consecutive to excessive strain of a man with an enlarged thymus (Mort subite par dilatation aigue du coeur consécutive au surmenage chez un homme porteur d'un gros thymus). Tricoire (R.), Bull. Soc. Méd. des Hôp. (Paris), 1919, **43**, 98-100.

A description of a case of sudden death of a young man with an enlarged thymus. Autopsy revealed a greatly dilated heart, and hypertrophied thymus. There were no other lesions.

The author suggests that "hyperthymisation" appears to lead to hypotonicity of the heart muscle whereby conditions of stress acting as secondary causes overwhelm the weakened heart leading to death by acute dilatation.—A. L. T.

THYROID and HEAT REGULATION (Schilddrüse und Wärmeregulation). Adler, Berl. klin. Wchnschr., 1919, **56,** 958; Münchner Med. Wchnschr., 1919, **66,** 1039.

When in warm-blooded animals the temperature rises one or two degrees, the excretion of carbonic acid is increased approximately 80-100 per cent; in frogs this is not seen. The author tried to explain this difference. He found that frogs from the Alps have a strongly developed thyroid. If these animals are kept at a high temperature, the thyroid becomes atrophic. Probably in frogs the thyroid has a regulatory function. In mammals the same function may be observed. In bats during hibernation, the colloid in the thyroid disappears and the whole gland shows a largely diminished function. If thyroid extract is injected in a hedge-hog during hibernation, 1½ hours after the injection respiration becomes more frequent; after approximately three hours the animal gets up and runs away. Extracts of other organs have no influence. Only extract of thymus may have some influence. A remarkable symptom in the hedge-hog is also that after the injection of extract of thyroid the temperature rises from about 9° to 34-35° C.

—J. K.

(THYROID) Radium therapy in hyperthyroidism with observations on the endocrinous system. Aikins (W. H. B.), Internat. J. Surg. (N. Y.), 1918, **31,** 217-224; Radium (Pittsburg), 1918, **11,** 81-90.

See Endocrin., **2,** 537.

(THYROID) Development of the thyroid glands of Bufo and their normal relation to metamorphosis. Allen (B. M.), J. Morph. (Phila.), 1919, **32,** 489.

The accumulation of colloid material of the thyreoid glands of toad tadpoles begins just as the hind limb buds appear. The colloid masses increase in size and number until the forelimbs break through the skin. The accumulation of colloid material is accompanied by a marked increase in the size of the

thyreoid gland, which appears in the main to be a direct result of it. The apparently paradoxical fact that there is a cessation in growth and actual diminution in the size of the thyreoid gland and of the colloid masses at the very time when the process of metamorphosis is most active might in part be explained as the result of a partial drying process due to the emergence of the tadpoles from the water were it not that they do not emerge upon the land until later. The reduction in size is thus under way before this factor can prove effective. It is much more probable that this diminution may be due to the absorption into the blood of an unusually large amount of stored colloid at this time when it would prove most effective. The tail steadily increases in size to a certain point, shows a slight diminution and then quickly disappears. Either the thyreoid secretion does not cause the shrinkage of the tail or it must reach a considerable volume before it is able to accomplish that result. It is certain that limb development in the process of this appearance of the tail follows the accumulation of colloid in the thyreoid glands of Bufo. (Author's abstract.)

It might be noted that anurans decrease in size during metamorphosis more than do their thyreoids, so that despite some actual decrease in the size of the thyreoids at this time there is a relative increase.—E. R. H.

(THYROID, HYPOPHYSIS) The relation of the pituitary and thyroid glands of Bufo and Rana to iodine and metamorphosis. Allen (B. M.), Biol. Bull. (Woods Hole), 1919, **36**, 405.

Hypophysis removal in the larval amphibia retards the development of the thyroid glands as was shown by Adler '14. Thyroid removal causes hypertrophy of the pituitary (shown by Hoskins and Hoskins '18, Rogers '18 and Larson '19). The author believes that the thyroid probably plays the rôle of iodine storage and controls its distribution and that it is possible that the pituitary might play the chief rôle in the utilization of iodine by the body, because tadpoles deprived of either the thyroid or pituitary fail to metamorphose on a normal diet but either group and those deprived of both these glands will metamorphose when iodine is administered. (One possible objection to Allen's theory is that larvae deprived of the thyroid can be brought to metamorphosis by the administration of pituitary substance, which is practically free from iodine.)

—E. R. H.

(THYROID) Hypothyreoidismus, Rachitis und Tetanie. Bauer (F.), Wiener klin. Wchnschr., 1919, **32**, 929.

A short note on a case with symptoms of myxedema, rickets and tetany.—J. K.

(THYROID) Basedow's disease and war (La maladie de Basedow et la guerre). Berard (Leon), Bull. Acad. de Méd. (Paris), 1916, **76**, 428-430.

Berard refers to the frequent occurrence of Basedow's disease among soldiers and also civilians under conditions of special stress. These may develop from a pre-existing goitre of varying size or may appear without any evident pre-existing abnormality. Proper treatment consists of: (1) complete isolation of the patient in such a situation as to induce complete security and comfort; (2) Hydrotherapy; (3) quinine sulphate, 1 gram, and sodium salicylate, 2 grams, given on alternating days. Some good results have been obtained by ingestion of fresh thymus, and by subcutaneous injections of serum of thyroidectomized animals.

If after five to six months of this methodical drug treatment the subject has not properly responded, he is submitted to surgical treatment—the ligation of thyroid vessels, or excision of portions of the glands. As anaesthetic Berard uses ether, with morphine and atropine.—A. L. T.

(THYROID) Neuroses and hormone therapy. Dysthyroidism as a factor in neuroses. The oculo-cardiac reflex as a control of hormone therapy (Névroses et opothérapie. La dysthyroïdie facteur de névroses. Le réflexe oculo-cardiaque régulateur de l'opothérapie thyroïdienne). Blanc (Jean), Progres Méd. (Paris), 1917, **32**, 95.

In certain psychoneuroses the author has studied the claim that the oculo-cardiac reflex of Aschner indicates the relative tonicity of the sympathetic as opposed to the parasympathetic nervous system. In hypothyroidism when pressure is made on the eye-ball there is a greater slowing of the heart than normal; on the other hand, in hyperthyroidism the decrease in heart rate is excessive. Occasionally after thyroid medication the result is "negative," i.e. instead of slowing of the heart there occurs acceleration. This was taken to indicate an excessive irritability of the sympathetic system. Blanc begins thyroid medication with doses of 0.002 mg.(!) given alone or with 1 mg. of parathyroid. These doses are given two or three times a day, results being followed or controlled by general clinical appearances and by the reflex of Aschner.—A. L. T.

(THYROID) The relation of neurocirculatory asthenia to hyperthyroidism as determined by the effects of injection of

epinephrin. Boas (E. P.), Arch. Int. Med. (Chgo.), 1919, **24,** 419-421.

Individuals suffering from neurocirculatory asthenia show a positive epinephrin reaction, as indicated by alterations in the pulse rate, blood pressure and augmentation of nervous phenomena. Some positive reactions are accompanied by precordial pain, vertigo, headache, epigastric distress and nausea. In four cases of palpable thyroid only one gave a positive epinephrin reaction. On the other hand, individuals showing a negative epinephrin reaction may have well defined goitres. Hence, it is impossible to predict from any criteria at present available whether or not any particular case of neurocirculatory asthenia is sensitive to epinephrin.—H. W.

THYROID gland, Malignant epithelial growths of the—. Bonn (H. K.) J. Ind. State Med. Assn. (Ft. Wayne), 1919, **12,** 67-69.

Reviews the literature on malignant tumors, discussing the pathological and histological diagnosis, and reports one case of squamous cell carcinoma, three of adeno-carcinoma and one of sarcoma of the thyroid. Bonn concludes that early diagnosis of malignant thyroid growths may be made when a goitre long quiescent suddenly increases in size, accompanied by a change in consistency.—L. F. W.

(THYROID) Surgical treatment of exophthalmic goitre. Crile (George W.), Proc. Clin. Congress Am. Col. Surgeons, 1919, Abst., J. Am. M. Assn. (Chgo.), 1919, **73,** 1633. Discussion, Lewis (Dean D.); Mayo (Charles H.)

Of 2,250 thyroidectomies, 50 per cent were subjected to ligations. In 333 cases, ligation was first done, then a thyroidectomy. Among 116 ligations, one death occurred in the stage of dissolution. In the first 100 cases the mortality was 16 per cent. With the use of gas and oxygen anesthesia this was reduced to 2.5 per cent. By the adoption of special management of cases, the mortality has been further reduced to 0.6 per cent. Since the war, special precautions have been added against postoperative hyperthyroidism due to excessive chemical activity and destruction by oxidation. With each degree of rise of temperature this chemical activity is increased 10 per cent. With a temperature of 106 F., metabolism is increased 70 per cent. Another point of importance was the discovery by the British research department that the wound can be left open in statu quo, by the use of a dressing of 1:5,000 flavine. This permits the surgeon to stop at any point at which he considers the patient is not enduring the operation

well. Lobectomy is performed under analgesia, as the inhalation anesthesia interferes with internal respiration in a patient already suffering from suboxidation. Hypersensitiveness is sufficient to destroy the patient. Complete team work is essential to success. The operation is performed by the hospital and not by the surgeon. The differential diagnosis is greatly aided by the Goetsch epinephrin test and basal metabolism determination.

DISCUSSION

Tachycardia without exophthalmos does not differ from ordinary thyreotoxic goitre. Hyperplasia of the thyroid epithelum presents the four classical signs of goitre. Surgeons are likely to want to operate too soon. The exercise of judgment makes all the difference between one surgeon's success and another's lack of it. I have seen patients die after ligation. I have not seen anything that will control that.

—D. D. L.

The Surgeon-General's report showed that 15 per thousand is the rate of goitre in the northern Pacific States. There is almost no goitre in New Hampshire and Vermont. There are perhaps more mistakes in diagnosing exophthalmic goitre than any other condition. The thyroid is not essential to life, but it is synonymous with making life worth living. The cell changes in the thyroid are due to increase of biochemical products by bacteria, coming from different parts of the body and acting on the thyroid. Two-thirds of the cases are simple hyperplastic glands. A second type is caused by areas of degeneration throughout the gland. A hyperplastic gland sometimes goes with myxedema—a sort of burned-out condition. In hyperthyroidism there is a burning of fats, a rapid oxidation, and these people literally destroy their own cells. The thyroid gland bears relation to the elimination of nitrogen. Nitrogen, if retained, leads to tetany. Creatin and creatinin have almost the same chemical constitution as the thyroid secretion. There is, however, no positive determining factor to tell what is the controlling influence in thyroid action. We do not all agree as to methods, but the important point is that the mortality has been brought down.—C. H. M. (Quoted).

(THYROID) Nervous cretinism. Crookshank (F. G.), Lancet (Lond.), 1917 (ii), 604-605.

Nervous cretinism was first described by McCarrison as occurring in India. The author describes a number of cases observed by him in English children. In almost every case there is evidence of dysthyreosis in the mother or other members of her family. The earliest manifestations of mild ner-

vous cretinism are generally regarded as tetany and occur towards the end of the second year of life. Sometimes a pale puffiness representing the myxoedematous phase of dysthyreosis is present; this is usually transient. Later there may ensue a stage of weakness, with tottering gait, and a more persistent spasm that passes into a condition not to be distinguished from "congenital spastic diplegia" or "Little's disease" of moderate degree. In the more severe cases mental defect is obvious almost from the first, and the early appearance of spasm with nystagmus leads to the diagnosis of congenital spastic diplegia. All cases of nervous cretinism are found to improve under thyroid medication.—L. G. K.

The THYROID gland, Local anesthesia in operations upon—. De Courcy (Joseph L.), Am. J. Surg. (N. Y.), 1919, **33**, 245-248.

De Courcy advises early operation whenever possible on the ground that in skilled hands there is no more danger in removing a simple adenomatous or benign (not exophthalmic) goitre than there is in interval appendicectomy; and benign goitre should be considered as potentially dangerous as a simple appendicitis or a hernia. Preliminary observation and treatment in all cases of exophthalmic goitre with intensive study of the heart, kidneys and blood, are important. If case does not respond to internal medication and rest, arterial ligation should be performed. As a general rule the author does not perform thyroidectomy when the pulse after a moderate amount of exertion exceeds 120 per minute. He believes that a greater risk can be taken when local anesthesia is used than is possible under general narcosis, and that arterial ligation will be less often indicated. Removal of both lobes and isthmus gives the best results in exophthalmic goitre and causes less reaction following operation. Thyroidectomies can be done painlessly and thoroughly under local infiltration.—R. G. H.

(THYROID) Endemic goitre (Vom endemischen Kropf). Deist (H.), Schmidt's Jahrbücher (Bonn), 1919, **330**, 1.

A general review of the theories as to the cause of endemic goitre. The author supports the well known theory of Bircher. He believes that it is absolutely necessary that all researches done on goitre in the whole world be international and judged by a central international commission.—J. K.

(THYROID) A case of Graves' disease (Ein Fall von Morbus Basedowii). Falta (W.), Wiener klin. Wchnschr., 1919, **32**, 157.

Description of a case with exophthalmos of only one eye. There are 109 of these cases reported in the literature.—J. K.

THYROID aplasia (Ein Fall von Thyreoaplasie). Falta (W.), Wiener klin. Wchnschr., 1919, **32**, 157.

A new-born baby suffered with marked constipation. Later there was no growth of the hair. Thyroid treatment had a good effect. During war it was impossible to get thyroid tablets. The child became worse and worse; obstipation reappeared, the psychic development became bad. A piece of a thyroid of a patient with Graves' disease was transplanted without success. As soon as it was possible, thyroid tablets were regularly given. The success was complete.—J. K.

(THYROID) Myxoedema. Fischl (R.), Berliner klin. Wchnschr. 1919, **56**, 479.

A case of myxoedema with retarded ossification of the bones of the hands was benefited by the administration of thyroid preparations. A short note.—J. K.

(THYROID) Paralyse chez une hypothyroïdienne. Fournier (J. C. M.), Rev. Neurol. (Paris), 1918, **25**, 62-65.

Published elsewhere. See Endocrin., **2**, 536.

(THYROID) The operative treatment of simple enlargements and tumors of the thyroid gland. Frankau (C.), Brit. Med. J. (Lond.), 1919 (i), 792, 794.

Operation is rarely necessary in colloid goitre since it yields fairly readily to medical treatment. Surgical treatment should be carried out only when there are definite symptoms or deformity. No palliative treatment gives relief in diffuse adenoma, hence operation is justifiable if the enlargement is marked, even if no symptoms are present. Cysts of the thyroid form the most frequent class operated on, since they may grow to a very large size and dyspnoea is usually present.

A certain amount of detail concerning the surgical technique is included in the paper.—L. G. K.

(THYROID) Mental symptoms predominate in some cases of myxoedema. French (H.), Guy's Hosp. Gaz. (Lond.), 1918, **32**, 72-73.

Brief description of two cases of myxedema presenting marked mental disturbances. The first case cleared up on thy-

roid opotherapy and continues normal. The second case was diagnosed as frontal lobe tumor and was trephined, but no tumor was found. Dying of erysipelas, the patient was autopsied and the only abnormality found was that the thyroid gland existed as a trace only, the right lobe being fibrous tissue and all weighing about 0.7 gram. The left lobe weighed still less. The conclusion is that this latter case might have been benefited by thyroid treatment and that myxedema may have mental and cerebral symptoms as its predominant features.
—F. S. H.

THYROID, Malignant tumor of—. Graves (S.), Ky. Med. J. (Bowling Green), 1919, **17,** 325.

A case report.—H. W.

(THYROID) Toxic, non-exophthalmic goitre. Haggard (William D.), Proc. Southern Med. Assn., J. Am. M. Assn. (Chgo.), 1919, **73,** 1796.

This type of goitre is quite as dangerous, if not more so, than exophthalmic goitre, because the toxin seems to have a selective action on the heart, causing the so-called "goitre heart," thyrotoxic, instead of the mechanical "goitre heart" from pressure. It is more likely to be overlooked on account of the absence of exophthalmos. Many simple adenomas are prone to degenerate and produce toxic symptoms. An atoxic goitre may be of long duration before producing toxic symptoms. There is danger in administering iodin in a case of goitre of long standing. It may set up toxic and sometimes fatal symptoms. Toxic, non-exophthalmic goitre occurs in one out of four goitres that are not hyperplastic. Toxic goitre is not definitely improved by ligation. Operation for toxic goitre is quite as dangerous, if not more so, than in the exophthalmic type, owing to the condition of the patient. In my last series of 100 toxic cases, exclusive of the so-called simple goitre, two deaths occurred in thirty-three operations, and only two deaths in sixty-seven exophthalmic cases.—Quoted.

(THYROID) Struma apoplectica. Hering. Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1061.

A very short note on hemorrhage into the thyroid observed in a patient after severe coughing.—J. K.

THYROID, A case of acute purulent inflammation of the— (Ein Fall von Thyreoiditis acuta suppurativa). Höpfner (H.), Berliner klin. Wchnschr., 1919, **56,** 944.

Description of a not very important case of an abscess in the thyroid, cured by incision.—J. K.

(THYROID) Growth and development of amphibia as affected by thyroidectomy. Hoskins (E. R.) and Hoskins (M. M.) J. Exp. Zool. (Phila.), 1919, **29**, 1.

The thyroid anlage was removed from very young embryos of Amblystoma punctatum and Rana sylvatica. The technique is described. In some larvae the gland regenerated. When correctly performed, this operation will inhibit metamorphosis more or less indefinitely if the animals are kept on a normal diet. Thyroidless larvae grow more rapidly than the controls and ultimately become two to three times as large. Inhibition of metamorphosis in these animals is attributed to a defective metabolism, especially of calcium, since the earliest and most striking effects were noted in the skeleton which calcified and ossified less completely than normal. Other characteristics of thyroidless amphibians are: retention of the larval form, and the ability to regenerate lost parts; the brain develops slowly; the hypophysis hypertrophies; the thymus persists and becomes relatively large; the epitheleoid (parathyroid) bodies and kidneys become relatively large; the spleen is not affected; the internal gills persist; the lungs develop and become functional; the intestine retains its larval character; the ovaries differentiate and form large oöcytes which do not completely maturate; the testes develop to maturity, producing spermatozoa which escape through the kidneys. The changes in the body and organs of normal larvae during metamorphosis are described and also the histology of the endocrine glands and organs of normal and thyroidless animals.—Author's abstract.

(THYROID) An experimental and clinical study of the isolated thyroid hormone. Janney (Nelson W.), Dental Cosmos, (Phila.), 1918, **60**, 133-139.

An address covering the work of the speaker and his coworkers on the subject. The data were previously reported in the following articles:

The anabolic action of the thyroid gland. Proc. Am. Soc. Biol. Chem. (N. Y.), 1916, **11**, 6.

An experimental and clinical study of the isolated thyroid hormone. Sec. on Ped., N. Y. Acad. of Med., 1917, April. See Med. Rec. (N. Y.), 1917, **91**, 1161.

hormone. Apr. Dental Cosmos (Phila.), 1918, **60**, 133-139

An experimental and clinical study of the isolated thyroid

The blood sugar in thyroid and other endocrine diseases Arch. Int. Med. (Chgo.), 1918, **22**, 160.

The influence of thyroidectomy and thyroid diseases on protein metabolites. Ibid, 1918, **22**, 174.

In addition experimental data were mentioned which militate against acceptance of the well known theory of endocrine function of Falta, Eppinger and Rudinger of the Viennese school. Probably the endocrine glands have (1) a general somatic action on the building and replacement of the protein molecule and (2) a specific action as exemplified by development of the secondary sexual characteristics at the time of functioning of the sex glands.

(THYROID) Arhythmias in Graves' disease (Arhytmien beim Morbus Basedowii). Huber, Ztschr. f. klin. Med. (Berlin), 1919, **87**, 465.

Very often in Graves' disease, extrasystoles may be observed. They are nearly always seen after injection of adrenalin. Also tachycardia of the sinus and arhythmia perpetua may be observed. Digitalis has a good influence.—J. K.

(THYROID AUTONOMIC N. S.) Voluminous goitre, compression of trachea and sympathetics. Exaggeration of the oculocardiac reflex [Goitre volumineux, compression trachéale et sympathique (Syndrome de Claude Bernard-Horner). Exagération du réflexe oculo-cardiaque]. Jacob (P.) and Labeaume, Bull. Soc. Méd. des Hôp. (Paris), 1919, **43**, 446.

On the side of excessive pressure, ocular signs indicate sympathetic nerve trauma or paralysis, as shown by exophthalmos, miosis and narrowing of the palpebral fissure. Aschner's eyeball-heart reflex appeared more prominent on the injured than on the normal side, producing a slowing of the heart from 88 to 52, while the slowing on the uninjured side was from 88 to 72. This was taken to indicate that the sympathetic nerve injury on the left side upset the balance between the sympathetic and vagus in such a way as to leave the vagal effects predominant.—A. L. T.

(THYROID) Symptoms of hyperthyroidism observed in exhausted soldiers. Johnson (W.), Brit. Med. J. (Lond.), 1919 (i), 335-337.

Observations were made on 50 soldiers who left the firing line complaining of weakness, uncontrollable nervousness, throbbing headaches, dizziness, palpitation and precordial pains, more especially on exertion. Occasionally digestive dis-

comfort and diarrhoea or frequency of micturition were complained of. Sleep was irregular and easily disturbed. Dreams, in which the patient would wake up in a profuse perspiration, were common.

On examination these patients appeared pale, looked ill and were exhausted. The mental state was usually one of subdued excitement. More or less prominence of the eyes was exhibited by all the cases. Tremor was a constant phenomenon. Other signs of "hyperthyroidism" were also generally present.

It was found that after a rest in bed (with full diet, suitable tonics and occasionally Dover's powder at night) the condition of all the patients rapidly improved in ten or twelve days. The exophthalmos greatly decreased or disappeared. The pulse remained rapid and excitable, and the general subjective symptoms always appeared to be within call if the patient experienced any excitement. These cases then merged into the group labelled "neurasthenia," and were indistinguishable from them.

The author advances the following hypothesis.

1. That a large number of so-called psychoneuroses are cases in which the symptoms are due to a state of disordered internal secretion, the result largely of emotional exhaustion, and, to a less degree, of physical exhaustion. 2. That many cases which are later diagnosed irritable heart, "D. A. H." soldier's heart and neurasthenia are really cases of this class, and that possibly many have passed through a slight state of exophthalmos without its importance being realized.

The phrase "exhaustion syndrome" is suggested as a suitable term to apply to this group of symptoms, and exhaustion is declared to be the active etiological factor in all these cases of breakdown.—L. G. K.

(THYROID) Pit in the thorax in a child with Graves' disease. (Dellenförmige Einziehung der Herzspitse bei Basedow). Just, Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1119.

Demonstration of a girl of 9 with Graves' disease and a pit in the thorax at the location of the cardiac apex. Of no special endocrine interest.—J. K.

(THYROID) Local anesthesia for operations for goitre. Keller (A. A.) New Orleans M. & S. J., 1919, **71**, 305-310.

The author discusses the dangers of general anesthesia. He believes that local anesthesia offers greater safety and is particularly suited to thyroidectomy. He has employed novocain and aposthesine with good results, and observes that there

is less post-operative pain and a shorter convalescence after local than after general anesthesia. He reports forty-five operations on the thyroid under local anesthesia.—L. F. W.

(THYROID) Isolation of the iodine compound which occurs in the thyroid (first paper). Kendall (E. C.), J. Biol. Chem. (N. Y.), 1919, **39,** 125-149.

The original must be consulted for details in isolating the active principle "thyroxin" in quantity from the glands. Thyroxin is shown to be 4, 5, 6—trihydro—4, 5, 6, triiodo—2 oxy, betaindole-propionic acid and exists in three forms: (1) the keto form with the carbonyl group adjacent to the imino; (2) a tautomeric enol form of this, with an alpha hydroxyl group and double bonded nitrogen, with no hydrogen attached to the imino, and (3) a form in which there is an open ring structure, the elements of water entering between the imino and the carbonyl with the formation of an amino and carboxyl group.

Five chemical reactions are involved in controlling the conditions of its isolation. (1) Iodine breaks off from the acetyl derivative when an acid suspension is neutralized by NaOH. Temperature greatly influences this reaction. (2) Pure thyroxin is easily reduced, yielding free iodine, when hydrolysis is carried on in metallic containers. (3) CO_2 causes two distinct reactions. It precipitates thyroxin from its impurities and, by forming the monometallic derivative form from the dimetallic, produces an optimum condition for the closing of the indole ring. (4) Increase in temperature during CO_2 treatment results in liberation of free iodine. (5) Glands vary in their thyroxin content, the yield being 400-500% higher in summer than in winter. Deamination and decarboxylation are believed to be the cause of the loss in therapeutic power of desiccated glands. This loss may be brought about by bacteria without change in the iodine content.—V. K. L.

(THYROID) Survey of thyroid enlargement among students of the Puyallup Indian School. Kerr (W. T.), Northwest Med. (Seattle), 1919, **18,** 110-112.

Of 310 Indian students representing 43 tribes from six states and Alaska, 10.6 per cent showed definite enlargement of the thyroid. The survey shows that in full-blooded Indians the incidence of goitre is very low as compared with part blood or the pure Caucasian race.—H. L.

(THYROID) A preliminary survey of the thyroid gland among two thousand, one hundred and eighty-two recruits at Camp Lewis, Washington. Kerr (W. J.), Arch. Int. Med. (Chgo.), 1919, **24**, 347-358.

Study of recruits from eleven northwestern states. Incidence of simple goitre was found to be highest in Washington and Oregon and lowest in California and Nevada. Endemic goitre was found largely confined to Pacific Northwest. Exophthalmic goitre was rarely seen, subjects having this condition being rejected by local boards. Twenty-one per cent of all troops showed definite enlargement of the thyroid gland, of which twenty-seven per cent were rather large. Goitres had been noticed in other members of the family, especially the females. Tremor and tachycardia were occasionally noted. No definite conclusions as regards etiology could be drawn.

—B. T. S.

THYROID, Influence of extract of—on certain secondary sex characters in the Triton (Influence de l'extrait de thyroïde sur certaines caractères sexuels secondaires des Tritons). Kollmann (Max), C. R. Soc. de Biol. (Paris), 1919, **82**, 793.

Male tritons when in full sexual activity possess a dorsal crest and large nictatory membrane. These secondary sex characters disappear in the intervals between sexual periods. This recalls the regression of the caudal membranes in tadpoles, which is the first external manifestation of metamorphosis. A group of Molge vulgaris were treated with injections of thyroid extract. The results showed an opposite effect to that expected. Instead of accelerating the disappearance of the crest and membranes, thyroid extract seems to favor their permanence, even after the close of the period of reproduction.

—T. C. B.

(THYROID) The influence of thyroidin on normal metabolism. Krogh (Marie), Ugeskr. f. Laeger (Copenhagen), 1916, **72**, 2237-2341.

Correction of reference in Endocrin. **2**, 73, 200.

(THYROID) Diarrhea in Graves' disease (Durchfälle bei Basedowscher Krankheit). Koslowsky, Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1219.

The author observed two cases in which diarrhea was the first symptom of Graves' disease. The other symptoms were not very distinct. Treatment with ovary tablets had a good influence on the diarrhea.—J. K.

(THYROID) Some details of the acceleration of metamorphosis in Anura under the influence of thyroid extract (Quelques précisions sur l'accélération de la métamorphose des Bactracien Anoures sous l'influence de l'extrait de thyroïde). Kollmann (Max), C. R. Soc. de Biol. (Paris), 1919, **82**, 1009.

Having shown that simply adding thyroid extract to the water produces the same effect as feeding thyroid, the author points out that aside from other factors it is necessary to consider the age of the tadpoles and their state of nourishment. The desirability of the maintenance of a constant temperature is emphasized, and the stage of development of the posterior extremities is taken as a criterion of age.

A large number of tadpoles was selected, as nearly alike as possible, and was then divided into eight lots. Lot 1 had no visible traces of the posterior extremities; lot 2 with whitish buds indicating the posterior extremities; lot 3, posterior extremities visible but very small; lot 4, legs longer, but straight; lot 5, like the preceding, but longer legs; lot 6, legs flexed in the adult position; lot 7, like the preceding, but the body commencing to take the adult form; lot 8, the anterior extremities present. Each lot was divided into two groups; one group was kept in ordinary water, the other had added 2 cc. extract of thyroid for each 100 cc. water.

Under these conditions the extract seems to exert no effect on groups 1, 2, 3 or 4, except in rare individual cases in lot 4, due to the fact that specimens at the identical stage of development cannot be rigorously selected. In lots 5 and 6 it is the rule to have metamorphosis rapidly produced in the "thyroidized" animals, while it is exceptional in the controls. The other lots remain uninfluenced by the thyroid extract.

In regard to nourishment (giving food in addition to thyroid extract), alimentation simply furnishes the material necessary to attain a condition where the animal becomes sensitive to the action of the extract.

Kahn's assertion that the left anterior extremity appears before the right, is not confirmed.—T. C. B.

(THYROID) Demonstration von Kretinen. Lange, Münch. med. Wchnschr., 1919, **66**, 945.

The author demonstrated at a medical meeting some cretins treated with thyroid with very little success.

Probably the patients were too old when treatment began; such patients ought to be treated at as early an age as possible. In countries where cretinism is frequent, popular lectures ought to be given to teach the public that treatment must begin when the first symptoms are observed.—J. K.

(THYROID) The little signs of thyroid disturbance. Leiner (Joshua H.), Med. Rec. (N. Y.), 1919, **96,** 99-101.

The author calls attention to the "little signs" of thyroid disturbances, believing that numberless cases are unrecognized that might be benefited by early recognition and judicious therapy. Most physicians diagnose correctly outspoken syndromes such as Graves' disease, myxedema, cretinism, but neglect the mild incipient modifications. He cites a few illustrative examples.—H. L.

(THYROID) Suppurative thyroiditis due to the bacillus paratyphosis A (Thyroïdite suppurée a bacille paratyphique A). Lemierre (A.) and Taberlet, Bull. et Mem. Soc. Méd. des Hôp. (Paris), 1919, **43,** 513.

A case report of a suppurative thyroiditis occurring in the course of paratyphoid fever.—A. L. T.

(THYROID) Making the cure of goitre safe. Levy (Louis), New Orleans M. & S. J., 1919, **72,** 170.

The author emphasizes the importance of careful preliminary treatment for exophthalmic goitre before operation in any case. To prevent shock he uses local or nitrous oxid anesthesia and, following the operation, gives enough morphine to keep the patient quiet, even though the respirations go down to 10-12 per minute. This morphine treatment is usually continued for three days.—L. F. W.

THYROID, Effect of extract of, on tadpoles. Lim (R. K. S.) J. Physiol. (Lond.), 1919, **53,** Proc. xxvi.

Precocious metamorphosis as described by Gudernatsch was observed. Microscopic sections show concomitant changes in the viscera, and a remarkable number of mitoses, indicating rapid cell proliferation.—T. C. B.

Preliminary THYROID operations. Link (G.), J. Ind. State M. Assn. (Ft. Wayne), 1919, **12,** 64-66.

The author believes that better results follow thyroidectomy when it is preceded by ligation of one or more arteries or by the injection of boiling water. He observes that increased mortality is often due to neglect of this measure.

—L. F. W.

(THYROID) The use of laboratory methods in the diagnosis of early hyperthyroidism. Lueders (C. W.), Arch. Int. Med. (Chgo.), 1919, **24**, 432-444.

A study was made to discover a means of differentiating early or borderline hyperthyroidism from functional cardiac disorder. The tests used were sugar tolerance, epinephrin test, nitrogen loss and test for acidosis.

The results showed that the laboratory affords a most reliable aid toward the recognition of early hpyerthyroidism. The sugar tolerance test is an important aid in detection of borderline cases. Epinephrin tests did not prove diagnostic of hyperthyroidism. Tests for nitrogen loss and acidosis seemed suggestive aids. Also creatinuria determinations in conjunction with other tests were of value.—B. T. S.

(THYROID) Some points in the surgical treatment of goitre. Mackenty (J. E.), Laryngoscope (St. Louis), 1917, **27**, 912-914; Tr. Am. Laryngol. Assn. (N. Y.), 1917, **39**, 215-227.

Advises operative measures as the surest cure of goitre and thinks that the rhinolaryngologist should do neck surgery. —H. W.

(THYROID) The basal metabolism in hypothyroidism. Means (J. H.) and Aub (J. C.), Arch. Int. Med. (Chgo.), 1919, **24**, 404-418.

Determinations of basal metabolism in untreated cases of myxedema showed definite reduction below that of normal individuals. Studies on a cretin and a case of cachexia strumipriva showed the same. Thyroid therapy brought the basal metabolism up to normal. Basal metabolic determinations form a convenient method of governing the dosage of thyroid preparations in hypothyroidism and may be of value in diagnosis. —B. T. S.

(THYROID) A note on the question of the secretory function of the sympathetic innervation to the thyroid gland. Mills (C. A.), Am. J. Physiol. (Balt.), 1919, **50**, 174.

The evidence regarding the innervation of the thyroid being conflicting, the object of the experiments was to determine whether the thyroid could be stimulated to greater activity by the use of cocaine according to the method of Froelich and Loewi. Daily injections of 10 mgm. cocaine per kilo, body weight, were given over a period of days and the thyroids were examined histologically for evidence of hyperactivity. No such

evidence could be observed, and the writer considers this an indication of a lack of secretory function of the sympathetic fibres to the gland.—T. C. B.

(THYROID) Radium. Mowers (S. W.), Northwest Med. (Seattle), 1919, **18,** 153-156.

In mentioning the many therapeutic indications for radium, the author states that it is very useful in exophthalmic goitre. The majority of the cases are clinically cured and a very large percentage have an actual decrease in the size of the goitre. Others have reported similar success, but further confirmation and longer observation is necessary.—H. L.

(THYROID) Ligation of the vessels in toxic goitre. Noble (T. B.), J. Ind. State M. Assn. (Ft. Wayne), 1919, **12,** 230.

Noble urges an early diagnosis of the mild forms of toxic goitre, and prompt surgical interference if the best results are to be obtained. Formerly the condition of the patient was determined by the intensity of the four cardinal symptoms. At the present time it is possible to determine the metabolism rate and thus place the patient on a definite scale of toxicity, selecting the treatment best suited to his needs. Ligation should be reserved for the severe forms of goitre when the life of the patient would be jeopardized by a lobectomy. In the average case lobectomy should never be preceded by a ligation.

—L. F. W.

(THYROID) The toxic element in goitre. Pern (S.), Med. J. Australia (Sydney), 1918, **5,** 276-278.

A report of twenty-three cases purporting to substantiate the author's opinion that the cause of goitre lies in a defensive reaction of the thyroid accompanied by hypertrophy due to toxins engendered in the system from infectious processes largely in the teeth and tonsils.—F. S. H.

(THYROID) The blood picture in exophthalmic goitre. Plummer (H. S.), Collected Papers of the Mayo Clinic (Rochester, Minn.), 1918, **10,** 359.

This paper is based on the study of the blood counts in 578 patients with exophthalmic goitre. The hemoglobin, erythrocytes, and the total leukocytes are all within normal limits. There is, however, both a relative and an absolute mononucleosis, together with a percentage decrease in the polymorphonuclear neutrophiles. The eosinophiles are slightly under the

normal average. Although some writers still maintain that anemia of the chlorotic type is a characteristic of this disease, this is neither borne out by the author's findings nor those published by Kocher. The author concludes that there is much to indicate that the changes in the leukocyte formula are owing to two more or less independent variables. One which causes a lymphocytosis and another which influences the neutrophilic count. The first may be found in a hyperplasia of the lymphoid tissues, and the second in a fluctuating abnormal distribution of the neutrophiles in the vascular tree.

—J. F.

(THYROID) Ueber Volumen pulmonis diminutum. Pollitzer (H.), Münchener med. Wchnschr., 1919, **66**, 1103.

In diseases with chronic contraction of the blood vessels in the lung the volume of the lungs may seem diminished. When the left lung diminishes in volume, it gives the impression that the heart is dilated. This may be observed in chlorosis, chronic malaria and Graves' disease.—J. K.

(THYROID) Factors for safety and ultimate results in goitre operations. Potter (C.), J. Missouri M. Assn. (St. Louis), 1917, **14**, 506-511.

Of surgical interest only.—A. R. T.

(THYROID) Thyroidism and Graves' disease as a form of traumatic neurosis (Thyreoidismus und Morbus Basedowii als eine Form der traumatischen Neurose). Pulay (E.), Ztschr. f. klin. Med. (Berlin), 1919, **88**, 87.

According to the author Graves' disease is a form of increased irritability of the sympathetic system. But the increased irritability does not alone cause Graves' disease unless the patient has also a "status degenerativus" and unless there occurs also a special stimulation of the sympathic (psychical, traumatic, or infectious). This stimulation gives rise to the beginning of the disease. It is not true that the cause of the disease is abnormal functioning of the thyroid. The thyroid malfunction is, rather, a result merely of augmented sympathetic activity, as are the many other Graves' symptoms. No value is to be attached to various theories which ascribe a primary etiologic role in the disease to the thymus or the pancreas.

J. K.

THYROID therapy in skin diseases. Pulay (E.), Therap. Monatshefte, 1919, **33**, 115.

A large number of dermatological conditions have been correlated with disturbances in thyroid function. Among these are erythema, hyperhidrosis, alopecia, atrophy of nails, and especially scleroderma. Administration of thyroid substance has been advocated in these cases. In the author's experience there is no specific or favorable result noted after such therapy.—Chem. Abst.

(THYROID-PARATHYROID-ADRENAL) The role of the thyroid-parathyroid apparatus in uremia (Du role de l'association thyro-parathyroidienne dans l'uremie). Remond (A.) and Minvielle. Bull. Acad. de Méd. (Paris), 1917, **77**, 504-507.

In an effort to study the mutual interrelationship between the thyroid, parathyroid and kidney, three series of experiments were performed: (1) nephrectomy, (2) nephrectomy with thyroidectomy, (3) thyro-parathyroidectomy with nephrectomy. It was found that survival of animals was the same in simple nephrectomy as in thyro-parathyroidectomy with nephrectomy, while in thyroidectomy with nephrectomy the survival was about half that in the other two series. The urea content of the blood was essentially the same in the first and third series, but in the second, the urea was much decreased while the chlorides were slightly increased. Summary:

	Nephrectomy	Thyroid-nephrectomy	Thyro-parathyroid-nephrectomy
Survival in hours.....	77	34	68
Urea in blood, per liter	5.97	1.99	5.69
Chloride, per liter.....	7.37	8.22	7.31

Thus, the removal of the parathyroid glands delays the early onset of intoxication occurring in the removal of kidneys and thyroids. In this the authors see an inhibitory action on the adrenal glands. Removal of thyroids with the kidneys has but little effect on the adrenal glands, while after removal of the parathyroids the adrenal appears to have been intensely active.—A. L. T.

(THYROID) Two cases of nephritic exophthalmos (Deux cas d'exophtalmie néphrétique). Rondopoulo (P. J.), Bull. Soc. Méd. des Hôp. (Paris), 1919, **43**, 4.

Two cases are described in which exophthalmos occurred in nephritics. That the exophthalmos was of thyroid origin was indicated by the presence of two of the Graefe, Möbius and Stellwag signs. The frequency of occurrence of exoph-

thalmos in nephrities was estimated to be about 3 per cent, occurring mostly in subacute or chronic nephritis.—A. L. T.

(THYROID) Case of myxedema. Saunders (A.), West London Med. J., 1917, **22**, 129.

A case of myxedema in a child of seven was shown. She had an enlarged thyroid at the age of two. At the age of five the left lobe was removed, after which the symptoms of myxedema developed. Her hair came out in patches and what was of additional interest were attacks of cyclic vomiting, which occurred every four months; simultaneously she became puffy over her entire body. Under persistent treatment with thyroid extract all her symptoms mentioned above vanished.—J. H. L.

(THYROID) Exophthalmic goitre. Schioetz (C.), Med. Rev. (Bergen), 1917, **34**, 1-20.

Report of a case of exophthalmic goitre, where the patient died after rapid loss of weight, vomiting, jaundice and albuminuria. Autopsy revealed an hyperplastic thyroid, thymus and anterior lobe of the pituitary; ovaries and pancreas were atrophic, liver and kidneys degenerated.

General remarks are offered as to the pathogenesis of the disease. The effect of thyroidin upon the protoplasm consisted of two phases: first, stimulation and later on destruction—analogous to the effect of certain inorganic poisons, e.g., mercury.—K. M.

(THYROID) Riedel's goitre (Riedelscher strumitis). Schloffer, Wiener. klin. Wchnschr., 1919, **32**, 930.

Description of a patient with an enormous goitre, hard as iron. No swollen lymph glands were detected. The clinical diagnosis "strumitis" (in the form described by Riedel) was confirmed by histological examination.—J. K.

THYROID gland, Influence of the—upon metabolism. I. Carbohydrates. Sekita (N.), Tokyo Igakukai Zisshi, 1918, **32**, 1-49; Jap. Med. Lit., 1919, **4**, 34.

From a study of thyroid functions, adrenaline glucosuria, and their relationship, the conclusion is drawn that the influence of the thyroid on carbohydrate metabolism has not been proved.—Chem. Abst., **13**, 2070.

(THYROID) Operation for thyroid tumor. Sherrill (J. G.), Ky. Med. J. (Bowling Green), 1919, **17**, 323-325.

Case report.—H. W.

(THYROID) Trauma and Graves' disease (Trauma en Morbus Basedowii), Simons (A.), Tijdschr. v. Ongevallen-Geneeskunde (Amsterdam), 1919, **4,** 247.

Description of two cases: 1st. A man fell with the abdomen against an engine. Twelve years before the accident he had been suffering from a Graves' disease which had disappeared after treatment. After this accident an acute Graves' disease developed. Some weeks after this he developed psychosis and died. The author believes that the trauma had an influence on the parasympathetic and sympathic systems and that the disease is caused by a disturbed equilibrium between these two systems. 2nd. A man fell in the water and developed, a fortnight later, acute Graves' disease. The patient died of cachexia. Autopsy showed a large thyroid with only a little colloid and status thymicus (large thymus and narrow aorta).

J. K.

(THYROID) A brief study of goitre based on 1000 cases operated upon. Sloan (E. P.), Ill. Med. J. (Chgo.), 1919, **35,** 226-227.

Summarizes the results with special reference to the onset of symptoms, age, sex, etc. Nothing new.—L. F. W.

THYROID gland, The function of the—in relation to infections. Sohmer (A. E.), St. Paul M. J. (St. Paul, Minn.), 1917, **19,** 297-301.

The author calls attention to the various known thyroid functions, developmental and metabolic. He cites experimental and clinical evidence that thyroid secretion has bacteriolytic and anti-toxic properties. He lays stress on the thyroid enlargement accompanying chronic infections, and concludes that it is only a step from this chronic irritation of the gland to the formation of a goiter with elaboration of toxic secretions.—A. R. T.

(THYROID) Familial exophthalmic goitre. Souques and Lermoyez (J.), Rev. Neurol. (Paris), 1919, **26,** 20-26.

Souques and Lermoyez relate that in the family described there have been seven cases of exophthalmic goitre among the sixteen members of the family in three generations. They give illustrations of the four members they have personally examined. The tendency seemed to be transmittd by the males.

There were no signs of inherited syphilis; the trouble must be some inherited predisposition rendering the thyroid peculiarly susceptible to diverse infections and intoxications. They list the few similar familial cases on record. In one, dating from 1884, eleven of the sixteen members of the family had developed exophthalmic goitre.—J. Am. M. Assn., **73**, 799.

THYROID treatment of alopecia areata. Strandberg (J.), Acta Medica Scandinavica (Stockholm), 1919, **52**, 165-176.

Strandberg now has a record of nine cases in which endocrine disturbances seemed to be responsible for malignant patches of alopecia. All were in men except three, but there was nothing to indicate positively endocrine disturbance. Two of the patients had dementia precox and one signs of syphilis. Thyroid treatment was applied in every case, but only briefly in two; in three of the cases the hair grew again under the thyroid treatment. In one man with dementia praecox the hair began to grow in as the mental condition improved. One woman who was not benefited by the thyroid had her hair drop out again during a pregnancy, and also when menstruation returned. The article is in German.—J. Am. M. Assn., **73**, 1736.

(THYROID) A new ocular muscle symptom in exophthalmic goitre. Suker (G. F.), J. Am. Med. Assn. (Chgo.), 1917, **68**, 1255.

"After extreme lateral rotation of the eyes, with fixation on an object at this point maintained for a second or two, on attempting to follow this fixation point as it is rapidly swung into the median line, one of the eyes fails to follow the other in a complementary manner into proper convergence. An apparent divergent strabismus is momentarily manifest." (Quoted.)

(THYROID) An urgent tracheotomy (Een spoed-tracheotomie). von der Tak (H.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63**, (II), 1448.

In a case of malignant goitre a very acute attack of dyspnea made immediate tracheotomy necessary.—J. K.

(THYROID) Chagas' disease in Venezuela. Tejera (E.), Gaceta Méd. de Caracas, Venezuela, 1919, **26**, 103.

Tejera presents conclusive evidence that the trypanosome thyroiditis described by Chagas in 1907 as common in children

in certain parts of Brazil prevails also in Venezuela. He reports two cases, in an infant and a boy of 2, belonging to the states of Trujillo and Zulia. His extensive study of the subject has demonstrated further that it is transmitted by a different insect from the one responsible for it in Brazil, Lamus (Conorhinos) megistus, as this does not seem to occur in Venezuela. The bug responsible for the transmission in Venezuela is Rhodnius prolixus Stal, as he determined by extensive experimental research and these clinical experiences. These insects in nature may harbor Trypanosoma cruzi. The insects are called by various names, pito, chupon, quipito, chinche de monte and chipo. It is a night-biting insect of the reduvidae family. Some specimens sent to Paris in 1913 from Venezuela were artificially infected by feeding them with Trypanosoma cruzi sent from Bahia, Brazil. Rincones presented Tjera's report sent from the laboratory of the Caribbean Petroleum Company at Mene Grande, and he added that a few years ago he urged research in Venezuela to find whether this American trypanosomiasis was restricted to Brazil alone. Tejera mentions in conclusion that, as goitre seems to be endemic in the Santander district in Colombia, Chagas' disease probably could be discovered there also. He was examining the rhodnius for Leishman bodies, in a study of American leishmaniosis, when he was surprised by the discovery in them of Trypanosoma cruzi of Chagas' disease. But his clinical cases of the latter came from a different district, and he found the trypanosome likewise in specimens of rhodnius from the environment of the patients. Rats, cats, monkeys and other animals inoculated from the insects developed the trypanosomes in large numbers in the blood. Ayala added that Tejera's research seems to exculpate the drinking water in respect to endemic goitre. He appealed further for research to decide whether there may not be some plant which serves as a host for the trypanosome like the euphorbia for the leptomonas (Iturbe), suggesting some zoological affinity between plants, Leishman bodies and trypanosomes.—J. Am. M. Assn., **73**, 565.

(THYROID) Hyperthyroidism in influenza. Todd (A. T.), Lancet (Lond.), 1919 (ii), 733-734.

Among 1500 cases of influenza 16 cases of hyperthyroidism developed. In all but one fatal case it appeared during convalescence. The onset was sudden in all cases.—L. G. K.

(THYROID) Relation between water-supply and goitre. Tolman (Mayo), Eng. News-Record, 1919, **83**, 516.

The cause of goitre is unknown, but has frequently been laid at the door of the water supply. T. claims that volcanic formations, the crystaline rocks of the Archaic period, and all deposits laid down in fresh water are free from goitre-producing characteristics. In the United States the greatest endemicity is found in Paleozoic areas. An estimate is made of 12,000 cases of goitre in West Virginia.—Chem. Abst., **13**, 3228.

(THYROID) The psycho-neurotic syndrome of hyperthroidism. Woodbury (M. S.), J. Nerv. & Ment. Dis. (N. Y.), 1918, **47**, 401-410; Clifton Med. Bull. (Clifton Springs), 1918, —, 18-23.

An excellent review and bibliography of the nervous and mental symptoms occurring in the course of Graves' disease. The author concludes that there is no distinct thyrotoxic psychosis, but that certain well-defined neurotic and psychotic symptoms arise in well-defined thyrotoxic cases. In the exophthalmic toxic cases, these symptoms are of the overcerebration and overstimulation type, dependent upon (1) cerebral hyperemia, (2) thyrotoxicosis per se, (3) toxicity from the increased waste products of metabolism. In the non-exophthalmic toxic cases, the mental picture is rather one of depression minus delusions. The latter cases comprise the adenomatous type of goitre and run a more sluggish course. They are distinguishable from non-endocrine neurasthenoid states by means of studies of the basal metabolism and the adrenin chloride test of Goetsch.—A. R. T.

(THYROID) Iodin content of human thyroid glands (Sur la teneur en iode du corps thyroide de l'homme). Zunz (E.), Réunion soc. belge biol., 1919, 22 Fév., 894-895.

The iodin content of the thyroid glands of normal human subjects, 21 to 34 years of age—men killed in war—was determined. In the majority of cases the range was 1.5 to 3 mgm. of iodin per gram of dry gland, or 0.46 to 0.84 mgm. per gm. of moist gland. The entire gland contained from 3.15 to 44.49 mgm., averaging 15.53 mgm. Diminution of the iodine content was noted in cases of bronchopneumonia.—Physiol. Abst., **4**, 338.

(VAGOTONIA) Ueber Vagotonie und Sympathikotonie. Klieneberger (C.), Berliner klin. Wchnschr., 1919, **56**, 719.

No new data. Cases of vagotonia, as described by Eppinger and Hess are very rare. The theory of vagotonia is very interesting, but it is only a theory. A great part of the liter-

ature on this subject shows a lack of critical sense and of pharmacological and physiological knowledge.—J. K.

(VAGOTONIA) Ulcer of the stomach and autonomic nervous system (Ulcus pepticum und vegatitives Nervensystem). Lehmann (G.), Berl. klin. Wchnschr., 1919, **56**, 772.

The author tried to find whether there is a relation betweel vagotonia and ulcers of the stomach. He found that the theory that the vagus and sympathic are antagonists is certainly not true. Most patients who are very sensitive to adrenalin are just as much so to pilocarpine. In modern literature we often read that patients with ulcers of the stomach show symptoms of vagotonia. The author could not confirm this. It is, however, true that such patients may show a disturbed function of their involuntary nervous system, but this is rare. In these cases the author believes that the ulcer is the cause of the change in the nervous system (through hemorrhage, under-feeding, etc.) The theory that ulcers of the stomach are caused by an abnormal function of the nervous system has never been proved and is not probable. Approximately 80 per cent of patients with ulcers show no symptoms whatever of so-called vagotonia. The clinical value of the word "vagotonia" is very small.—J. K.

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ENDOCRINOLOGY

THE BULLETIN of the ASSOCIATION

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INTERNAL SECRETIONS

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HYPOPHYSEAL DISORDERS WITH SPECIAL REFERENCE TO FROELICH'S SYNDROME (DYSTROPHIA ADIPOSOGENITALIS)

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The question of obesity or its congener, fat dystrophy, has not received much study or attention until quite recently. This was undoubtedly due to the lack of knowledge concerning the fundamental principles involved in the process of fat metabolism. Formerly, excessive accumulation of fat was usually regarded as the result of surcharging by overeating and underexercising, a normal metabolic function, a condition designated exogenous obesity. Since a better knowledge has been gained of the physiological function of the endocrine glands, the fact has become definitely established that the vast majority are due to a disturbance of function of certain of these glands, which form is designated endogenous obesity.

Although it has been observed from antiquity that eunuchs show changes in skeletal development with a type of fat distribution differing from the normal, it was not until Reverdin and Kocher (1882-1883) associated a form of obesity with the loss of function of the thyroid after complete extirpation, and Froelich in 1901 described a syndrome with obesity and genital hypoplasia associated with hypophyseal deficiency, that its full clinical significance was comprehended.

The discussion in this paper will be limited to the hypophyseal form, presenting a review and correlation of the most valuable literature on the subject to date.

The obesity, as well as the other features embraced in the clinical syndrome described by Froelich in 1901, was previously recognized and referred to as cerebral adiposity, and although lesions of the pituitary were demonstrated in some of the cases, no definite relation between the two was suspected.

As regards the earlier literature, Dr. Garrison of the Surgeon-General's Library, stated the following: "The only early reference to pituitary obesity known to me is the case given by Barnhard Mohr in Wochenschr. f.d. ges. Heilkunde, Berlin, 1840, VI, 565-571. This is the solitary case of any importance before the time of Froelich." This patient, a woman 47 years old, had an enlarged hypopysis cerebri, due to sarcoma causing cerebral pressure, especially upon the optic nerve and chiasm producing visual disturbance. In addition she had vertigo, periodical headaches, clumsy movements, mental deterioration, and finally, symptoms of apoplexy. Unusual obesity developed with extraordinarily large abdominal dimensions, especially in the transverse diameter. Autopsy showed a very large degenerated pituitary gland, an enormous deposit of subcutaneous fat, 3½ inches in thickness, with increase of fatty tissue in the heart, liver, and about the intestines.

Froelich's case was that of a boy fourteen years old, who had suffered for two years with headaches, vomiting, and a rapidly developing obesity with infantilism of the genitalia. To this picture Bartels gave the name dystrophia adiposogenitalis. The hypophyseal origin of the disease was not unanimously accepted until Cushing and Ashner by experimental investigation successfully demonstrated that obesity and genital hypoplasia developed in hypophysectomized animals, and further they definitely stated that adiposity was due to posterior lobe deficiency.

Cushing explains these phenomena as follows: Functional hyperplasia of the anterior lobe stimulates tissue growth, especially the skeletal, cuticular, and subcuticular tissues; conversely, anterior lobe insufficiency should inhibit skeletal growth and sexual development. Functional hyperplasia of the posterior lobe appears to be more concerned with tissue metabolism, for when rendered inactive by disease or compression, meta-

bolic processes are checked, and high tolerance is acquired for carbohydrates, which are promptly stored up as fat.

Recent investigation by Robertson on the influence of the anterior lobe of the pituitary upon growth through its growth controlling constituent, tethelin, emphasizes the fact that over-activity leads to gigantism or acromegaly, according to the age when the disease first manifests itself; and he asserts that under-activity, the result of pathological conditions partially or totally destroying the function of the anterior lobe, produces the clinical picture of adiposity, underdevelopment of the skin, bones and sexual organs, and secondary sexual characters.

Goetsch obtained very interesting results from pituitary feeding experiments upon rats. Feeding of the anterior lobe extract caused increased weight and greater and more vigorous body growth and development over the control. The period of complete sexual development is shortened by at least one-third of its normal time, and the sexual instincts are early awakened. The feeding of the posterior lobe extract does not stimulate growth nor the development of the sex glands.

Feeding experiments of endocrine diets on normal and hypophysectomized tadpoles by E. Smith show that the latter were retarded in growth on all diets except the glandular lobe of the hypophysis. The retardation of growth in hyophysectomized tadpoles was entirely prevented by a diet of anterior lobe, so that these tadpoles exceeded in size either normal tadpoles on a control diet or controls fed glandular lobe.

SYMPTOMOLOGY

The most striking symptom in hypophyseal dystrophy is obesity with a fairly definite type of fat distribution. Fat is accumulated chiefly about the hips, upper thighs, lower abdomen, and mons veneris. In addition, Biedl observed a remarkable deposition of fat in the omentum and retroperitoneal space. There is a type in which the fat distribution is more general, involving the mammae, shoulders and supra- and infra-clavicular areas; the hands and arms, legs and feet remain normal. This occurs as a familial type and presents a picture of obesity somewhat intermediate between thyroid deficiency and hypophyseal deficiency, and is probably due to a functional hypoplasia of the sex glands, secondary to hypopituitarism.

Integumental changes are also quite characteristic. The skin is remarkably delicate and white, sometimes described as alabaster. It is mostly cool to the touch, usually dry and sometimes exfoliates. The hands and feet are usually small. The fingers taper and the nutrition of the nails is normal, although

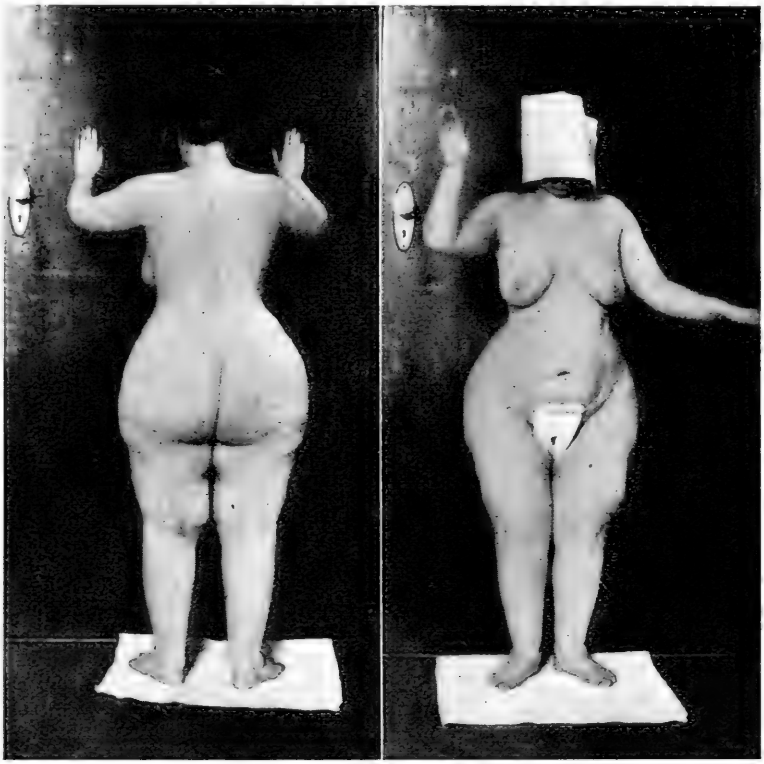

Fig 1 and Fig. 2—Illustrate case of dystrophy adiposogenitalis in which the fat is accumulated below the waist.

the crescents at the base are often absent. If the disease manifests itself before puberty the stature remains small; sexual development is delayed, which delay may result in permanent sexual infantilism.

Hewett, in a study of infantilism as related to pituitary disease, states that the symptoms may be roughly divided into two classes: Those due to mechanical effects of the tumor and those which seem to be due to an altered internal secretion. To

the former group belong the headache, vomiting and visual disturbances. The most characteristic of them, primary optic atrophy and unilateral or bilateral temporal hemianopsia, are due to direct pressure on the optic chiasm or nerves. To the latter group belong the sexual disturbances, (retarded sexual de-

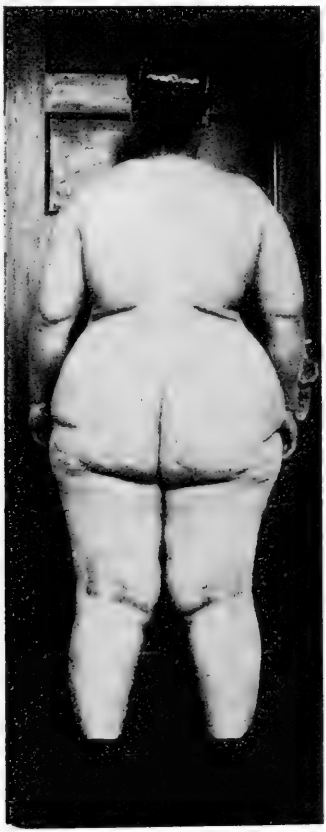

Fig. 3—Represents a type of case in which the fat distribution is more general.

velopment, cessation of menses, etc.) the obesity, the stunted growth, and possibly the occasional diabetes insipidus—these are due, in part at least, to diminished secretion of the anterior lobe of the gland. He concluded that infantilism associated with disease in or near the pituitary gland may resemble either the Brissaud or Lorain type.

The Brissaud type of infantilism in which the characteristics of infancy or early childhood are especially retained is described as follows: "Round, chubby face, lips projecting and plump, small nose, smooth face, fine clear skin, fine hair, eyebrows and eyelashes scant, eyes prominent, large round cheeks, infantile face and head, skeleton under-developed, neck short and chubby, body long and cylindrical, abdomen prominent, limbs round and large, layer of fat over the whole body, infantile pelvis, lumbar lordosis, rudimentary sexual organs, no hair except on head, high-pitched voice, thyroid small, mind slow, retardation of ossification, absence or retardation of second dentition."

The Lorain type, has been described as follows: "Small stature, delicately formed, slender skeleton, skin soft and pale, large shoulders, lower extremities long and slender, trunk relatively small, infantile sternum and pelvis, epiphyses normally united, no fat, abdomen normal, finely chiseled face, voice high, neck long, genital atrophy, absence of or slight secondary sexual characteristics."

In the female the menses are irregular or absent, and if the condition arises before puberty there are hypoplasia of the genitalia and deficient development of secondary sexual characters with absence or deficiency of hirci and crines pubis; the latter if present assume the angular outline or masculine tendency.

The male in early life shows the same disposition to sexual infantilism with absence or delayed secondary sex characters, such as the absence of hair on the face or body-hair, etc. The tendency to reversal of sex type is more marked in the male. In addition to the beardless face, horizontal crines pubis and delicate skin, other signs of feminism present are broad pelvis, moderate degree of genu valgum, rounded limbs, small feet and hands with tapering fingers and occasionally well developed breasts.

If the disease develops in adult life, retrogressive changes take place in the sexual organs with a corresponding diminution or loss of functions, with the same tendency of the features to revert to the opposite sex. Sugar tolerance is very much increased. The metabolic functions are below normal, which accounts for the subnormal body temperature, subnormal blood pressure, slow pulse and diminished carbon dioxide exchange. The basal metabolic rate as observed by Plummer is usually from

16 to 18 per cent below normal, and frequently 25 per cent or more.

Pardee describes as one of the first symptoms of pituitary disease, headache, which he calls "Pituitary" headache. It has three characteristics: (a) Its location; (b) Its duration and persistence; (c) Its relief under specific medication.

His conclusions are as follows: (1) Pituitary disturbances constitute a fairly common cause of headache; (2) Pituitary headache is located between the temples, deep in behind the eyes and is accompanied by dyspituitary signs; (3) Abnormality of the sella turcica is demonstrable in almost every case of pituitary disease; (4) Administration of the whole gland cures these headaches and the accompanying symptoms in a large percentage of cases, provided there is not a progressive neoplastic growth.

Cushing observed certain mental disturbances in hypopituitarism ranging from mild psychosis to extreme mental derangement, epilepsy, impairment of memory, lack of concentration and drowsiness. And Beverly Tucker ascribes certain forms of adolescent psychosis to hyposecretion.

Polyuria is a frequent symptom, and occasionally a true diabetes insipidus develops. The condition has been attributed to posterior lobe deficiency as a result of some lesion. Since the exhaustive studies of Houssay and Leschke this view is open to doubt. Houssay experimentally established a cerebral basal zone within which pricking generated polyuria. The posterior lobe of the pituitary may constitute a part of this zone, although he does not deem it probable. This zone is limited in front by the optic chiasma and behind by the penduncle protuberance.

Leschke pointed out the fact that while lesions of the hypophysis, such as trauma, sarcoma, metastatic carcinoma, tuberculosis, syphilis, etc. have been demonstrated in cases of diabetes insipidus, similar lesions in the midbrain, especially those involving the tuber cinereum may produce diabetes insipidus with the hypophysis intact. Removal of the gland itself does not produce polyuria; on the other hand a piqure in the tuber cinereum does produce polyuria. He regards the hypophyseal lesion as incidental, and if associated with diabetes insipidus, the latter condition is due to pressure or extension of the lesion into the tuber cinereum. Cases of diabetes insipidus have been

reported by Schüller and Christian, in which extensive pathological changes occurred in the bones of the skull. Dr. McLean and myself reported a case of cranial bone lesion in a girl with lues, who had severe diabetes insipidus and well marked dystrophy adiposogenitalis, but no abnormality of the sella turcica.

The degree of fat dystrophy varies according to the extent of the impairment of the function of the hypophysis. In this respect it is somewhat analagous to thyroid deficiency. When the functional impairment is slight a mild form develops (forme fruste) with very little genital hypoplasia or fat dystrophy, corresponding in degree to Kocher's thyreopenia. When the functional capacity is very much lowered Froelich's syndrome develops with its characteristic clinical picture. This phase corresponds to Gull's disease of the thyroid or the myxedematous syndrome.

Many of the cases advance into a state of cachexia. Most of the reports of this condition have appeared in the German literature and are described as hypophyseal cachexia. Simmonds published the reports of three cases of severe chronic cachexia ending fatally, in which the pathological findings showed total destruction of the hypophysis,—in two of the cases from neoplasm, in the other from an old embolus. In a later article he attributes cachexia to destruction of the anterior lobe and cites four cases in support of this view. The cachexia usually occurs in the fatal cases, although recoveries from the symptoms of cachexia under hypophyseal feeding have been reported.

INTERRELATION OF GLANDS

Many of the symptoms of dystrophy adiposogenitalis are dependent upon the close interrelationship between the function of the pituitary and other ductless glands. This feature is especially important in its relation to the sex glands. Clinically and experimentally it has been demonstrated that anterior lobe deficiency produces hypoplasia of the sex glands or the genital syndrome, and posterior lobe deficiency lowers the carbohydrate metabolism.

After primary change in the sex glands, as in pregnancy or after castration, there is a consequent hyperplasia and hypertrophy of the pituitary gland. The interesting contribution on this subject by Goetsch has been of great therapeutic value in the treatment of functional conditions of both glands.

In underfunction of the thyroid, as in cretinism or myxoedema, Eichorst observed changes very similar to those following loss of function of the gonads. At first the pituitary becomes larger and hyperaemic, hemorrhages are often observed, the glandular cells grow, the chromophile cells degenerate. Later, connective tissue changes take place with glandular cell atrophy; necrosis and cysts are formed in the connective tissue; the gland becomes smaller.

TREATMENT

The advancement along the lines of therapy in pituitary disease has kept pace with the progress made in the study of the physiology and symptomology. Treatment has become more rational, and, as is the case in disorders of other glands of internal secretion, organotherapy is most efficacious in the deficiency syndromes.

In hypopituitarism these include:

Anterior Lobe Deficiency—

1. Disturbance of growth (infantilism).
2. Development of obesity (dystrophia adiposogenitalis).
3. Genital hypoplasia (infantile genitalia with frigidity, sterility, and amenorrhea).
4. Temperature anomalies.
5. Cachexia Hypophysopriva.

Posterior Lobe Deficiency—

1. Hypotension.
2. Increased sugar tolerance.
3. Diminution of basal metabolism rate.

In addition there occur pressure symptoms—headache, vertigo, vomiting, etc.

Polyuria (diabetes insipidus), which was formerly attributed to posterior lobe deficiency or hypoactivity of the pars intermedia, is not included in the above classification of symptoms, owing to the results of the clinical and experimental studies of Houssay and Leschke mentioned previously.

Fortunately most of these indications, if they can be influenced by treatment, are controlled by the administration of the hormones of the thyroid, pituitary and gonads, either singly or combined. The thyroid is probably the most important. This gland has been called a sex gland because it is a powerful stimulant to the sex organs; and the presence of the thyroid hormone,

as well as the pituitary, is essential to normal function of the gonads. The thyroid is the greatest stimulator of metabolism known, acting, probably, by its effect in increasing muscle tonus through irritation of the automatic nervous system. The thyroid is also a stimulator of the pituitary function. It is thus easily conceivable how thyroid extract would favorably influence the majority of the groups of symptoms above mentioned. Through its influence on metabolism it has a tendency to improve the fat dystrophy, decrease sugar tolerance and increase the rate of basal metabolism. The changes in the metabolic rate will favorably influence the subnormal temperature, slow pulse, hypotension, dry skin, etc. Through its accelerating influence on the pituitary and sex glands it will augment the effect of pituitary and ovarian extract upon sexual hypoplasia and hypogonadism, as well as on infantilism of hypohyseal origin.

Anterior pituitary lobe has its greatest value in cases of dystrophy adiposogenitalis. In combination with thyroid it has the effect of redistributing the fat and increasing the functional activity of the sex glands, besides correcting some of the anomalies due to hypoplasia of the genitalia.

Most of these cases are not pure hypopituitarism; symptoms referably to thyroid and ovarian deficiency are frequently present. It is owing to this fact that better results are obtained by combining the respective hormones than by giving them singly.

In a study of a group of cases with hypophyseal fat dystrophy it has been the writer's experience that mere loss of weight is no adequate criterion as to the effect of treatment on the fat dystrophy. Patients under treatment must be systematically measured and measurements recorded. The most striking example was a woman whose hip circumference was reduced 7½ inches while under treatment, without her losing weight. By mensuration it was definitely established that the fat is actually redistributed in certain types of these patients. As a rule the measurements of circumference increase from the waist up, and decrease from the waist down. The dose employed in the treatment of these cases was 2½ grains of anterior pituitary lobe, (Parke, Davis & Co.), 2 or 3 times a day, and thyroid from one-half to one grain 2 or 3 times a day. Small doses of ovarian or testicular extract were added in some cases. To my mind the latter is of doubtful value.

Polyuria. The chief symptom of diabetes insipidus, which is occasionally associated with hypopituitarism, can best be controlled by the hypodermic administration of extract of the posterior lobe and infundibulin. In my personal experience it has

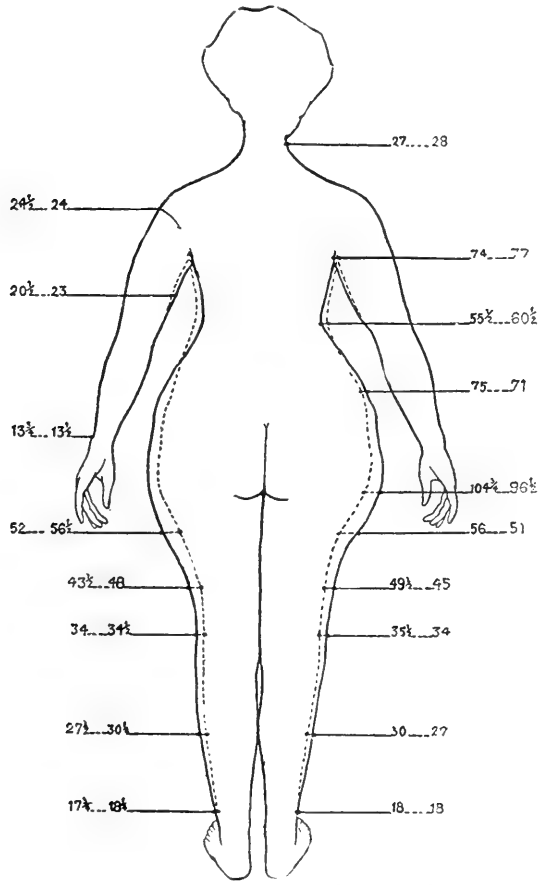

Fig. 4.—The dark continuous line and figures represent the body outline and circumference measurements before the administration of anterior pituitary lobe and thyroid gland. The dotted lines and figures represent the same 8 weeks later.

Note the increase in circumference from the waist up and decrease below the waist.

been found that 1 c.c. of pituitrin every day or two will absolutely control this annoying symptom, but the amelioration is only temporary. The remarkable effect of a single dose of 1 c.c.

pituitrin promptly reducing the 24 hour urine from 13000 c.c. to 1800 c.c. the next day led to the view that diabetes insipidus is due to posterior lobe deficiency; the oral administration has no effect.

The so-called pituitary headache is often promptly relieved by the administration of pituitary extract; Pardee recommends whole gland in doses of ½ to 2 grains three times a day. When the headache is relieved the dose is diminished. Timme in his article on a "New Pluriglandular Compensatory Syndrome" lays stress on the importance of recognizing these cases at their onset when the best results are obtainable by the early administration of pituitary substance. He considers pituitary gland almost a specific. The whole gland in doses of 2 to 3 grains, three times a day, is given in appropriate cases. This he supplements at times with pituitrin hypodermically, 0.5 to 1 c.c. per day or alternate days, for one or, at most, two weeks. With genital delay he occasionally feeds anterior pituitary lobe, which gives fair results. Atropine is recommended in those cases with vagotonic symptoms. Timme states that pituitary feeding in itself alone produces highly satisfactory improvement in almost every case; headache disappears, fatigability diminishes, blood pressure and blood sugar content increase.

The whole gland substance is indicated in cases with symptoms of both anterior and posterior lobe deficiency. With the use of thyroid and pituitary, de Schweinitz and How obtained good results in a case of pituitary disease with the onset of blindness; vision was restored. Other observers reported similar results. The feeding of pituitary substance exerts a favorable influence on the cachexia. Cases are reported in which the symptoms were entirely relieved.

Except for the fact that operations on the hypophysis are fraught with considerable danger, the mortality rate being 10-16 per cent, the indications for surgical treatment of disease of this gland would be practically comparable to those for diseases of the thyroid. The complete removal of the gland or any process which totally destroys the substance will lead to the condition known as cachexia hypophysopriva; operations, therefore are restricted largely to tumors and are resorted to more frequently in conditions associated with hyperfunction.

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THE RELATIONSHIP BETWEEN THYROID AND PARATHYROIDS

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The present communication is in the nature of a recantation.

We shall make no attempt to give a complete historical account of the discussion of this subject. Such an account up to the year 1912 has been given by Vincent (10) and up to 1913 by Biedl (1).

The earlier investigators looked upon the parathyroids as embryonic thyroids and a belief in some kind of morophological and physiological relationship between the two glands has persisted up to the present time. But since the appearance of the papers of Vassale and Generali (7, 8, 9) the majority of authors have regarded the parathyroids as organs *sui generis*.

The experimental evidence for and against this view has been somewhat contradictory. Vincent and Jolly (11, 12) found that on microscopical examination of parathyroids left *in situ* after removal of the thyroid an alteration in structure had occurred. The parathyroid approximated in appearance to ordinary thyroid tissue. Their experiments were carried out on cats. Similar changes after thyroidectomy were found by Halpenny and Thompson (4) in the parathyroid of a dog. Halpenny (3) later reported a somewhat more doubtful instance occurring in a rabbit.

These results have not been generally accepted. Although the rabbit, among laboratory animals, lends itself in a special way (from anatomical considerations) to experiments bearing upon this problem, we can find in the literature very few detailed accounts of work directed towards this point carried out upon the animal in question.

It was in rabbits that Gley (2) rediscovered the external parathyroids, and it is undoubtedly true that it is largely to this author that we owe our present knowledge of the importance of these bodies. In his earlier papers on the subject, Gley sup-

ported the view that the parathyroids could (after removal of the thyroid) develop into thyroid. Later on he changed his view though he has maintained a belief in some kind of relationship between the two structures. Biedl (1) reports that, although he has noticed very considerable hypertrophy of parathyroids (in the rabbit) left behind after removal of the thyroid, yet he has never seen any structural changes in the former under these circumstances.

The present series of experiments has been carried out upon rabbits of different ages, some of them being full-grown, others only half-grown. The thyroid has been carefully extirpated under aseptic conditions, and with it, of course, both internal parathyroids, leaving behind one or both external glandules. The animals have been kept under the best possible conditions after the operation for periods varying from seven to eight hundred days, but of twenty-two animals which survived the operation for more than twenty-four hours, two have died within a few weeks of infections which are so common after thyroidectomy. The rest, to the number of twenty, have survived for periods varying from eighteen to eight hundred days, after which time the parathyroids were removed and examined microscopically. In some instances the animals were allowed to live after the second operation.

Our results are briefly as follows:

In none of the parathyroids have we found any distinct traces of vesicle formation. It is possible that there are changes of other kinds and of less significance in the glandules which had been left behind, but on this point we do not wish to be positive.

This series of experiments, then, does not lend support to the view that parathyroids left behind after thyroidectomy become converted into thyroid tissue. It is possible that the anatomical differences between rabbits on the one hand and cats and dogs on the other, involves also a difference in the potentiality of parathyroid to change into thyroid. Notwithstanding these considerations, and in spite of the fact that negative results are in such cases of less value than positive, we must confess that these experiments have led us to suspect the possibility that there were some errors of observation in the cases reported by Vincent and Jolly and Halpenny and Thompson. It is clear

that in dogs and cats where the parathyroids are in close proximity to the thyroid, there is a great danger of leaving behind a shred of thyroid tissue at the operation for thyroidectomy. This might subsequently be mistaken for transformed parathyroid. This suspicion is at any rate strong enough to suggest that further careful experiments upon animals other than rabbits ought to be carried out.

A few observations of another character bearing on the functions of the thyroid-parathyroid apparatus have been made in the course of these experiments. In the first place it may be desirable to call attention to the fact emphasized by Vincent and Jolly and other observers that after thyroidectomy, animals are particularly liable to various infective diseases, particularly of the respiratory tract. Again, stress must be laid upon the observation that none of our animals suffered from a condition which resembled in the remotest degree the disease known as myxoedema in the human subject. It is true that some of them suffered from falling out of hair and other skin diseases, but it is also true that many control animals suffered in the same kind of way. In none of the animals, young or old, was there any puffiness of the face or swelling of the subcutaneous tissue of any part of the body.

It is also important to note that we have not seen distinct tetany in any of the animals, and some have survived a removal of the remaining parathyroids for several weeks without symptoms. We are aware that tetany does sometimes occur in rabbits, but the precise conditions which determine its onset are by no means clear.

Noël Paton (5) has recently urged the functional distinctions between thyroid and parathyroids, and has suggested that in rabbits the explanations of a comparatively large proportion of survivals after complete thyro-parathyroidectomy is due to the fact that parathyroid tissue nearly always occurs in the thymus in these animals (Pepere, 6).

In our notes of the earlier experiments we find frequent record of hypertrophy of remaining parathyroids. But the measurements made in the later experiments did not lend support to the view that this hypertrophy is generally found. We thought it best, therefore, to omit all such statements, though

our impression is that in many cases there was distinct hypertrophy. This accords with the statement of Biedl *(vide supra)*.

It was suggested to us by Sir E. Sharpey Schafer that some experiments of the character described above should be carried out in dogs and cats. Such experiments can only be performed in selected animals, and we have had the misfortune to lose by accident two dogs which had lived for some time with only one parathyroid, the thyroid and three parathyroids having been removed.

We beg to acknowledge the valuable assistance of Mr. John Carmichael in all the experiments.

PROTOCOL OF EXPERIMENTS.

Exp. 1. Nov. 11th, 1916. Rabbit, female, full-grown. Thyroid and both internal parathyroids (as well as the left external body) removed. On Feb. 22nd (103 days) the animal was killed, and the right parathyroid examined. On microscopical examination it showed no structural changes.

Exp. 2. Nov. 17th, 1916. Rabbit, male, full-grown. Thyroid and both internal parathyroids removed, both external glandules left behind. The animal remained well till Jan. 6th (50 days), when the two external parathyroids were removed under aseptic conditions and the animal allowed to live till Jan. 17th, when it was killed. Tetany did not develop. The parathyroids removed on Jan. 6th showed no signs of vesicle formation. At the *post-mortem* no accessory bodies could be found.

Exp. 3. Nov. 18th, 1916. Rabbit, male, full-grown. Thyroid and both internal parathyroids removed, along with the right external parathyroid. The animal remained well until Jan. 18th (61 days), when the left external body was removed for microscopical examination. The animal was then allowed to live till Jan. 31st, when it was killed. The left glandule showed no structural changes. No symptoms of tetany developed after its removal, and on *post-mortem* examination, no accessory parathyroids could be found.

Exp. 4. Nov. 22nd, 1916. Rabbit, male, full-grown. Thyroid and both internal parathyroids removed. Both external bodies left behind. The animal remained well until Feb. 1st (71 days), when a second operation was performed and both the external parathyroids removed. No symptoms of tetany supervened and the rabbit was killed on Feb. 20th. Neither of the parathyroids showed any distinct structural changes.

Exp. 5. Nov. 23rd, 1916. Rabbit, female, full-grown. Thyroid and both internal parathyroids removed. Both external bodies left *in situ*. On Dec. 9th (16 days) the animal died of pneumonia. The external parathyroids showed no changes.

Exp. 6. Nov. 23rd, 1916. Rabbit, female, half-grown. The thyroid, both internal, and the right external parathyroids were removed. On Dec. 1st (8 days) the animal died of pneumonia. The external parathyroids of the left side had undergone no structural changes.

Exp. 7. Nov. 25th, 1916. Rabbit, male, full-grown. Thyroid with the two internal parathyroids was removed, leaving behind both external bodies. The animal remained in good health till Feb. 28th (95 days) when it was killed. No vesicular formation could be detected.

Exp. 8. Dec. 1st, 1916. Rabbit, male, full grown. Thyroid and internal parathyroids removed. Both external glandules left *in situ*.

Remained well till Mar. 27th (115 days). No sign of vesicle formation was found in the external glandules.

Exp. 9. Dec. 2nd, 1916. Rabbit, male, full-grown. Thyroid and internal parathyroids removed, the two external bodies left *in situ*. Remained well till Mar. 27th (114 days) when the two external parathyroids were removed. They showed no structural changes.

Exp. 10. Dec. 4th, 1916. Rabbit, male, full-grown. Thyroid and internal parathyroids removed. External glandules left *in situ*. On Feb. 28th (86 days) the animal was killed. No changes in external parathyroids.

Exp. 11. Dec. 7th, 1916. Rabbit, female, full-grown. Thyroid, both internal and left external parathyroids removed. On Feb. 20th (75 days) the rabbit was killed and the right external parathyroid examined. This showed no structural changes.

Exp. 12. Dec. 7th, 1916. Rabbit, male, full-grown. Thyroid and internal parathyroids removed, both external parathyroids left behind *in situ*. On Jan. 28th (52 days) the animal died of intercurrent disease. Parathyroids showed no structural changes.

Exp. 13. Dec. 18th, 1916. Rabbit, female, full-grown. Thyroid, internal parathyroids and left external body removed. Killed on Mar. 27th (99 days). No change in right external parathyroid.

Exp. 14. Dec. 18th, 1916. Rabbit, male, full-grown. Thyroid, both internal and right external parathyroids removed. Died on Mar. 2nd (74 days) of pneumonia. During the last few months the hair had been falling out, first in patches round the neck, then on one side of the body. The parathyroid left behind at the operation showed no structural change.

Exp. 15. Feb. 3rd, 1917. Rabbit, male, half-grown. Thyroid and internal parathyroids removed, both external glandules left behind *in situ*. Animal remained well till Mar. 26th (52 days) but did not increase in size or weight. The parathyroids did not show any changes.

Exp. 16. Feb. 10th, 1917. Rabbit, male, half-grown. Thyroid and internal parathyroids removed. Both external parathyroids left. Remained well till Mar. 26th (44 days) but did not increase in size or weight. The external parathyroids did not show any structural changes.

Exp. 17. Oct. 14th, 1917. White rabbit, female, young and in good condition. Wt. 1.5 K. Thyroid and internal parathyroids removed. Both external parathyroids left. The right glandule measured 7 mm. x 2.5 mm. and reached from the 10th to the 14th rings of the trachea. The left body was 7 mm. x 2.75 mm. and extended from the level of the 5th tracheal ring to that of the 10th.

On Dec. 23rd, 1919, the animal, whose weight had reached 2 K, was killed. The right parathyroid measured 5.5 mm. x 2 mm., the left 7.5 mm. x 2.5 mm. Both were found to be unchanged histologically.

Exp. 18. Oct. 30th, 1917. Rabbit, light brown, female, young. Wt. 2.1 K. Thyroid and internal parathyroids removed. Both external glands left behind. The right one measured 8 mm. x 3 mm. and lay opposite the 7th-11th rings of the trachea. The left measured 9 mm. x 3.5 mm. (Tracheal rings 9-14).

On Dec. 23rd, 1919, the animal was found to weigh 2.2 K and was in excellent condition. The right parathyroid now measured 8 x 3 mm. and the left was almost exactly the same size.

On examining the parathyroids histologically, we were astonished to find undoubtedly thyroid tissue in connection with the right glandule. But we are inclined to think that this really represented a true accessory thyroid which happened to be united to the external para-

thyroid. The left parathyroid was of normal microscopical appearance.

Exp. 19. Oct. 30th, 1919. Young white female rabbit weighing 1.6 K. The thyroid and both internal parathyroids removed. Both external bodies left behind. The left measured 7 x 2.5 mm. The right was not measured.

Dec. 23rd, 1919. The rabbit is normal and weighs 2.8 K. A shred of thyroid had been left behind. The left glandule measured 9 x 2.5 mm., the right 8 x 2.5 mm. The bodies were unaltered in structure.

Exp. 20. Dec. 23rd, 1917. Male rabbit, white, weighing 1.5 K. Thyroid, both internal parathyroids and the right external glandule removed, the left external parathyroid being left behind. The latter measured 8.3 mm. at one operation.

Dec. 23rd, 1919. The animal was killed. Wt. 1.8 K. Left gland now measured 15 x 4 mm. On microscopical examination appeared to consist of lymphoid tissue. (It is remotely possible that this body was not the parathyroid, but a lymph gland.)

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GYNECOMASTIA

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The term "gynecomastia," derived from the two Greek roots γυνή-feminine and μαστός-mamma, is applied to the occurrence in the male of a unilateral or bilateral mammary development resembling that of the female in its gross anatomical characteristics, with or without the production of milk.

This enlargement of the male mamma is not by any means a rarity, the phenomenon having been an object of recorded interest since the time of Aristotle (1), who reported having himself examined several individuals possessing the anomaly.

The surgical removal of the overdeveloped tissue was advocated at an early date, the procedure for which was apparently first described by Paulus Aegineta (2). Later the Persian physician, Ali-Ben-el-Abbas (3) and the Arabian, Abul-Casimir el Zahrâwi (4) reported the methods of operation in vogue in their respective countries, and Fabricius ab Aquapendente (5) developed a technique that savors much of modernity.

From the time of these early contributions to the subject down to the present medical literature contains many reports of the occurrence of abnormal enlargements of the male breast. Doubt, however, is thrown upon the validity of the interpretations of many of these cases as true gynecomastia, since there is often an evident failure to differentiate between the chronic or acute pathological conditions, such as carcinoma or breast abscesses, and the physiological mammary enlargement or *gynecomastia vera* unaccompanied by pathological stigmata.

In 1884-1885 Schuchardt (6) (7) (8) reviewed the literature concerned with new tissue formation in the male breast in three papers, two of which were devoted to the enlargements of the mammae due to obviously pathological conditions, while one detailed 272 cases which in all probability were authentic examples of true gynecomastia.

Gruber (9) who studied the subject intensively considered that true gynecomastia is a physiological phenomenon, and is

generally characterized by the non-painful and non-inflammatory character of the growth and the fact that it presents to the touch the characteristic lobulation of the female organ, unaccompanied by any of the usual clinical stigmata of pathological import.

Among the pathological causes of the enlargement of the male breast, carcinomata seem to occupy the center of the stage. But enchondromas, adenomas, fibromas, myomas, fibro-adenomas, lipomas, atheromas, cystic formations, tubercular growths, simple hypertrophy, calcification, and gummas have all been found at one time or another among those conditions leading to what Schuchardt (6) (7) calls the "Neubildung" of the male breast; while chronic induration and chronic mastitis can also be included if the term is taken in its widest sense.

In addition to the differentiation made between these and other pathological enlargements of the male mamma and gynecomastia there should be introduced a second group of overgrowths in which the enlargement consists simply of an additional deposition of fat or fibrous tissue in the mammary region. This latter type of increase was justly called by Gruber (9) adventitious or spurious gynecomastia.

Early studies of the gross and microscopic anatomical characteristics of the human breast were made by Gruber (9), Langer (10), Luschka (11), Momberger (12) and others. These seemed to show that there are no demonstrable differences in the manner of growth and development of the mamma of the two sexes up to the beginning of puberty. Even the post-partum enlargement as described in Halban's (13) diagram of mammary growth occurs irrespective of sex, as has been noted by Albers (14), Steifensand (15), de Sinèty (16), Opitz (17), Storch (18), Scanzoni (19) and others. Although the mode of development is apparently the same in the two sexes up to the commencement of the pubertal period, the degree of the enlargement is normally somewhat less in the male. At puberty, however, a marked quantitative differentiation appears to take place, and although the development and ramification of the glandular tissue occurs in both male and female, that of the former is normally of slight degree. Nevertheless, there does take place a progressive advancement in the development of the mammary elements of the male over the condition found in the infantile

stage, and the same type of change occurs which in the female leads to the production of the mammary volume characteristic of the sex. The main histological difference seems to lie in the apparent cessation of glandular growth just prior to the formation of the alveolar fundaments and a lessened fat and fibrous tissue infiltration.

On the other hand histological studies of Kölliker (20) seem to indicate that the growth of glandular tissue in the male with the formation of the end-bulbs is more extensive than is that of young nulliparous women of the same age. While this change is taking place the milk passages are ramifying by lateral buddings, as well as by multiple dichotomic terminal divisions, so that there are now found single canals connected with small groups of "Bläschen" of the second and third order. The ratio of the end-bulbs and the fundaments of the glandular "Läppchen" to the breast mass as a whole in young women and nulliparae is consequently very much less than in the male of the same age, while the glandular tissue development to and beyond the degree found in the male occurs in the female only during pregnancy and lactation. Although these two sets of observations have led to apparently conflicting conceptions of the differences of the glandular development occurring in the two sexes, a review of the observations on which the ideas were based would seem to indicate a greater degree of completeness in those of Kölliker (20). This latter investigator has clearly differentiated the histological structure and the developmental changes taking place in the female breast before, during and after childbirth, while the other workers are somewhat hazy in respects to these points. Accepting the histological studies of Kölliker (20) as being the more accurate, it is evident that this tissue presents similar morphological potentialities for assuming the function of milk-production as does the virginal mammary gland. Under certain, though rare, conditions this potential function apparently becomes actual, as will be later discussed. That it is the exception rather than the rule for this phenomenon to occur, the same being true for the enlargement of the male breast to a volume and texture resembling the female breast, may be due either to the presence in the organism of a chalone-producing tissue inhibiting the hyperplasia or to the absence of a specific hormone capable of bringing about such growth.

Turning now to the histological studies of the male breast in gynecomastia, it is seen that they have generally failed to take into account the glandular conditions found by Kölliker (20) in the normal male mamma during the second and third decennium as compared with those found in young nulliparous women. For while it is usually admitted that the manner of glandular ramification and end-bulb formation is the same in the gynecomast as it is in the female, it is frequently stated, with no added comparative evidence of a direct nature, that the degree of glandular tissue development in gynecomastia is not as great as is that in the female at puberty and during pregnancy, thus, obviously sliding over the differential histological picture obtaining during these two periods.

The most comprehensive summary of the microscopic conditions occurring in the abnormal physiological enlargement of the male mamma is given by Stieda (21), who considers that the term gynecomastia is only justified insofar as it is concerned with the outer form and volume increase of the male breast: that it should not include or express a histological uniformity or similarity of such a breast with the functioning female organ. The condition consists in a hyperplasia of the normal tissues of the male, primarily the connective tissue, which invades the surrounding fat tissue: the fat and the glandular tissue take some part in the hyperplasia it is true, but it is a minor one. Structures similar to acini are found but not to the same degree as in the normal female breast. In general this conception is supported by the histological findings of Scheiber (22), Ingleby (23), Galliet (24) and others, although the statements made comparing the findings with the female breast do not take into account the original structure as described by Kölliker (20). It is accordingly highly probable that the gynecomastic breast is but little if any different in its glandular development from the breast of the young virginal or nulliparous female and is accordingly potentially capable of assuming the elaboration of milk provided the appropriate stimulus be afforded.

The onset of this anomaly may take place apparently at any time after the organism commences the development of the sexual changes accompanying puberty, although Foot (25) reports a case of so-called pre-pubertal gynecomastia of the right breast that was painless, non-inflammatory and presented a dis-

tinctly lobulated structure in a boy of twelve, and Ingleby (23) and Moorehead (26) have recorded similar occurrences in boys of eleven and twelve years, all of whom presented no other signs of approaching puberty. Such a designation if tending to dissociate the phenomenon from the influence of pubertal stimuli is hardly justified since it is pretty generally accepted that the first faint stimuli heralding the approach of puberty are beginning to make themselves felt at this time, or even earlier (Heyn 27). However, it is during puberty that gynecomastia makes its appearance most frequently, Villeneuve (28), Bertherand (29), Gruber (9), Weber (3) and others citing many instances of the anomaly occurring at this period.

But the occurrence of the anomaly is not restricted to the pubertal period, since Curveillier (31), Galliet (24), L'Abbé (23) and Bryant (33) have all noted its development in men from 20 to 30 years of age. It is possible that these individuals were examples of a delayed sexual development (27). The same objection cannot be raised to the cases reported by Scheiber (22) and others in which the enlargement did not occur until well along into middle life nor to those individuals who had reached a ripe old age before the development of the gynecomastia as reported by Hall (34), Gorham (35) and Villeneuve (28). These cases are evidently definitely dissociated from direct connection with the changes taking place in the organism at puberty.

Since the incidence of gynecomastia in most cases is near the time of puberty, one is inclined to consider the phenomenon as in some way associated with an abnormality of the endocrine stimuli concerned with adolescence—particularly since it is during this period that the gross enlargement of the female mamma occurs. This latter phenomenon is generally agreed to be due to stimuli derived from glands of internal secretion. Such a conception, however, does not exclude the possibility that those cases occurring later than the adolescent period are also associated with abnormalities in gonad activities, the nature of which is unknown.

Gynecomastia may occur either unilaterally or bilaterally. No attempt has been made to compile the statistics relative to the locus of incidence, but it is interesting to note that out of forty-five cases Gruber (9) found that ten were unilateral, five being on the right side and five on the left.

The condition seems to be rarely hereditary in character, and those instances in which it has occurred in more than one generation may be considered as expected under the general law of probability. Savitsky (35) has reported a peasant gynecomast whose father, elder brother, and cousin were also similarly afflicted.

The familial occurrences of the phenomenon are also rare, Schaumann (20) finding but two instances where the anomaly occurred in more than one member of the family. This lack of definite, positive evidence that either hereditary or familial characteristics are concerned in gynecomastia allows the assumption that it is an untransmissible sport.

Whether actual milk production occurs in gynecomastia has been questioned. Stieda (21) and others seem to have failed to observe any consistent or valid evidence of this. Nevertheless, the literature contains many presumably authentic reports of instances of the secretion of milk and nourishment of the young by gynecomasts, Humboldt, Franklin (37), Schmetzer (38) and others giving excellent descriptions of personal observations of such cases.

The chemical analysis of "buck-milk," as the secretion of the male breast is usually called, shows that it can hardly be considered as a complete food for the growing infant. One analysis given by Schmetzer (38) in 1837, showed 1.23 per cent of fat, 3.58 per cent of alcoholic extractives, 1.50 per cent of water extractives and 1.18 per cent of insoluble materials. Nevertheless, there are instances reported of infants thriving on milk obtained from gynecomasts and it is accordingly within the bounds of probability that if the reported analyses had been derived from such specimens quite different results would have been obtained.

It is a generally accepted theory that for milk to be secreted there must be produced by or introduced into the organism a substance or substances stimulating the mammary glands to take up and carry on the function of lactation. Although it is well known that there are substances elaborated by endocrine glands common to both sexes that have been found to act as galactagogues, the source of the actual stimulus to lactation in the male is decidedly uncertain.

Gruber's (9) studies of the individuals coming under his observation and reported in the literature led him to consider that true gynecomastia is the result of a physiological process. He divided the gynecomasts into two groups depending upon whether or not there was a concurrent abnormality of the genitalia. Those whose genitalia appeared normal were classed as essential gynecomasts, while those with abnormal genitalia were considered as examples of acquired gynecomastia.

The anamnesis of the gynecomastic individuals coming to record gives validity to the conception that the condition may be acquired and associated with abnormalities of the genitalia. There is evident a strikingly frequent occurrence of defective or pathological states in these organs. Not every case of pathological or defective testicles exhibits a gynecomastia nor every case of the anomaly exhibits defective or pathological conditions of the genitalia, but there is found in many gynecomasts a simultaneous disturbance in function and structure of the procreative apparatus. Not only the testicles but also the penis seems to be incompletely developed in many cases. Schaumann (20) reports six cases of gynecomastia accompanied by immature genitalia. Malformations such as hypospadia and epispadia accompanied by atrophic testicles or penis are frequently noted. Definite mammary hypertrophy has been known to accompany testicular atrophy caused by orchitis following parotitis (Lereboullet 39); while Martin (40) was of the opinion that castration may bring about a similar result. It is not improbable, however, that the mammary enlargement in the latter cases is more in the nature of a spurious gynecomastia than of any other form. Laurent (41), Gorringe (42), Galliet (24), Weber (30) and Paulicky (43) all report similar cases in which there was atrophy, defect or pathological condition of the testicles accompanying the gynecomastia; and the evidence is sufficiently extensive to indicate the validity of Biedl's (44) summary conclusion that the anomaly is due in many instances to such conditions.

Turning for the moment to the so-called essential type of gynecomastia in which there is no evident abnormality of the genitalia, it is found that Coes (45), von Nelaton (47), Paulicky (43) and others have observed and reported such instances. Moreover, definite statements are frequently made that the sexual libido and potency in such individuals is entirely normal.

It is accordingly evident that gynecomastia may or may not be accompanied by a disturbance of the generative instincts and functions, from which it can be inferred that the stimulus to the anomaly formation does not necessarily lie in a perversion of any normal erotic hormone.

As might be expected, however, certain types of gynecomasts do present evidence of a lack of sexual desire and potency. A survey of the literature reveals that this expression of fundamental instinct was never developed at all or began to recede with the onset of the anomaly when accompanied or preceded by the appearance of defective genitalia. One case of sexual perversion is reported by Raggi (48) in which insanity was accompanied by a distinct mammary enlargement which receded to normal volume on recovery.

The mental trend and emotional reactions of the greater number of the gynecomasts seem to lie along those lines ordinarily reserved for the opposite sex. There are exceptions, but as a rule they give evidence of a preponderance of feminine traits where masculine would be expected. In many instances such an impression may have been enhanced in the observer by the lack of abundant hirsuties and the presence of a feminine voice. The degree to which this is true is indeterminable.

However, since the anomalous enlargement of the male breast is frequently accompanied by an atrophy, defect, or pathological condition of the male genitalia, and is usually associated with some deviation from the normal primary and secondary sexual characteristics of the male, the assumption is justified that the condition is a sequel of an abnormal endocrine trend in the organism. But two reports showing a possible direct associated endocrine disturbance accompanying gynecomastia, aside from those cases in which there are present abnormalities of the genitalia, have been found in the literature. The first one of Wagner (49) is, however, doubtful, due to the lack of general information existing at the time. Freeman (50) reports a hyperthyroidosis accompanied by enlargement of the mamma, but the existence of a causal relationship is hardly proven on the basis of this single observation. The results of the observations recorded up to the present may now be briefly summarized.

Gynecomastia is a physiological enlargement of the male breast to the volume and appearance of the normal female mam-

ma. It may be non-painful and non-inflammatory; to the touch it gives the feel of lobulation found in the female breast; it is not accompanied by pathological stigmata. It may arise at any time after the beginning of puberty or after the termination of the changes taking place at this period, but taken by and large, the greater number of cases have their incidence during the pubertal stage. It may occur as a one-sided enlargement, but possibly is more frequently bilateral. Heredity seems to play no part in its development. Apparently authentic reports give evidence that the gynecomastic breast may produce milk, which conclusion is supported by the histological studies of Kölliker. These seem to indicate a structural similarity of the development of the normal male mamma to the virginal or nulliparous breast. Finally, the anomaly may or may not be accompanied by atrophy, defect, or pathological condition of the genitalia.

Is there any experimental justification for the assumption that this anomaly is connected with endocrine dysharmony? Two facts seem to support the hypothesis that a disturbance of the normal internal secretory functions of the sex glands of the male is the chief contributing factor to its production. The first is that the onset of the phenomenon is usually so closely associated with the changes taking place in the primary and secondary sexual characteristics at puberty and the second is the frequent presence of defective genitalia in these individuals. This latter condition is associated with a tendency to femininity and lack of sexual desire and potency.

The normal pubertal enlargement of the female mammary glands is undoubtedly due to the elaboration of an internal secretion by the ovary. The experiments carried on by Halban (13), Kehrer (51), Hegar (52), Knauer (53) and others in which it was conclusively demonstrated that if the ovaries of young female animals be removed, normal mammary development fails to occur, while if the removed ovaries be again homologously implanted there follows normal development to functional capacity. This apparent relationship between the ovaries and the secondary sexual characteristics of the female is correlated in the male by the dependency, at least in part, of the usual development of the secondary sexual characteristics upon the presence of a certain amount of functioning testicular substance within the organism. The experiments of Foges (54)

with cocks and of Larcher (55) and Morgan (56) with hens indicate that the testicles produce an internal secretion concerned with the development of the male characteristics. Halban (13) has expressed the opinion that gynecomastia may be due to fundamental similarity in the nature of the internal secretory products of the ovaries and the testicles. Foges (57) criticises this hypothesis and the experiments of Aschner and Grigoriu (58) would tend to support the criticism. These latter investigators succeeded in producing a hyperplasia and so-called colostrum-secretion in the mammae of rabbits or guinea pigs by the injection of testicular extract, but similar results with extracts of spleen, muscle and liver indicate a lack of specificity of the reaction. If the normal internal secretion of the testicles is the same as that of the ovaries with reference to its relation to the development of the secondary sexual characteristics, why then are not all males possessed of mammae of volume equal to those of the female? It has been said that the anlagen of these characteristics, such as the beard, are predetermined and have but little if any initial relation to the sexual glands, Tandler (59) being one of the most strenuous opponents of the conception of a dependency of the secondary sexual characteristics upon the sexual glands. In the male the mammary anlagen are present to the same extent as in the female yet they fail to develop except in abnormal cases. On the other hand it is well known that boys may experience a slight tendency to swelling of the mammae at puberty, giving evidence of some sort of stimulus working at this time, affecting this tissue. And we also know that the castration of boys before puberty prevents the development of the male characteristics, but yet does not cause female tendencies to be produced.

It might appear at first sight as if the cases of acquired gynecomastia were such because of the removal of a substance produced by the testicles inhibiting the development of the heterologous secondary sexual characteristics such as the mamma. Steinach (60) seems to be of such opinion, in which he is apparently supported by Lipschütz (61). This opinion is based on a series of remarkable experiments. Young male rats and guinea pigs were castrated and ovaries from consanguinous animals were implanted and grew to the conditions normally found in the female. As a result of these transplantations the male

animals developed the physical and psychic characteristics of the normal female. The sexual appurtenances also, such as the mammae, became entirely feminine so that true, fat, rich milk was produced sufficient to nourish young and growing animals. From this it is evident that the implanted ovaries do not stimulate the growth and development of the male characteristics, but do give rise to the formation of the distinguishing female type, the penis remaining infantile in structure while the mammae evolve to the volume and function of the female type.

Similar experiments on the transplantation of testes into young castrated females resulted in non-development of the female characteristics and the evolution of the male type, in psychic, physical and sexual trend. Lipschütz (61) and Sand (62) observed that in such masculinized females the clitoris tends to develop into a penis. As previously stated, Steinach (60) considers the so-called "pubertal glands," that is, the internal secretory portion of the testes and ovaries, to be inhibitory to the development of the usual heterologous sex characteristics when implanted into the opposite sex, and to be specifically stimulative to the production of the sexual type normally accompanying the developing gland in the donor. Such an antagonism, however, is doubtful since Sand (63) has successfully transplanted a testicle and a consanguinal ovary into a young castrated male rat and obtained therefrom an experimental hermaphrodite. Hence by the simultaneous transplantation of male and female sexual glands into an infantile mammal the hypothesis of an inhibitory action of either on the other is not effectually substantiated. Moreover, the hypothesis of Halban (13) that the internal secretion of the sex glands is the same in both male and female would seem to be disproven by the fact of the development in the male of the female characteristics following implantation of consanguinal ovaries. If the secretion were identical for the two sexes there would be nothing to prevent the development of the usual female characteristics in the latter case. An interesting phase of these investigations is the influence of the heterologous sex gland secretion on the psychic reactions of the host, there being reported an evident adaptation of psychic sexual nature to that normally connected with the sex of the donor (64).

The experiments of Sand (62) showing the possibility of the simultaneous occurrence of both male and female characteristics in the same individual when both secretory testicular and ovarian substance are present are virtually experimental productions of the essential type of gynecomastia in animals. The studies of Steinach (60) (65) showing that in the absence of functioning endocrine testicular substance the presence of functioning endocrine ovarian substance causes the appearance of female sexual characteristics have a similar significance. Animal experimentation having thus demonstrated conclusively that it is possible to produce in males an enlargement of the mamma at puberty resembling that taking place in the female and that furthermore this development may continue to the point of milk production, the endocrine origin of the condition of gynecomastia is reasonably well established.

The source of the stimulus giving rise to the phenomenon of gynecomastia in man is in all probability connected with gonad hormone secretion. Since Steinach (60) has demonstrated that the internal secretion of the sexual glands is specific for the sex insofar as the production of the sexual characteristics is concerned, and since Sand (62) has shown the conception of an inhibitory function of the one on the expression of the function of the other is unsupported, it is possible to believe that in the gynecomasts there is present somewhere in the body in addition to testes an amount of functioning ovarian or ovary-like tissue sufficient to cause the abnormal development of the male mamma. This assumption would explain both the essential and the acquired types of the anomaly. For in the former cases it can easily be supposed that there is present a condition in which neither the testicular nor the ovarian stimulus is prepotent or insufficient so that both masculine and feminine characteristics are produced. In those cases where the anomaly arises in connection with an atrophy defect or pathological condition of the testes it is possible that an originally prepotent testicular secretion has been so weakened that the balance swings to the side of the ovarian stimulus, which, becoming prepotent, gives rise to the mammary enlargement as an expression of its function. Such a conception does not by any means imply acceptance of Steinach's (60) theory of the reciprocal inhibitory actions of the heterologous sex glands in the production of the characteristics

of the sex, this having been disproved by Sand (62). The conception is based on the facts demonstrated by the latter investigator that both secretions may be present and functioning in the same animal with the added, though gratuitous, assumption that in gynecomastia one or the other may be prepotent or that both may be equally potent and depending upon attendant circumstances give rise to either type of the phenomenon.

There has recently appeared a series of papers by Steinach (66) having to do in large part with an attempt to correlate homosexuality with gonadal endocrinology. One finding of particular interest in connection with the present discussion which tends to support the hypothesis previously proposed is the observation that the testicles of some five homosexuals showed the presence of certain cellular elements ordinarily foreign to the male glands and resembling in their structure and staining properties the cells of the corpus luteum, even to the presence of chromaphile material.

These observations, the results of the heterologous and homo-heterologous implantations of Sand, and the clinical reports of the literature, afford cumulative evidence validating the expansion of Novak's (67) expression that the phenomenon of gynecomastia is attributable to a diminution of testicular function into the conception that coincident with the lessened testicular function there exists a potent hormone-producing tissue resembling in its effects that of the female ovary and giving rise to the mammary enlargement characteristic of the sex.

Such being the present indications it remains for future investigations to show whether the production of the stimulus is due to a perversion of the hormone producing gonadal tissue of the male in the nature of its becoming similar to that of the female, or whether there is actually present in these individuals functioning ovarian endocrinal tissue.

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FRIGHT AS A CAUSE OF EPILEPSY AND HOW IT ACTS.

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That a fright may be the exciting cause of epilepsy, especially in the young, is a fact that cannot be too well impressed upon parents, teachers, and all who have the care of children. Most men who have given special attention to the malady believe that a predisposition to the disease exists in the cases of epilepsy that follow fright. In this they follow the teaching of Gowers, who wrote: "We must regard as the exciting cause of epilepsy, the condition or circumstances to which the first fit was apparently due. It may be again pointed out to prevent misconception, that these exciting causes cannot be regarded as the essential causes of the disease except in a very few cases. They would not have been effective had not a predisposition existed, due to inheritance or to causes which are generally beyond our recognition" (1). He also wrote: "Of all the immediate causes of epilepsy the most are psychical—fright, excitement, anxiety. Of these three forms of emotion, fright takes the first place. The relation of this cause to age, however, is very distinct. It is effective chiefly in early life, when emotion is so readily excited, and most powerful at the transition from childhood to adult life, while after middle life it is almost inactive" (2). And further on he states: "Predisposition usually exists. Hence in speaking of fright as a cause of epilepsy, it must be remembered (as already stated) that its effect is only that of the exciting spark" (3).

In this article, the writer reports a case, carefully investigated, in which a severe fright in a healthy boy, produced epilepsy, the first convulsion occurring two months after the fright. Moreover, he does not think his case unique, for Gowers himself, as above quoted, qualified his statement about predisposition by stating it "usually" exists, and that the exciting causes cannot be regarded as the essential cause of the disease "except in a very few cases." One of the twelve cases (Case 5) of epilepsy caused by fright reported by Paravicini in his valuable paper, "The Etiology of the Epileptic Psychosis" (4) apparently is of this nature since there was no bad heredity in the

case, and, insofar as predisposition to the disease went, was regarded by Paravicini as "immune."

In those cases in which fright causes epilepsy to arise in a previously sound nervous system, we may inquire whether there are any facts physiological, clinical, or pathological, that can illumine the genesis of this disease, facts that by the light they shed upon the pathway of our investigation help also to define the gaps that exist in our knowledge of the disease, and thus to emphasize the need of their investigation.

Research has shown that in idiopathic epilepsy the sympathetic nerve fibres are demonstrably diseased, that it is, in fact, a sympathicopathy. The demonstration that idiopathic epilepsy is characterized by objective signs—chronic vasoconstriction spots, demonstrable abnormalities of sympathetic nerve reactions—is an advance in our knowledge of the disease. It is a satisfaction that physical, objective phenomena that can be seen, measured, photographed, can now claim attention in place of the notions based on vagary (e. g., "the fit is the expression of the afflicted one's desire to return to its mother's womb") of which recent years have been so prolific. The demonstrable involvement of the sympathetic system is one of the facts that claim our consideration in an attempt to elucidate the genesis of the disease.

The next fact to claim consideration is that fear acts powerfully on the mechanisms of the body and that this action is by means of the sympathetic nerves. The physiologist, Cannon (5), teaches that impulses originated by emotion, flow over sympathetic nerves and cause an increase of the secretion of adrenin in the blood, accelerate the heart and dilate the pupils. The glycogen is mobilized and changed into sugar; the available energy of the skeletal muscles is increased by the extra adrenin produced; the coagulability of the blood is increased. All of these actions are produced by stimuli flowing over the sympathetic, and having for purpose the betterment of the individual's chances in the fight or flight, brought about by the original emotion. In other words, the bodily metabolism is profoundly influenced by terror, and an increased secretion of adrenin is demonstrably produced, which has itself a large share in the production of the demonstrable changes in the metabolism.

Another fact to claim consideration is that certain toxins produce convulsions. But adrenin, if toxic, is not in this class. Can its continued hypersecretion lead to a perverted metabolism in which a convulsant toxin is produced? This is one of the gaps in our knowledge that needs exploration. Suggestive experimentation, bearing upon the possibility of a hyperadrenin-aemia producing a convulsant is that noted in another connection, by Dr. Schaller of San Francisco. "He reported that in 1906, while working in the pathological laboratory of Dr. William Ophüls, he had undertaken some experiments to produce arteriosclerosis by repeated injections of adrenalin intravenously into the rabbit, following the experiments of Josué. By this method, striking specimens of arteriosclerosis were obtained. He had used doses of adrenalin maximal within lethal limits in order to produce maximum effects; and he had by this means frequently produced typical epileptic attacks in these rabbits. The attacks were manifested by periods of unconsciousness, by falling, tonic and clonic convulsions, dilation of the pupils, loss of sphincter control; in short, by typical epileptic attacks" (6). That adrenin can bring on attacks in human individuals subject to the malady has recently been demonstrated (7).

Another fact to bear in mind is that sudden anemia of the brain produces convulsions. Kussmaul and Tenner (8) proved "that sudden arterial anemia of the brain, as also faradization of the cervical sympathetic nerve, which determines permanent spasms of the blood vessels gives rise to epileptic fits." In epileptics, reflex vasoconstriction of the peripheral vessels can be frequently seen (as in the arm) to be more intense and to last minutes longer than that evokable in normal individuals. Is it not conceivable that this intensity of vasoconstriction as witnessed in the peripheral vessels of epileptics may also affect the cerebral circulation and with convulsive results?

The facts that we have under consideration we shall briefly review in their possible relation with the genesis of cases of epilepsy that have for sole cause a severe fright, first relating the history of a case coming within this category.

H. O., Swedish-American, male, aged 21 years. (Referred by Dr. F. W. McVey of Boston.) No mental or nervous diseases, alcoholism, or tuberculosis on the father's or mother's side. Both parents healthy. Five brothers, all healthy. In childhood the patient had no infectious disease except measles at eight years of age. When seven years old he suffered a severe fright. Three boys took him into the woods

near by his home. One held him while another held open his mouth, while the third boy poured a nasty fluid down his throat. He returned home very pale. For two months afterward he cried out nightly in his sleep. He was afraid all the time, showed constant pallor, and had to be coaxed daily to go to school, fearing the boys who had maltreated him. After two months had passed, one morning when ready to go to school, he came back into the kitchen very pale; he looked up towards the ceiling and became rigid, "like a stick" as his mother said, and she carried him to bed. This was his first convulsion. For a while after this, every three weeks he would have several convulsions near together. Then a period of five months elapsed without one; this was followed by a period in which two or three light attacks occurred every day for awhile. Since then, for a period of thirteen years, the convulsions have averaged two a month. An impediment of speech, slight stuttering, came on after his first attack and remained permanently.

We have now to consider, in the light of known extraneous facts, the genesis of epilepsy caused by a severe fright in a previously sound nervous system. As shown by the experiments of Cannon, fright influences the bodily mechanism through stimuli passing over the sympathetic nerves. The secretion of adrenin is increased, with the resultant effects previously mentioned. In our case, the sudden onset of quite constant pallor, showed that the sympathetic nerves were hyper-active in discharging stimuli which produced the evident peripheral vasoconstriction. Fear was constantly in the mind of the boy, evidenced by the night terrors, and the coaxing of the mother necessary to get him to go to school after the fright. Thus, while this fear lasted, a period of two months, there was a hypertonia of the sympathetic nerves manifested externally by the almost constant pallor. The period between the causative fright and the onset of convulsions (in cases of epilepsy caused by fright) is termed by Paravicini the intervalic period. During the intervalic period in the case here reported there was manifested a hypertonia of the sympathetic system—a fact not surprising in the light of Cannon's experiments. The writer has observed carefully several cases of incipient idiopathic epilepsy, in the etiology of which, however, fright played no part, and in them there was a hypertonia of sympathetic nerves present, demonstrated by neurological tests. Hence it is evident that hypertonia of sympathetic nerves is connected with the incipient or preconvulsive stadium of idiopathic epilepsy. It is the only abnormal physical condition that we can feel sure was present in the intervalic period of the case here reported.

Is sympathetic hypertonia in itself sufficient to cause con-

vulsions? That might depend on the sympathetic fibres involved in the hypertonia. Thus Kussmaul and Tenner's experiment of producing epileptic fits by "faradizing the cervical sympathetic nerve which determines permanent spasms of the blood vessels" is nothing but the artificial production of a hypertonia in the sympathetics innervating the blood vessels of a brain area; and anyone who has seen the intense and long lasting vasoconstriction evokable in some skin area of a chronic epileptic cannot but reflect, in the light of Kussmaul and Tenner's experiment, on the result of a similar vasoconstriction automatically produced in the epileptic's brain vessels. (That the brain, encased as it is in the unyielding cranium, cannot undergo vasoconstriction en masse is of course recognized. That differential distribution of the blood within the brain may, however, give results such as those herein postulated must also be recognized.)

The length of the intervalic period, two months in the case here reported, suggests the probability of some other factor in the production of the convulsions besides the hypertonia of sympathetic fibres, and thus we are led to inquire if the hyperadreninaemia present during that time could so vitiate metabolism that substances were formed which acted as irritants to the cerebral cortex. The periodicity of the convulsions in epilepsy suggests such a toxin formation. Very little, however, appears to be known of the metabolism of epilepsy, and a line of investigation that has enlarged our knowledge of diabetes mellitus and diseases of the thyroid, is conspicuous for its utter neglect in case of the epileptic. All that can be said, therefore, about the production of nerve-irritating substances by the hyperadreninaemia (caused by the hypertonia of the sympathetics lasting for a considerable period) is that such a production is possible.

Bringing these various facts, pathological, clinical, and physiological, into closer relation with our case report, we find that H. O., a healthy boy with no predisposition to epilepsy (no damaged nervous system from bad heredity or infectious diseases) suffered a severe fright (its severity manifested by night terrors for two months) which caused a hypertonicity of the sympathetic nerves (manifested by the marked and constant pallor of sudden onset). This was supposedly accompanied by a hyperadreninaemia—the normal accompaniment of emotional hypertonia of the sympathetics (Cannon's experiments). After

two months of this condition, convulsions occurred and have recurred for fourteen years. Physical examination now shows a diseased condition of the sympathetic nerves, manifested by chronic vasoconstriction spots and abnormal vasoconstriction reflexes, phenomena that investigations have shown to be characteristic of idiopathic epilepsy. We have therefore three outstanding facts: 1, a sound nervous system; 2, a severe fright, causing a hypertonia of the sympathetic nerves with a resultant hyperadreninaemia lasting for two months; 3, sixteen years after the onset of convulsions, a diseased sympathetic system.

While it may be assumed that in the intervalic period there was a hypertonia of the sympathetic system, the relation of this hypertonia with the outbreak of convulsions is as yet obscure. We do not yet know the topography of the sympathetic fibres in the brain. The fact that emotion is the cause of this hypertonia indicates brain connections with sympathetic fibres. Waiving the possibility of stimuli reaching the motor cortex from the hypertonic sympathetic fibres, are there other considerations that may aid in explaining the onset of convulsions in this case?

It is generally admitted that the convulsions in epilepsy originate in the cortex. The experiments of Tsiminakis (9) indicate that the cortical cells, especially the motor cells, of the normal brain react to anemia differently than do those of the epileptic. This investigator compressed the carotids for a minute in 30 normal subjects. Outside of a momentary unconsciousness there was no reaction of brain cells. He compressed the carotids likewise in 116 patients, mostly epileptics. The epileptics became unconscious more quickly than the others, at latest in thirty seconds, and the onset of unconsciousness was quickly followed by epileptiform convulsions, struggling or kicking movements for ten to forty seconds; later these were followed by the characteristic stare of epileptic somnambulence (''Absenz''). These experiments indicate two things: a greater irritability of the motor cells in chronic epilepsy, and the influence of anemia in provoking an outburst of stimuli from such over-irritable motor cells in the cortex, causing convulsions.

This leads to the question: What in the intervalic period might cause a hyperirritability of the motor cells in the cortex, the condition which is apparently present in chronic epilepsy,

the condition in which a momentary anemia so readily leads to convulsions? It may be that the hypertonia of the sympathetics caused a pallor of the motor cortex as it caused that visible in the skin during the intervalic period and thus led to the production of acid metabolites resulting in hyperirritability of the motor cells. Or the hyperirritability may have been caused by an irritant in the blood, a product of perverted metabolism due to the hyper-adreninaemia of the intervalic period. These are mere hypotheses used as stop-gaps in our chain of facts to explain the onset of the convulsions in our case of epilepsy. Once convulsions occur, their recurrence is facile, as Gowers has remarked.

If the convulsions are caused by spastic constriction of cortical vessels, and if the sympathetic fibres originate in the cortex [facts that point to such an origin have been described elsewhere (10)] the progressive character of idiopathic epilepsy is explainable, together with the cortical gliosis that accompanies the disease. For the recurrent spastic contraction of the cortical arterioles could have for results, the cortical gliosis that is found accompanying the disease, and the descending degeneration of sympathetic fibres that Echeverria found and described (11). The physical signs of chronic vasoconstriction spots, and abnormal sympathetic nerve reactions demonstrated by neurological testing, have previously been shown to go with this disease so constantly as to determine idiopathic epilepsy to be a sympathicopathy, a diseased condition of sympathetic neurones (12).

SUMMARY

Eliminating all theory from consideration (it has been used only in an endeavor to account for some of the facts) the facts in the genesis of our case are these: 1, a sound nervous system; 2, a severe fright; 3, a hypertonia of the sympathetic nerves for two months, a direct result of the fright; 4, outburst of convulsions at end of two months and their recurrence during sixteen years; 5, the present status, a chronic diseased condition of the sympathetic nerves, manifested by chronic vasoconstriction spots and abnormal vasomotor reactions characteristic of idiopathic epilepsy. It is concluded that severe fright can produce idiopathic epilepsy in a child without a predisposition to the disease. It acts by causing a hypertonia of the sympathetic nerves. A

hypertonia of sympathetic nerves is the evident beginning of the disease in the case reported.

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A CASE OF COMPLETE AMENORRHEA WITH FULMINATING SYMPTOMS: SURGICAL DEMONSTRATION OF OVARIAN ETIOLOGY †

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Most of the evidence as to the relationship of the ovaries to menstruation has been of negative character. By this I mean that we are better acquainted with the effects of destroying ovarian function than we are cognizant of the results of restoring activity to a functionless ovary. Being presented with an apparently unique case, any therapeusis undertaken must necessarily be an experiment.

The literature revealed no case similar to the one herein reported.*

In the midst of an attack the patient's condition presents a striking picture. She is seen at one time prostrated and the next moment half raised on the edge of a lounge giving the appearance of one with a wild, uncontrollable mentality, with an extremely flushed appearance and an almost suffocating cyanosis and widened palpebral fissures. Besides this her arms may be covered with blood from unsuccessful attempts to establish a flow of blood, unsuccessful because repeated venesection month after month had destroyed the continuity of the superficial veins of her arms.

Case No. 115. Chief complaint, complete amenorrhea. Age, 30; single; school-teacher. The family history was negative as to similar conditions, tuberculosis and cancer. Tonsillectomy was performed about 1909, appendectomy in 1915.

Menstrual history: The first menstruation was in 1903 at the age of twelve. For some reason not now known, the right breast was removed in 1905, the left one was removed in 1906. After the removal of the first breast, periodic attacks of numbness and unconsciousness ensued with complete amenorrhea for two and one-half years. Later there were some scanty menstruations. As time went on conditions became much worse. The menstruations became vicarious. Nose-bleeds were the chief source of the escape of blood.

In 1915 the patient underwent an operation for the ingrafting of a sheep's breast. This was soon absorbed, as could be expected, without

† Read at the meeting of the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

*"We are unable to find any literature dealing with amenorrhea following amputation of the breasts in a young woman."—Robt. E. Noble, Brig. Gen., Med. Dept., Librarian S. G. O.

any definite results. Following this, the patient consulted many physicians, but the only relief obtainable was artificial bleeding either from curettments or from venesection. There was a complicating leukorrhea which was first noticed by the patient on the day following a curettment, in Feb., 1919.

Prior to coming here the patient had not had a natural menstruation, unless started by a venesection of about a pint of blood or by a curettment, during six months. During the next six weeks, while the patient was under our observation, she had to be bled twice to relieve conditions of extreme cyanosis associated with unconsciousness and delirium. These symptoms entirely disappeared as soon as the first twelve ounces of blood were removed.

Physical examination: July 22, 1919; height 5 feet 2 inches; weight about 105 pounds; pupils react to light; mouth, numerous crowns, bridgework, pyorrhea and root abscesses; tonsils, no visible portions remaining; no superficial lymph nodes; thyroid, not enlarged; breasts, one-half of the right breast and one-fourth of the left breast were still present; heart, lungs, liver, spleen and other abdominal organs, negative; uterus, very hard; cervix, lacerated; vagina, small, leukorrhea; rectum, spine, joints, patellar reflexes, extremities and skin, negative.

Blood pressure 118, systolic and 78, diastolic; pulse 90; Wassermann test, negative. Vaginal smear was positive for Neisser infection. Urine analysis, sp. g., 1.026, acid, no albumin, no sugar. In a second test albumin and pus were present.

Blood count: Erythrocytes,

July 23, 1919; 10,000,000 per c.mm.

July 24, 1919; 12,000,000 per c.mm.

July 26, 1919; 5,600,000 per c.mm. (after venesection).

Operation: Aug. 1, 1919. Ether anesthesia. Low mid-line incision. Findings: Ovaries, normal in size and position; ovarian veins tortuous and congested; uterus, normal position; fundus, about four cm. in major diameter, and marked by several areas of hyperemia and of ischemia.

The operation comprised the incision of the peritoneum behind the ovarian vessels on each side, sectioning of the sympathetic nerves to the ovaries and the removal of the adventitia from the major ovarian vessels. One vein which became lacerated was ligated. The abdominal wound was closed.

Results: Normal menstruation, lasting for five days, began on the day following the operation. The next menstrual period was skipped but without any of the nervous and vascular symptoms as before. Subsequently, the menstruations became regular and normal, as follows:

Oct. 28-Nov. 1.

Nov. 22-28.

Dec. 18-24.

Jan. 17-21.

On March 6, 1920, the patient stated in a letter that she was "feeling fine" and had gained twenty-five pounds.

DISCUSSION

Prior to deciding upon a therapeutic plan, this case offered many perplexities. As the patient was demonstrably suffering from focal infections, it was considered advisable, before trying other means, to remove the foci. The patient, however, preferred to submit to an experimental abdominal operation rather than to lose her infected teeth. It was thought that the ovarian

nerves and perhaps the blood-vessels also, directly or indirectly, were being stimulated by the toxins of infection and thereby altering the circulation and hence the functions of the ovaries. With this as a hypothesis, the operation was undertaken with a view to eliminating the nervous and vascular control of the ovaries.

SUMMARY

A case is reported in which a patient suffered from amenorrhea for about fourteen years following the surgical removal of parts of both breasts, for reasons not now known. Sectioning of the sympathetic nerves to the ovaries and resection of the adventitia of the ovarian vessels was followed by the establishment of normal menstruation.

(PATHOLOGY OF THE SYMPATHETIC) PATOLOGIA DEL SIMPATICO, by Professors P. Castellino and N. Pende. F. Vallardi, Milan, Italy, 1915.

That the internal secretions will ultimately be proved to play an important role in the genesis of numerous disorders in addition to the well recognized endocrinopathies is a prophecy frequently and safely offered. The data justifying such a statement are widely scattered and confused. Castellino and Pende's widely quoted book is of interest to the endocrinologist primarily as an attempt to bring together these data and to organize them systematically. The attempt involves a considerable amount of theorizing which will be valued more or less in accordance with the temperament of the individual reader.

The book—of some 500 pages—is divided into two sections. In the first the anatomy, physiology and pathology of the endocrine-sympathetic system is discussed at length. The point is emphasized that the relations between them are so intimate that the two components can most profitably be treated together. In the concluding chapter of this section a critique is offered on the theories of vagotonia and sympatheticotonia as expounded by Eppinger and Hess. The conception is regarded as of restricted practical significance.

The second part of the volume begins with a chapter on the cyanoses and erythroses of the skin. The habitual acrocyanosis is related to hypothyroidism, as are chillblains and symmetrical gangrene. Chronic acroasphyxia and Raynaud's disease involve also "hyperadrenalism." Other conditions considered are acroerythrosis erythromelalgia, erythrophobia and acroerythrosis indolora. Quincke's disease is regarded as related to thyroid dystrophy and gonad alteration. Similarly the trophoedema of Meige may be allied to dysthyroidism, as demonstrated by forms passing into myxedema. Next the lipodystrophies are taken up, with a detailed description of Dercum's disease, which is considered as a pluriglandular syndrome with prevalence of hypophyseal symptoms. Then adiposis analgesica and lipomatosis symmetrica are treated with adenolipomatosis symmetrica and neurofibromatosis of V. Reklinghausen.

Scleroderma, sclerodactylia and hemiatrophy of the face are discussed in a chapter with hemihypertrophy, congenital and acquired, considered as trophoneuroses. As regards atrophy of the skin (idiopathic) hypoadrenalism is claimed to be a causal factor.

Trophoneurotic gangrene of the skin is treated in all its known varieties, in connection with Raynaud's disease. A very detailed chapter follows on skin dystrophies, with special emphasis on the adrenal as related to the pigmentary anomalies.

Hypertrichosis is regarded as of pluriglandular origin, but always mediated by the sympathetic system.

After a discussion of the causal action of various endocrine glands on sympatheticopathies of the locomotor apparatus (Dupuytren's disease, hydroartrosis intermittens of Moore. Paget's disease, osteomalacia and several angiomyopathies), hemicrania is considered as a cervical sympathetic disorder.

A short discussion of negative tenor is added on the possible connection between epilepsy and glaucoma and the sympathetic. The sympathetic conditions are not considered as causal; in regard to the glaucoma the operation on the cervical sympathetic did not lead to any encouraging result.

A long and detailed chapter on the heart follows; in this Castellino claims that the thyroid is cardio-exciting while the gonads are cardio-depressor. Other topics treated are asthma, laryngospasm, hysterical hemophthysis, coeliac and gastro-intestinal neuroses, urogenital sympathetic neuroses, chlorosis, Basedow's syndrome as an endocrine-sympathetic dystrophy and two pluriglandular syndromes.

The book as a whole does not lend itself to adequate analysis in a review of restricted scope. For many interesting details the original should be consulted.

—G. VERCELLINI.

(THE PUBERTY GLAND) DIE PUBERTAETS DRUESE UND IHRE WIRKUNGEN, by A. Lipschütz. Bern, 1919, pp. 456.

Lipschütz's book is a masterpiece of artistic and lucid scientific exposition. It will rank not only as the best on the particular subject treated, but is also one of the best in general medical literature. The illustrations are good, many even splendid. Much of the book is devoted to the experiments of Steinach, but the author details also his own work. He was the first to show that castration of female animals, followed by transplantation of a testicle, leads to development of the clitoris to an organ resembling a penis. The theory that sex is already determined in the ovum is discussed at length and finally rejected. New theories on hermaphroditism and homosexuality are given. Lack of space renders impossible an adequate discussion of them. They are well deserving of careful attention in the original.

The literature is not very completely reviewed. The author does not seem to know, for example, of Blair Bell's interesting book "The Sex-gland." This is regrettable for there are some contradictions between the two authors; it would have been interesting to have them discussed by Lipschütz.

—J. KOOPMAN.

(A THEORY OF CANCER) LA DYSCYTOGENESE HYPOCYTOPOIETIQUE DYSEUTROPHIQUE OU CANCER. Naamé, Maloine et Fils. Paris, 1919, pp. 43.

Dr. Naamé offers a theory of the etiology of cancer. The thesis is based on a review of the literature and on personal therapeutic observations. It is largely a speculative development of the conception that "Cancer is a dyscytogenesis with local hypocytopoiesis and glandular dyseutrophy." By this verbalistic feat the author would seem to have formulated a conception with which many would agree. By "dyseutrophy" apparently is meant functional imbalance which Naamé believes can be more or less constantly corrected by judicious organotherapy. He reports the successful treatment of uterine cancer by "mammo-hypophyseal and thyro-mammary extracts" and of breast cancer by "thyro-ovarian" extract, and, more recently, a few other successes along similar lines. In view of the dubious history both of organotherapy and of "cancer cures" only an overwhelming mass of detailed evidence would carry conviction of the validity of the method proposed.

—R. G. H.

(GOITRE IN THE WHITE RAT) DER KROPF DER WEISZEN RATTE, by Th. Langhans and C. Wegelin. Bern, 1919, pp. 131.

This book would perhaps be more interesting if there did not exist quite a number of similar books and booklets on the same topic and with the same general content. Langhans and Wegelin fed white rats with water (boiled and not boiled) or with milk from districts in Switzerland where goiter is prevaalent. The effect was at times the development of goiter, but often no effect was seen. So the conclusion is, as in most other publications, that the water may have some relation to goiter, but that it is certainly not the only cause and that, after all, we know little about the matter It seems extremely doubtful whether a new book was needed to reiterate this. It was found, however, that minute doses of iodids protect the rats from goiter. The corroboration of this observation and the excellent illustrations are perhaps the most valuable features of the work.

—J. KOOPMANN.

ABSTRACTS

(ADRENAL) Hematoma de la cápsula suprarrenal. Baciga-lupo (J.) and Perazzo (E.). Prensa Med. Argentina, 1919, **6**, 161.

Anatomical observations of technical interest upon a newly born child.—R. G. H.

(ADRENAL) Addison's disease. Balen (M. J.). J. Am. M. Assn. (Chgo.), 1920, **74**, 82-83.

A brief case report with the following points of interest: A male, age 48, tailor, six months before admission complained of marked fatigue, dizziness, and headache, accompanied by a gradually increasing brownish pigmentation of the skin, especially on the face, chest, hands and abdomen. The heart action was very feeble, blood pressure low (systolic by mm. Hg). The lungs showed evidence of chronic tuberculosis. Death occurred 24 hours after admission.

Necropsy more than 24 hours after death, showed extensive miliary and many calcified tubercular lesions of the lungs. The spleen was greatly enlarged, but without tubercles. The adrenals were greatly enlarged, especially the left, and one section showed a diffuse fibrocaseous degeneration of the medullary portion, with marked cortical atrophy. The cortex on microscopic examination showed a number of small but typical tubercles.
—F. C. P.

(ADRENALS) Urea excretion after suprarenalectomy. Bevier (G.) and Shevky (A. E.), Am. J. Physiol. (Balt.), 1919, **50**, 191-203.

The removal of the suprarenals in rabbits is followed by a depression of the rate of urea excretion. The result is like that obtained by subcutaneous injection of optimum doses of pituitrin and contrary to that obtained after injections of epinephrin. It is suggested that these findings support the hypothesis that there is an epinephrin-pituitrin balance in the blood which may regulate the rate of kidney function.—T. C. B.

(ADRENALS) The development of the urogenital system in the Marsupialia with special reference to Trichosurus vul-

pecula. Buchanan (G.) and Fraser (E. A.), J. Anat. (London), 1918, **53,** 35.

The discussion deals almost entirely with the urinary apparatus, but there is a brief description of the adrenals also. The development of these is quite as in other mammals.

—E. R. H.

(ADRENAL SYMPATHETIC SYST.) The treatment of sea-sickness (Sur le traitment du mal de mer). Cazamian (P.), Bul. gen. therap. (Paris), 1919, **170**, 782-784; Bull. Soc. Med. des Hôp. (Paris), 1919, **43,** 638-640.

In a study of over fifty subjects suffering with sea-sickness C. found normal urine and blood. There was generally present blood pressures higher than normal, and an inversion of the oculo-cardiac reflex. Lumbar punctures were without effect, and showed varying degrees of pressure in the cerebro-spinal fluid, which was otherwise normal.

He considers that the majority of subjects presented a fundamental sympathicotonia by virtue of hyperadrenalism induced by the stimulating effect of the rolling of the ship acting upon the vegetative nervous system. It is only when the suprarenal cortex is exhausted that the sympathetic tone decreases and the arterial tension is lowered. Apparently among adults the sympathicotonics are predisposed to mal de mer, while the vagotonics have a chance to escape.

The majority of medicaments utilized against sea-sickness have no relation with the fundamentals of the disorder. Basing treatment on the above considerations it was found that in the cases showing faulty action of the sympathetico-adrenal system, 1-2 mg. of neutral sulfate of atropine given subcutaneously was entirely satisfactory, when supplemented by adrenalin (6 mg. in 3 doses) orally administered at half hour intervals.—F. S. H.

(ADRENALS) Physiological action of the adrenalin discharged as the result of the stimulation of the splanchic nerve (Acción fisiológica de las descargas de adrenalina por excitacion del nervio esplácnico). Cevera (L.) and Houssay (B. A.), La Prensa Med. Argentina (Buenos Aires), 1919, **5,** —— (Nov. 20).

Stimulation of the splanchnic nerve in chloralized dogs produces a greater elevation in arterial pressure when the adrenal veins are free than when they are obstructed. If the obstruction is removed during stimulation there is observed a sharp elevation of the pressure preceded by a brief fall. Rarely this step (described by V. Anrep and others) occurs with the veins occluded. When the veins are unobstructed a constric-

tion of the paws is to be observed which does not take place when the adrenal veins are compressed; in the latter case the volume of the paw follows the variations in pressure; even if a marked hypertension is produced by intense stimulation of the splanchnic nerve.

Medullary puncture in dogs having the spinal cord destroyed to the level of the 12th dorsal vertebra, produces hypertension, particularly if the vagus nerves have been previously cut. At the same time there is a marked and long continued constriction of the paw deprived of its nerves. This constriction does not occur if the adrenals have been removed or their veins obstructed.

All these experiments demonstrate that excitation of the splanchnic nerve and bulbar puncture produce a discharge of adrenaline capable of producing vascular effects which are added to the vaso-constrictor action of nervous origin.—B. A. H.

(ADRENAL) Clinical notes from France. Cumston (C. G.), N. Y. Med. J., 1920, **111**, 154-157.

The vomiting of pregnancy is found clinically in three forms: "simple," "incessant" and "incoercible." Suprarenal vomiting of pregnancy may offer in a general way all the classical characters of gravid vomiting, but the symptomatology of suprarenal disturbance is superadded. Apparently the adrenals do not participate in the genesis of the simple type. In all instances of the adrenal form, vomiting is incessant or incoercible and offers the aspect of a very serious type of cases. Good therapeutic results are claimed for the control of adrenal vomiting by the administration of extracts of the entire adrenal gland. Adrenalin hydrochlorate by mouth (5 to 10 drops) and hypodermatically (0.5 to 1 mg.) is also of great service in these cases.
—H. W.

(ADRENAL) Endocrine imbalance with predominant adrenal deficiency (A proposito di un caso di squilibrio endocrinico pluriglandolare con prevalente insufficienza delle glandole surrenali). Farmachidis (C. B.), La Riforma Medica (Naples), 1919, **35**, 829.

The case belongs to those which Pende calls "pluriglandular syndrome with uniglandular predominance." In the present case adrenal symptoms were particularly in evidence but polyuria from dysfunction of the hypophysis and several disturbances referable to the celiac plexus were also manifested.

Although the Wassermann reaction was repeatedly negative, owing to the hardening of the peripheral arteries and the enlarged spleen and lymphatics the patient was tentatively

treated with mercury and the effect was a slow, but total recovery.—G. V.

(ADRENAL) Acute peritoneal form of adrenal insufficiency during the course of chronic adrenalism (Insuffisance surrénale aiguë a forme péritonéale au cours d'une surrénalite chronique). Fiessinger (N.) and Leroy (E.), Rev. gen. de clin. et de therap. (Paris), 1917, **31**, 325-328.

The autopsy findings in this case showed marked lesions of the adrenal bodies justifying the diagnosis of acute adrenal insufficiency made at the onset of the disorder. The case record reports frequent emesis of bile-containing matter, accompanied by the facies and pulse of the peritoneal type. The treatment consisted of subcutaneous injections of 2 mgm. adrenalin per day, but this was unavailing.—F. S. H.

(ADRENAL EDOCRINE ORGANS) The functional connection between the reproductive organs and other glands of internal secretion. Hewer (E. E.), Brit. Med. J. (London), 1920, (i), 293.

The paper gives a preliminary summary of the results of injecting white rats with various preparations of suprarenal cortex. In nearly every case the hair began to come out, although the coat was usually very fine and glossy. In a few cases so much hair came out that the coat appeared ragged. Most of the animals were perfectly healthy. The thymus was found to become more vascular. In the pancreas an inconstant hypertrophy of the islets of Langerhans was observed. The adrenals were not altered in size, but the cortex was unusually vascular. Large spaces containing blood and debris were seen between the cells in the zona glomerulosa. Signs of disintegration were found in the two outer zones of the cortex. Very marked degeneration was obtained in the testes. The spleen and liver were not affected. In another series of experiments, feeding the animals with desiccated suprarenal cortex brought about some change in the rate of growth.—L. G. K.

(ADRENAL DIABETES) The relation between blood pressure and blood sugar (Over de vorhouding ausschen den bloedsdruk en het suikergehalte van het bloed). Hovens Gréve (C.), Inaug. Dissertation, Leiden, 1919.

It is well known that adrenalin has an influence both on the blood pressure and on sugar metabolism. Increases in blood pressure after injection of adrenalin may be accompanied by glucosuria. On the other hand, the low blood pressure in Ad-

dison's disease is accompanied by a diminished amount of blood sugar. Therefore the author examined the blood in nephritis, in hypertonia without nephritis and in diabetes. In many cases no relation between blood sugar and blood pressure could be detected. There are, however, striking cases of hypertonia without demonstrable anatomical lesions with hyperglycemia.

In diabetes there are two forms, those with and those without increased blood pressure. It is possible that this last form is of chromaffin origin. The treatment of these patients requires perfect psychic rest. Perhaps atropine or pilocarpine is of some use.

When a patient has increased blood pressure and hyperglycemia we have, however, no right to speak of a "latent diabetes." The author proved that when a large amount of carbohydrate was given to such a patient, the influence on the amount of blood sugar was much smaller than when even a very small dose was administered to a true diabetic.—J. K.

ADRENAL, syndrome, Dystrophies and necrotic lesions in—(Dystrophies et lesions nectrotiques dans les syndromes surrenaux). Hutinel (P.), Bull. Med. (Par.), 1916, **30**, 573-585.

The author postulates an endocrine factor in various infections and intoxications, which modifies altogether the aspect of the morbid process. The adrenals are especially charged with this abnormal reaction and the resulting groups of signs and symptoms are together spoken of as a suprarenal syndrome. This consists chiefly of cardiovascular phenomena, giving rise to general malnutrition of all of the tissues which prolongs the duration of the original disorder. The symptoms of myocardial insufficiency are closely simulated in some respects: The skin shows signs of malnutrition and may show diffuse pigmentation. The urine changes resemble those of acute febrile conditions. In some cases there are said to be marked psychic changes of various kinds.—I. M.

(ADRENAL) Endocrine tropisms. Adrenotropisms. Kaplan (D. M.), N. Y. Med. J., 1920, **111**, 241-248.

The author ascribes certain "thyro-rheumatic," "thyro-endocardial" and "pituito-appendical" syndromes to a tonsillopathy requiring endocrine interpretation and attention. The result of indiscriminate tonsillectomies is not immediate but an insidious cachexia tonsilloprevia which may assume the clinical form of unmanageable headache, cardiac distress, osseous or articular manifestations, obscure leucocytoses, peculiar febrile rigors or a fulminating appendiceal infection.

Individuals dominated by their adrenal apparatus, are "adrenotropic." Manifestations of adrenotropism are: Pigmentation of the skin, hyperchlorhydria, biotrophic tendencies to diphtheria, influenza and tuberculosis—or rather their preferential selection of the adrenals—weak toleration of depressant coal tar derivatives, tobacco tolerance, physical and psychical vigor, energy and persistence, hirsutism, long and pointed canines, dark complexion, red hair, carbuncles, asthma, adrenal diabetes, adrenal Basedow's disease, epinephroma, anencephalia, hyperchlorhydria adrenopathica, masculinism, vascular hypertension and hypotension, pulmonary edema, acroparesthesia, erythromelalgia, dementia praecox, psychasthenia, polychromatophilia, "pernicious anemia," certain hernias, carcinoma and other conditions!—H. W.

(ADRENAL) The hyperglycaemia of asphyxia, and the part played therein by the suprarenals. Kellaway (C. H.), J. Physiol. (Lond.), 1919, **53**, 211-235.

The difference of opinion between Stewart and Rogoff and Cannon and Hoskins as to the part played by the suprarenals in the hyperglycemia of asphyxia has led to a reinvestigation of the subject. The observations were made on cats without anesthesia, and the paradoxical pupil reaction was taken as an index of the output of adrenalin. The author has satisfied himself that asphyxia causes an increased output of adrenalin, and has attempted to determine the responsibility of this output for the hyperglycemia which follows asphyxia. The conclusions drawn are as follows: (1) The increase of adrenalin and of sugar in asphyxia are mainly due to lack of oxygen. (2) The main effects in ordinary anoxemia are due to action on the central nervous system, through the splanchnics. (3) In severe anoxemia with the splanchnics cut, both effects are produced by peripheral action. (4) The increase in blood sugar is only in part due to adrenalin.—T. C. B.

(ADRENAL) The treatment of Addison's disease (Zur Behandlung der Addisonischer Krankheit). Quincke (H.), Therap. Halbmonatshefte (Berlin), 1920, **34**, 42.

A description of two patients who had lived during the war in extremely bad environment. Both showed all the classic symptoms of Addison's disease and were cured by the administration of 100 mgm. of desiccated adrenals daily. The author suggests that in these cases there is no anatomical lesion but a diminished function of the adrenals caused by undernourishment.—J. K.

ADRENAL deficiency and adrenalin in cholera and seasickness (Insuffisance surrénale et adrénaline; "Cholera et mal de mer"). Naamé, Paris Med., 1917, **7**, 415-416.

Naamé agrees with several of the French observers that the symptomatology of cholera is due largely to acute adrenal insufficiency and that administration of adrenalin is the logical treatment.

A theory is offered that sea-sickness is due to inhibition of the adrenal glands brought about by the action of the undulatory movement upon the solar plexus. In substantiation of the theory, the observation is recorded that the administration of adrenalin has an excellent effect upon the malady. Numerous successes are reported. Large doses should be employed, 5 to 6 mgm. in 24 hours, the doses being given at half-hour or hour intervals, especially when the stomach is empty. The nausea is promptly relieved and the normal ability to retain food is restored.—R. G. H.

(ADRENAL) Action of drugs on the output of epinephrin from the adrenals. V. Curara. Stewart (G. N.) and Rogoff (J. M.), J. Pharm. & Exp. Therap. (Balt.), 1919, **14**, 343-354.

Curara in doses sufficient to paralyze the skeletal muscles in the cat depresses the output of epinephrin from the adrenals to a marked degree. The depression begins promptly and may be still well marked when the paralysant effect on the muscles has begun to disappear. Although precise calibration was not attempted it was found that the output of epinephrin was depressed markedly at a time when stimulation of the vagus caused cardiac inhibition.—F. F.

(ADRENAL) Asthmatic spasm treated by adrenin (Crise d' asthme, traitement par l' adrenaline). Thiroloix (J.), Bull. gen. de Therap. (Paris), 1916-17, **169**, 97-98.

T. reports six cases in which the subcutaneous injection of 1 cc. of adrenaline relieved the asthmatic spasms completely. He recommends the drinking of black coffee by the patient after the administration of the drug to relieve the after effects of the large dose given.—F. S. H.

(ADRENAL) Morphology and cytology of the chromaffine system of saurians (Nuovo contributo alla conoscenza del sistema cromaffine dei Sauri. Studi morphologici e citologici sulle capsule surrenali, con speciale riguardo ai paragangli omonimi.) Trinci (G.), Arch. ital, Anat. e Embryol. (Firenze), 1916, **14**, 513.

An anatomical study of the adrenal, and inter-renal chromaphil tissue and paraganglia of reptiles; of technical interest.
—E. R. H.

(ADRENAL) The hypertrophy of the suprarenals in the pregnant rabbit should not be attributed to the presence of the foetus (L'hypertrophie des capsules surrénales chez la lapine gestante ne doit pas être attribuée a la présence du foetus). Watrin (J.), C. R. Soc. de Biol. (Paris), 1920, **82**, 1405-1407.

In previous experiments the action of the corpus luteum and the unattached ovum were studied. In this paper another factor, the placenta, is considered.

The placenta consists of cells of maternal origin, and cells of foetal origin, either of which may have an action on the suprarenals. By making an incision in the uterus of a rabbit whose ovaries contain corpora lutea, it is possible to produce cellular elements in the absence of the foetus, that are identical with those of normal maternal origin. Under these circumstances it is found that the placental elements of maternal origin have no action by themselves, and the hypertrophy of the suprarenals must be due to uterine traumatism.

It is impossible to produce the foetal placenta in the absence of the foetus, but if we submit a rabbit to a fecundating coitus and on the 10th day remove the embryo through a small incision in the uterine wall, the wound heals quickly and the placenta continues to develop. If we examine the suprarenals 10, 15, or even 20 days after the operation, they show hypertrophy equal or superior to that observed in a normal gestation. As the foetus has been removed and the traumatism is slight, we must look to the placenta as the cause. This is in opposition to most biologists who make the foetus the direct factor in the hyperfunctioning of the suprarenals.

The author thinks this "hypertrophie gravidique" is of the same order as the hypertrophy of other glands of internal secretion, such as the thyroid and hypophysis. It is a reaction to specific substances secreted by the attached ovum and by the elements of the foetal placenta. It is believed that the capsules have been "sensitized" by the secretion from the corpus luteum.
—T. C. B.

(ADRENAL) A case of Addison's disease (Een geval van ziekte van Addison). Wertheim Salomonson (J. K. A.), Nederl. Tijdschrift v. Geneesk. (Haarlem), 1919, **63** (ii), 1930.

A description of a classical case.—J. K.

ADRENIN, Unusual action of — in elderly persons (Ungewöhnliche Wirkungen des Adrenalins in höheren Lebensalter). Arnstein (A.) and Schlesinger (H.), Wien. klin. Wchnschr. (Vienna), 1919, **32**, 1179.

Precaution is necessary in the giving of adrenalin to elderly persons since frequently after the injection of small doses of this drug the rise of blood pressure is followed by a sharp fall and the heart-beat may become very slow for some hours. Tachycardia may be produced in individuals having cardiac insufficiency and when there is present a sclerosis of the coronary arteries the injection of even small doses may be followed by severe attacks of stenocardia. In rare cases glycosuria results. —J. K.

(ADRENIN) Adrénaline et dissociation auriculo-ventriculaire (Etude a l'electro-cardiographe). Arrillaya, Thése de Paris, 1918-1919; Abst. Presse med., **27**, 389.

By means of the electrocardiagram, Arrillaya studied the reactions of six subjects of auriculo-ventricular dissociation to injections of adrenin. In the records the auricular and ventricular beats could, of course, be differentiated. It was found that adrenin caused a simultaneous increase in the rate of both auricles and ventricles. It did not ever result, however, in a recomposition of the cardiac rhythym. In four cases the auricles and ventricles began to react simultaneously and in two, the ventricles reacted more promptly. It is stated that the reaction to adrenin is more marked in patients exhibiting adrenal deficiency. Although not able to restore synchrony in the activity of the two parts of the heart, adrenin has a beneficial symptomatic effect, especially in dissociation due to intoxication with salicylates, digitalis or emetine.—R. G. H.

(ADRENIN PITUITRIN) Permeability of the blood vessels (Über die Durchlässigkeit der Gefässe). Bauer (J.) and Aschner (B.), Wien. klin. Wchnschr. (Vienna), 1919, **32**, 1204.

The injection of adrenalin caused an increase in the permeability of the blood vessels towards water and chlorine while pituitrin had no such effect.—J. K.

(ADRENIN) Studies on the regulation of the blood diastase. Fugimoto (B.), Am. J. Physiol. (Balt.), 1919, **50**, 208-215.

The object of the investigation was to determine if possible how the blood diastase is regulated. Among other things the effect of injections of adrenalin was tried. After injuring

the liver by hepatotoxin, injections of adrenalin had no effect on the diastase content of the blood.—T. C. B.

(ADRENIN) The secretion of adrenalin is not necessary for the maintenance of arterial pressure (La sécrétion surrénal d'adrénaline n'est pas nécessaire au maintien de la pression artérielle). Gley (E.) and Quinquaud (A.), C. R. Soc. de Biol. (Paris), 1919, **82**, 1175-1178.

The experiments of Strehl and Weiss have been repeated with negative results. When the right suprarenal was removed, and the vein of the left ligatured to prevent circulation, there was no fall of blood pressure as reported by Strehl and Weiss. —T. C. B.

ADRENALIN, The action of — on the heart. I. Action on the turtle heart. II. The modification of the action of adrenalin by morphine. Heinekamp (W. J. R.), J. Pharm. & Exp. Therap. (Balt.), 1919, **14**, 17-24, 327-342.

Heinekamp finds that adrenalin exerts a direct stimulating action on the vagus centers of the turtle. After repeated use it loses this effect. Injected directly into the heart muscle it increases both rate and amplitude, principally affecting the systole.

It was found that adrenalin has a direct central action and is synergistic with morphin. Morphin to a degree sensitizes the vagus center. The aggravated adrenalin action following morphin is due, therefore, both to the morphin sensitization and the adrenalin-morphin synergism. The increased blood pressure plays but a slight part in affecting the inhibition of the heart. —F. F.

(ADRENIN) Cecal stasis with betaiminazolylethylamine (histamine) intoxication in relation to dementia precox; indications for treatment. Holmes (Bayard), Am. Med. (Chgo.), 1916, **11**, 405-413.

Holmes discusses the problems connected with the etiology and treatment of dementia precox with special reference to the association of the disease with functional disturbances in the glands of internal secretion and with constitutional toxemia. The fact that dementia precox cases manifest the adrenalin paradoxes observed in animals or persons under the influence of toxic amines, such as those in ergot, suggested the possibility that this disorder might be due to excessive amounts of such substances in the body. With the assistance of a chemist, a number of patients were examined and a large excess of βiminazolylethylamine was found in their feces.

Study of the motor activity of the intestines of these same patients gave definite evidence of spasm of the colonic sphincter and exaggerated cecal stasis, which favor the production of the toxic histamine from histidine by bacillus aminophilus intestinalis and its absorption into the blood stream. From these results Holmes suggests that the treatment of dementia precox cases be directed against the production of the toxic substances in the cecum and proposes appendicostomy with protracted irrigation of the proximal colon through the artificial opening until better means can be found.—I. M.

ADRENIN treatment of influenza (Adrenalinbehandlung der Grippe). Jaksch-Wastenhorst, Deutsche med., Wchnschr. (Berlin), 1920, **46,** 112. Münch. med. Wchnschr. (Munich), 1920, **67,** 31.

Many authors have recommended the use of adrenalin in the serious cases of influenza but J. has never obtained good results from its use and warns against employing this drug in the disease.—J. K.

(ADRENIN) A new conception of asthma. Knapp (M. I.), N. Y. Med. J., 1920, **111,** 55-59.

Asthma is considered the result of gastrointestinal disturbances, especially insufficientia pylori. The use of adrenalin in controlling asthmatic attacks is not justifiable, in the author's opinion, because of the transitory relief given and the effect upon structures other than the lungs.—H. W.

(ADRENIN) The mode of action of adrenaline on the bacterial toxins (Du mode d'action de l'adrénaline sur les toxines bacteriennes). Marie (A.), Ann. l'Inst. Pasteur. (Paris), 1919, **33,** 645-656.

Although adrenaline renders innocuous bacterial toxins such as those of diphtheria and tetany, and is also antagonistic to the vegetable poisons crotine, and abrine, it is not effective in preventing the fatal effect of the alkaloids, strychnine sulfate or morphine chlorhydrate in the usual lethal dose. The same can be said for its lack of neutralizing action against nicotine, cocaine, and tuberculin. Marie bases this difference in protective effect on the fact that the one group produces antibodies in the blood, while the other group, the vegetable alkaloids, does not so do, and although adrenaline does not destroy the antigenic properties of the tetanus toxin, it does neutralize doses ordinarily fatal. The mode of action is tentatively given as one of preliminary oxidation of the toxin by the adrenalin, facilitating its absorption by the antibodies.—F. S. H.

ADRENIN, The effect of — upon the rate of locomotion of Planaria and of toad larvae. Moore (E. L.), Biol. Bull. (Woods Hole), 1919, **37**, 157.

Planaria, so far as known, do not produce any secretion corresponding to adrenin, yet they are made more excitable by dilute solutions of this substance, with resultant early fatigue. The increased excitability resulted in in-coordinated movement and in many cases interfered with locomotion. Toad larvae which have adrenals tended to react to adrenin in the same manner as Planaria.—E. R. H.

(ADRENIN PITUITRIN) Action of certain drugs on the brain circulation in man. Raphael (T.) and Stanton (J. M.), Arch. Neurol. & Psych. (Chgo.), 1919, **2**, 389-392.

Records of the pulsations of a subtemporal cerebral hernia were made after the inhalation of amyl nitrite and the intravenous injection of epinephrin, caffein, and pituitrin. Epinephrin induces a primary constriction of the brain vessels, followed by a marked dilatation. Pituitary extract injections result in a dilatation of the brain vessels.—F. C. P.

(ADRENIN PITUITRIN) Cardiac death due to diphtheria. Rohmer (P.), Berl. klin. Wchnschr., 1917, —, 1059; Abst., La Pediatria.

Owing to the adrenal insufficiency found in paralysis of the heart, Rohmer recommends adrenalin hypodermically (not intravenously since this proves too often dangerous). One to 3 cc. of 1:1000 adrenalin hypodermatically used very often, or adrenalin and pituitrin in association, is claimed to be of a great usefulness.—G. V.

(ADRENIN) The occurrence of epileptic seizures after the injection of adrenalin preparations (Nella provocazione degli accessi epilettici coi preparati surrenali). Silvestri (T.), Gaz. degli Ospedali. (Milan), 1919, **40**, 852.

A claim for priority of recorded observation of the production of epileptical seizures by the administration of adrenalin to epileptics. (See Endocrin. **3**, 349).—J. K.

(ADRENIN PITUITRIN) Rhythmic contractions of vessels. Soloveitchik (D. E. A.), Dissertation, Petrograd, 1917, pp. 82.

A method of Kravkov (isolated ear of a rabbit) was used with a modification which consists in excluding the veins by ligaturing them in order to observe only the changes of arterial

aperture. Spontaneous contractions of vessels can be observed while perfusing the preparation with Locke's solution; their strength varies within wide limits; sometimes they are totally closed. If the ear is kept at the temperature about 0° it is possible to observe the contractions even 6 to 10 days after the operation. The temperature of the body is more favourable for these contractions than lower ones. Oxygen does not produce any visible influence on these contractions. Adrenaline augments the spontaneous contractions at body temperature, but has little effect at room temperature. Atropine antagonises adrenaline. The most efficient concentration of a drug is that which produces a strong vaso-constrictor action. Histamine, ergotoxine, and pituitrin augment these contractions; rabbit serum in concentrations which produce a strong vaso-constrictor effect, extracts of suprarenals and of the heart of rabbits augment the contractions. Strophanthin and digitalin augment them if the pressure of the perfusion liquid is increased after the contraction of vessels evoked by the drugs used. Nicotine and strychnine augment the contractions, veratrine lowers them. No visible influence is produced by pilocarpine, eserine, caffeine, quinine, chloroform, camphor, barium chlorate, or lactic acid. The contractions described above are spontaneous in a real sense; the constituents of the blood merely regulate them. It is an inherent property of the muscular fibres.—Physiol., Abst., **4,** 388.

(ADRENIN) Hemophilia. Sugiura (J.), Jikwa Zasshi, 1916, **199,** 1-22; Jap. Med. Lit., 1917, **2,** 6.

A case is described in which fibrin factors were normal, but in which the blood contained a large amount of adrenin.—Physiol. Abst., **3,** 536.

ADRENIN treatment of influenza (Grippebehandlung mit Adrenalin). Wagner (G. A.), Münch. med. Wchnschr. (Munich), 1920, **67,** 31.

The use of adrenalin in influenza is indicated only when the case is complicated with penumonia and the lungs are rapidly invaded by a serous exudate. The drug should never be given intravenously since it causes a diminution of the blood vessel permeability.—J. K.

(ADRENIN OVARY) Treatment of osteomalacia of pregnancy with adrenalin (Behandlung der Schwangerschaftsosteomalazie mit Adrenalin). Wagner, (G. A.), Münch. med. Wchnschr. (Munich), 1920, **67,** 31.

This is a report of a case of a pregnant woman with bronchitis, bronchiectasis and thoracic pain accompanied by

symptoms of osteomalacia. After a few injections of adrenalin the pain disappeared. During 58 days a total of 91cc. of adrenalin had been injected. After a premature confinement the patient's ovaries were removed. The interstitial cells of both were found to be enormously developed.—J. K.

AUTONOMIC NERVOUS SYSTEM, The arrangement of. Langley (J. N.), Lancet (Lond.), 1919, (i), 951.

Prof. Langley points out that since the appearance of Gaskell's book, "The Involuntary Nervous System," there has been a tendency among writers to consider that the main problems of this system were settled by Gaskell. The truth is that Langley himself worked out a great many of the facts of fundamental importance attributed to Gaskell.—L. G. K.

(BLOOD SUGAR DIABETES) The influence of muscle activity on the amount of blood sugar (Der Einfluss von Muskelarbeit auf den Blutzuckergehalt). Brösamlen (O.) and Sterkel (H.), Deutsches Arch. f. klin. Med. (Leipzig), 1919, **130**, 358.

The authors found that in normal persons the blood sugar concentration with the subject at rest and with empty stomach shows, when examined at different moments, but few variations. In diabetes these variations are more pronounced but never very great. In normal persons much activity diminishes the amount of blood sugar: this may be preceded by a very short moment of hyperglycemia. The blood sugar reaches the lowest amount, approximately an hour after the end of the muscle activity. In diabetes the same influence may be observed, though extremely rarely; nearly always muscle activity is followed by hyperglycemia, lasting for many hours.—J. K.

A BLOOD SUGAR tolerance test. Janney (N. W.) and Isaacson (V. I.), Proc. Soc. Exp. Biol. & Med. (N. Y.), 1917, **15**, 15-16.

It is considered that the hyperglycemia response to ingested sugar is a better test of sugar tolerance than the appearance of sugar in the urine. The test is carried out by first determining the blood sugar of the patient who has fasted over night, and then administering pure glucose in the ratio of 1.75 gm. per kgm. of body weight in a 40 per cent aqueous solution, with the addition of a lemon, and again determining the blood sugar at the end of two hours. In normal subjects the blood sugar has by this time returned to its fasting level. If hyperglycemia still persists, the blood sugar tolerance is lowered. Preferably half hourly observations are made following the

glucose ingestion as well as the sugar eliminated in the urine, and for the twenty-four hours.

Glycosuria which is normally absent under the conditions of the test is not a necessary accompaniment of decreased tolerance. A normal blood sugar curve accompanied by glycosuria usually indicates renal diabetes. All cases of Graves' disease examined show a prolonged blood sugar curve, as do certain cases of chronic interstitial nephritis. Hypoendocrine conditions such as cretinism and muscular dystrophy are characterized by increased sugar tolerance with the ordinary urinary test, but blood sugar determinations showed hypoglycemia and a delayed tolerance curve.—F. S. H.

(CAROTID GLAND) The function of the so-called carotid gland (Über die Funktion der sogenannten Carotisdrüse). Massaglia (A.), Frankf. Ztschr. f. Pathol. (Wiesbaden), 1916, **18**, 333-347.

The author being unable to obtain the chromaffin-reaction in the carotid-gland after fixation in potassium bichromate and formalin, studied the effect of its cauterization or removal from cats, dogs, and rabbits, with particular respect to the production of glycosuria. The cauterization, removal, or cutting of the nerves to the gland caused but a transient glycosuria in cats and dogs, and but little, if any, effect in rabbits. This is explained on the basis of a stimulation of the sugar center as a result of the operation and not as due to the glandular properties of the tissue itself. The author concludes that on the basis of this evidence the so-called carotid-gland should be considered as a paraganglion.—F. S. H.

(CORPUS LUTEUM) Organotherapy in uterine hemorrhages (Zur Organotherapie der Gebärmutterblutungen). Hannes (W.), Monatsch. f. Geburtsh. u. Gynäk. (Berlin), 1919, **50**, 199-205.

The logical course of treatment of menorrhagia not due to a tumor formation or disturbance of pregnancy is essentially organotherapeutic, and dependant upon the use of some preparation of the corpus luteum. It was found that the subcutaneous injection of the contents of a 1.1 c.c. ampoule representing 1 gm. of fresh tissue gave satisfactory results. As examples three cases are cited in which the hemorrhage in a 24 year old, a 25 year old, and a 44 year old woman had lasted for 3 weeks, 2 weeks, and 20 days respectively. In all three cases the hemorrhage was brought to a complete stop by one injection of the extract. All cases do not necessarily respond so quickly, but, by and large, the final results are the same. It frequently happens

that the first menstruation after the treatment is somewhat delayed while the duration of the period is usually shortened.
—F. S. H.

CORPUS LUTEUM, Menses-increasing substance from—. Seitz (L.) and Wintz (H.), U. S. Patent 1,318,698, Oct. 14, 1919.

A menses-increasing substance is obtained from corpus luteum by separating the watery liquid containing the active substance from a mixture of alcohol extracts and $CHCl^3$ extracts obtained by successive extraction of ovaries with cold alcohol, hot alcohol, $CHCl^3$ and boiling alcohol, by adding an excess of $CHCl^3$ to the mixture of extracts, and then isolating the active substance by evaporating the aqueous liquid and purifying the residue with ether. U. S. 1,318,699 relates to a modification of the method, according to which there is separated from the alcohol extracts obtained by extracting ovaries successively with alcohol, acetone, cold and warm ether, $CHCl^3$ and hot alcohol, first the H_2O and constituents soluble in H_2O by the addition of an excess of $CHCl^3$ and then there is recovered from the remaining alcohol $CHCl^3$ mixture the menses-controlling substance by evaporating and extracting again the residue of the evaporation with both the ether extracts previously obtained, evaporating the extract thus obtained to dryness, redissolving the orange-yellow mass obtained, filtering the solution and evaporating it in vacuo until a mass of uniform consistency is obtained.—Chem. Abst.

(CORPUS LUTEUM) Ueber die Beziehungen des Corpus Luteum zur Menstruation. Seitz (L.) and Wintz (H.), Monatschr. f. Geburtsh. u. Gynaek. (Berl.), 1919, **49**, 1-23.

Correction of reference, Endocrin. **3**, 353.

DERCUM'S DISEASE following exposure to war, with biopsy of the tumors (Morbo di Dercum in seguito a vita di guerra, con biopsia di qualche tumore). Boschi (G.), Riv. Pathol. nerv. e ment. (Firenze), 1918, **23**, 161-192.

In his original description of adiposis dolorosa Dercum mentioned the possibility that it is primarily of endocrine origin. A case is described by Boschi which throws light upon the problem. A young soldier having this disease showed, among other things, swelling of the thyroid approximately contemporaneously with the first appearance of lipomata, hyperidrosis, frontal and bitemporal headaches, asthenia and hypoaphrodisia. The illustration published shows transverse crines. Blood pressure was 160/100. These findings are interpreted as indicating a pluriglandular etiology of the disease, in which the hypophysis

played the principal role. The psychological, neurological and somatic findings are reported in detail and the etiology discussed at some length.—R. G. H.

DERCUM'S DISEASE, Researches on metabolic exchange in —(Di alcune ricerche sul ricambio nella malattia di Dercum). Martelli (C.), Patholgica, 1916, —, 189.

The author noted that in a case of Dercum's disease the nitrogen and mineral components of the urine were in general diminished. After thyroid-adrenalin therapy they were increased. The increase was noted in both urea and non-urea nitrogen, but the quantity of amino acid nitrogen was decreased.—Riv. Patol. nerv. e ment., **22,** 503.

(PANCREAS DIABETES) Diet reduction with retention of protein to relieve glycosuria in diabetes mellitus. Fenlon (R. L.), Boston M. and S. J., 1920, **182,** 168-171.

The tendency to develop acidosis is decreased by keeping the protein intake of the diet at a "necessary level." This is considered to be 0.12 grams of nitrogen per kilogram of body weight. The patients complain less of hunger on such a dietary measure than when this factor is ignored. The author believes the protein indirectly maintains the serum protein of the blood and possibly aids in the nutrition and functioning of the kidney during diet reduction.—H. W.

DIABETES, The lime deficiency of—. Kahn (Max) and Kahn (Morris H.), Arch. Int. Med. (Chicago), 1916, **18,** 212-227.

The object of the investigation was to show the importance of lime deficiency in diabetes. Much evidence that calcium deficiency occurs with great frequency is cited from the literature. Studies were made on early cases of diabetes. These showed that calcium was being lost constantly from the body. Calcium chloride injected intravenously caused marked improvement in the symptoms. Glucose excretion fell markedly and glycemia gradually declined. The quantity of urine was reduced and acetone bodies did not appear in the urine of any of the patients.—I. M.

(DIABETES) The "Allen" treatment of diabetes modified by the administration of alikalies in full doses. Mulvany (T. E.), Practitioner (Lond.), 1918, **101,** 171.

A brief report of a case of diabetes in a man of 19 years. The Allen starvation treatment only temporarily cleared the urine of sugar and the patient appeared to be on the verge of

coma. Starvation was then tried again and a teaspoonful of bicarbonate of soda in a glass of water was administered every four hours. In four days the patient was sugar-free, and at the time of writing, about five months later, the patient's health was excellent and he was still sugar-free.—L. G. K.

(DWARFISM) An unusual case of dwarfism in twins. Goldstein (H.) and Schneck (M.), N. Y. Med. J., 1920, **111**, 98-100.

Case report of dwarfism in one of twins. The authors conclude this case to be one of a class of dwarf growths, showing no evidence of any preverted internal secretion or defective constitutional condition. The case is considered one of achondroplasia or chondrodystrophia (Kaufman).—H. W.

ENDOCRINE disturbances, Multiple—(Sindrome pluriglandolare). Fici (Vincenzo), La Riforma Medica (Naples), 1919, **35**, 778-782.

Fici reports a case of pluriglandular syndrome (hypoadrenalism, hypopituitarism, hypo-ovarianism, status lymphaticus and splenomegally) in a woman of 33. The illness began seven years ago. The only antecedent symptom that might be connected with the later syndrome had been a fit of diarrhea, vomiting, and cramps in the lower limbs, which lasted about twenty days. The patient ascribed the beginning of the malady to sorrow over losing a child. She had severe headaches and intractable eczema of the eyes, probably ascribable to pituitary or other endocrine anomalies. Injections of pituitary, ovarian and thyroid extracts failed to elicit a reaction. There was only a slight response to adrenalin, but a marked one to atropine and a partial one to pilocarpine. These latter findings, together with a tendency to vomiting, diarrhea and asthma, indicate vagatonia. As to etiology nothing beyond psychic trauma was discovered. Tuberculosis, which is frequently found in such cases, was absent in this.—G. V.

ENDOCRINE GLANDS, Studies on the conditions of activity in —. V. The isolated heart as an indicator of adrenal secretion induced by pain, asphyxia and excitement. Cannon (W. B.), Am. J. Physiol. (Balt.), 1919, **50**, 399-432.

This is the full report promised by Cannon in a short article in Science (May, 1917, 45, 463) delayed on account of his absence. It is an answer to the criticisms of Stewart and Rogoff and others, and should be read in the original. The positive evidence in favor of adrenal secretion during pain, emotion and asphyxia is reviewed and criticisms of the catheter method are considered. The author defends the use of the isolated heart as

an indicator of adrenal secretion, criticises the methods yielding negative evidence, and reaffirms the emergency theory of the function of the adrenals.—T. C. B.

(ENDOCRINE INSUFFICIENCY) The clinical picture of inanition osteopathy (Zum klinischen Bilde der Hungerosteopathie). Hamel (O.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 68.

Five cases are described in this paper, two of which showed tetanic symptoms. The probable cause is endocrine insufficiency resulting from undernourishment.—J. K.

ENDOCRINE neuroses and their treatment. Rogers (J.), N. Y. Med. J., 1920, **111**, 229-232.

The autonomic nerve and plates spray out like fingers around the receiving cells. Between these cells and the nerve spray lies the circulating lymph and blood with all the nutrient matter and endocrine products. The impulses discharged from the nerve spray can be imagined as pushing nutriment into the receiving cells. In this process the product of the thyroid, and probably other organs, seems to accelerate the cell chemistry, while that of the adrenal, and possibly the pituitary, seems to retard the cell's metabolism. The thyroid products acts only through or upon the terminal sprays of the vagus system, while the adrenal is limited in its inhibition to the terminal sprays of the sympathetic. A circle drawn around the receiving cells and the terminal neuron or spray of the motor and vagus and sympathetic nervous systems seems now to indicate the point of action of at least the pituitary, thyroid, parathyroid and adrenal glands. The circle also necessarily includes the point at which nutriment gains access to the cells and the products of their metabolism are excreted. The parasympathetic seems by vasodilation and stimulation of functional activity to drive all the organs, while the sympathetic seems to check them, and this drive influence is vastly reinforced by the thyroid. The adrenal, on the other hand, exhibits an equally strong influence upon the sympathetic check. These opposing effects are most clearly shown in the stomach and pancreas. (See abstract Endocrin., 1919, 3, 409.)

The moist and flushed skin, the overacting heart, abnormal appetite (vagus hunger contractions), frequent bowel movements and the diuresis of hyperthyroidism all point to excessive thyroid drive. Such cases usually appear to begin with an initial hypothyroid disturbance which, in turn, has its origin in fatigue or an acute infection of traumatism. Apparently both groups of nerves fail in the initial stage of these disorders. Then if the fatigue or toxemia continues, the check upon the metabol-

ism becomes more deficient than the drive and the result is hyperthyroidism. If, on the other hand, the drive becomes more and more deficient, the primary hypothyroidism deepens into a myxedema. To say that there is an excess of drive or excess of check in any instance, is probably not strictly correct. For what appears as an excess of drive may really be a lack of check, and the excess of check, a lack of drive upon the metabolism.

The treatment not only of thyroid disturbances, but of all functional disorders of the viscera, is or should be, primarily that of reinforcing the deficient drive or the deficient check. The thyroid nucleoproteins, in doses of 1 50 to 1/10 grain frequently repeated, are most satisfactory. The liquid residue or noncoagulable part of an aqueous extract (as prepared by the author) sometimes proves better. The commercial preparations made by desiccation of the entire gland tend to be inert or toxic. The thyroid nucleoproteins or residue are useful in all frankly hypothyroid or deficient drive conditions and in many so-called mixed hypothyroid and hyperthyroid disturbances in which there is evidence in some viscera of good or active functioning and in others of deficiency. The residue is clinically better than the nucleoproteins in the hypothyroid or mixed thyroid disorders which are accompanied by a high blood pressure and also in cases with gastric hypofunctioning. Thyroid and other neuroses such as those of the stomach and intestine, which show excess of the drive over the check upon metabolism, can be benefited by almost any adrenal derivative; adrenalin is the least satisfactory. The adrenal nucleoprotein in doses of 1/10 to 1/2 grain every 2 hours, or the adrenal residue in doses of 5 to 20 minims every 2 hours, are the most useful of the adrenal derivatives for medical treatment of hyperthyroidism.

Whenever hyperthyroidism is present and not speedily changed to the preceding hypothyroid disturbance, surgery is indicated, particularly, ligation of thyroid arteries. In recovery these patients always pass again in the order of the development of symptoms through the initial stage of hypothyroidism.

The pituitary, at least in the stomach and some parts of the intestine, seems to reinforce or support the adrenal check. The parathyroid apparently reinforces the thyroid drive, but not exactly at the same anatomical point. Hence, in the present state of knowledge, it is legitimate, when the drive or check symptoms cannot be helped by either thyroid or adrenal feeding, to experiment with the associated derivatives.—H. W.

(ENDOCRINE ORGANS) An introduction to the study of the endocrines in gynecology. Bandler (S. W.), N. Y. Med. J., 1920, **111**, 221-225.

Menstruation is dependent upon the normal development of the genitalia and the normal trophic control of these structures. Every menstruation is a crisis in which the ovary, thyroid and pituitary participate. Menstruation is preceded by premenstrual changes varying in intensity and degree according to the action and interaction of these glands. Women whose menstrual periods occur every 35 days are in need of endocrine stimulation. They are more likely to begin labor at a date later than estimated. Women with hypoplasia of the uterus and those who become pregnant after endocrine therapy often have a long and tedious labor. Those who have repeated miscarriages are probably hyperpituitary and when they finally carry a viable child may not go to term.

Disorders most amenable to endocrine therapy are actual or relative amenorrhea, lactation atrophy, menorrhagia, metrorrhagia, dysmenorrhea, sterility, "one child sterility," threatened and habitual miscarriage, disturbances of the climacterium, fibromyomata, and hyperthyroidism, dyspituitarism and similar conditions. Nervous and irritable gynecological patients usually are suffering from thyroid or pituitary disturbances. The relation between the various endocrine structures is less stable in women than in men, hence alterations in the cyclic functions of the sex apparatus result in endocrine disturbances manifested as changes of the body, altered nervous function and psychic instability.—H. W.

(ENDOCRINE ORGANS) Trauma and constitutional disease (Trauma en constitutioneele ziekten). Broex (D.), Tijdschr. v. Ongevallen Geneesk. (Amsterdam), 1919, **4**, 257, 289, 321.

A general discussion, without new data, on the relation between trauma and diseases of the endocrine organs.—J. K.

(ENDOCRINE ORGANS EMOTIONS) Biochemical researches in normal and in frightened animals (Richerche biochemiche in animali normali ed in animali emozionati). (Preliminary report.) Buscaino (V. M.), Rivista di Patologia nervosa e mentale (Firenze), 1920, **24**, 400-403.

In the previous issue of this Journal Buscaino's earlier researches on the histo-chemistry of the endocrine organs were reported. The present paper deals in a preliminary way with some of the results obtained by the application of these methods to the study of the reactions of the various organs to the emotions. In addition to numerous negative or dubious findings there are reported a variety of positive results. Confirming earlier investigators, it was found that frightened guinea pigs and cats become glycosuric. Likewise the oxidizing power of

the blood serum is increased, especially in animals showing objective signs of fright.

Guinea pigs as well as dogs show diminution of the yellowish color assumed by pieces of central nervous substances treated with Lugaro's solution. Parallel to this runs a diminished affinity of all the nervous tissue for the toluidin blue. In guinea pigs augmented nuclear activity of the nervous cells occurs as shown by an increase of the granular contents in the cerebral cortex and still more in the nuclei of the base. The neuroglia cells become richer in fats.

Vascular congestion in the liver (cats), diminished glycogen (guinea pigs, cats), increased neutral fats (guinea pigs), diminution of neutral fats (cats), increased lipoids (guinea pigs, cats), increased fuchsinophil formation of the protoplasm (guinea pigs, cats), increased argentophil formation of same (guinea pigs, cats), marked nuclear variations and increase of special nuclei in guinea pigs as well as in cats were seen.

In the adrenal cortex there were noted vascular congestion (cats), increase of neutral fats and stearin (guinea pigs), diminution of neutral fats and stearin (cats), increased lipoids (cats), increased fuchsinophil formation of the protoplasm (guinea pigs, cats), marked nuclear variations and increase of a special form of nuclei in cats as well as in guinea pigs.

Similarly, the thyroid reacted by vascular congestion (guinea pigs, cats), increased volume of the protoplasm (cats, guinea pigs), marked nuclear variations and increase of the special nuclei (cats). In the interstitial cells of the testis (guinea pigs) only increase of the cellular size was noted. In the interstitial cells of the ovary (cats), there was increase in size of the cells, marked nuclear changes and increase of the special nuclei.—G. V.

(ENDOCRINE ORGAN) Glands and emotions under bombardment (Glands et emotions de bombardments). Etienne (G.) and Richard, Revue med. (Paris), 1918, —,— (Oct. 12), Reprint, pp. 7.

During the bombardment of Nancy the populace was subjected to intense emotional stress. The authors had several opportunities to observe striking endocrine defects which resulted in patients so excited. Various instances of mammary depression and of chlorosis were seen; these were ascribed to perturbation of ovarian functions. Two cases are described in which marked transcient glycosuria resulted. In two cases Graves' disease with hypertension and two with hypotension were seen. These also are described. In the light of Cannon's researches the authors regard the adrenal glands as playing a major role in the genesis of the maladies.—R. G. H.

(ENDOCRINE ORGANS) Arterial pressure and emotions of war (La pression arterielle et les emotions de guerre) Etienne (G.) and Richard, Paris med, 1919, **9**, 109. Reprint, pp. 13.

The authors had extensive opportunity during the war to study the genesis of hypertension as a reaction to emotional stress. They believe that the initial hypertension is due to excitation of the vasomoter system directly, but that continued stress leads to changes in the endocrine organs whereby the initial effect is augmented and continued. As evidence, cases are mentioned in which sudden shock resulted in amenorrhea, glycosuria, and swelling of the thyroid gland. Especial importance in this connection is ascribed to the adrenal glands, which can both reinforce the vasomotor impulses directly and secondarily stimulate other endocrine organs.—R. G. H.

(ENDOCRINE ORGANS) Must the extracts of glands in the study of endocrinology be substituted by blood or lymph, coming from these glands (Gli estratti ghiandolari devons essere abbandonati e sostituiti dal sangue o dalla linfa defluente dalle rispettive ghiandole, negli studi endocrinologici)? Ghedini (G.), Gazzetta degli Ospedali (Milan), 1919, **40**, 9.

The author warns once more against identification of the pharmocological action of an extract of an endocrine organ with the physioligical function of the organ itself. No new facts are adduced.—J. K.

(ENDOCRINE ORGANS, BLOOD SUGAR) The significance of a small amount of sugar in the urine. Hamman (L.), Can. Med. Ass. J. (Toronto), 1919, **9**, 961-967.

The author points out the advantage of studying the fasting blood sugar and the blood sugar following a meal rich in carbohydrate in order to distinguish the hyperglycemic from the renal type of glycosuria when only a small amount of sugar is present in the urine. The following test is advised: The blood sugar is determined in the morning after the night fast and the urine is examined. Immediately thereafter 100 grams of glucose are administered in lemonade and one-half hour, one hour and two hours thereafter, the blood sugar is determined and the urine examined for sugar. Normal persons react to this test with a rapid rise in the blood sugar which seldom exceeds 0.14 per cent. The high point is usually reached at the end of one-half hour and the original fasting level after an hour or hour and a half. No sugar appears in the urine.

Patients with a lowered carbohydrate tolerance react with a much higher rise of the blood sugar and the elevation persists much longer. The blood sugar reaches 0.18 per cent or more and remains above the original fasting level for three, four or more hours. When the blood sugar exceeds about 0.17 per cent sugar appears in the urine and continues to be excreted until some time after the blood sugar has fallen below this level.

The mild cases of renal diabetes are characterized by slight and usually transient glycosuria. On the other hand the hyperglycemic diabetics respond to the test not only by excreting sugar in the urine, but by displaying as well a low glucose tolerance. Disturbances of thyroid and hypophyseal function, hypertension, nephritis and diseases of the brain are also accompanied by a mild glycosuria which is of the hyperglycemic type. These conditions must be distinguished from diabetes by the clinical picture and this is not difficult if the physician is aware of their association with hyperglycemia. (See also. Endocrin. 1919, **3**, 63.)—L. G. K.

(ENDOCRINE ORGANS) Observation on the frequency of some constitutional diseases in the tropics (Enkele opmerkingen naar aanleiding van de menigvuldigheid van eenige constitutieziekten in de tropen). De Langen (C. D.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (ii), 1638.

The author observed that some diseases (diabetes, Graves' disease, hypertrophy of the prostate) are extremely rare in the tropics. Among 422,943 patients he never saw a case of myxedema.—J. K.

(ENDOCRINE ORGANS) Cranio-facial deformities considered as a syndrome of dysfunction of the endocrine glands in children (Les dysmorphoses facio-craniennes considérées comme syndrome du dysfunctionnement des glandes endocrines chez l'enfant). Robin (Pierre), C. R. Soc. de Biol. (Paris), 1920, **83**, 13-15.

The faulty functioning of the endocrine glands may, among other manifestations, alter the form and volume of the bones of the head and face. When we examine subjects of such skeletal alterations we find some trouble with the endocrine glands. If we examine the photographs and radiographs of children attacked by endocrine disturbances, we are struck with the fact that they are all cranio-facial dysmorphies. These deformities cause functional disturbances of respiration, digestion, vision, audition, olfaction and mastication, arrest of development, adenoidism; in short, a more or less pronounced disequilibrium of the psychic and vegetative functions. These react in turn on the endocrine glands, and a vicious circle is established.

The author finds that early treatment of the jaws and dental arches brings about an amelioration of the symptoms and a re-establishment of the biological equilibrium.—T. C. B.

(ENDOCRINE ORGANS) The influence of experimental hypofunction of one or more endocrine glands upon growth processes in very young cats and dogs (Il processo della crescenza nell'ipofunzione di une o piú ghiandole endocrine provocata sperimentalmente nei gatti e cani giovanissimi). Pugliese (A.), Bioch. e terap. sperim. (Milan), 1919, **6,** fasc. 3.

The simultaneous extirpation of one adrenal and one thyroid, with or without splenectomy, does not cause any apparent trouble in adult dogs and cats. The mono-thyro-parathyroidectomy in very young animals favours increase in body weight; this is retarded by the mono-adrenalectomy alone. The simultaneous extirpation of one adrenal and one thyroid is fatal in kittens of less than four months, and a progressive cachexia follows in 80 to 100 days. The bones of such kittens are smaller than those of the controls, and show a diminuation of nitrogenous and fatty substances with increased percentage of ash, Ca, and phosphorus. The same operation, if performed in very young dogs, only retards their growth and diminishes their organic resistance.—(Physiol. Abst. 4, 400.)

(ENDOCRINE ORGANS) The ductless glands in cardivascular diseases and dementia precox. Sajous (C. E. deM.), Med. Rec. (N. Y.), 1917, **91,** 82-84.

A general presentation of the subject is given with special reference to the frequency with which general arteriosclerosis and dementia precox are associated with well-known endocrine disturbances. Attention is called particularly to the occurrence of arteriosclerosis in "hyperadrenia" in which overwork, mental strain and emotional disturbances are said to be the cause. Arteriosclerosis in diabetes and myxodema is suggested to be a possible result of undernutrition in the vessel walls. Abnormal activity of the thymus, the adrenal bodies and the thyroid in dementia precox is spoken of as being of possible causal significance.—I. M.

(ENDOCRINE ORGANS) Osteomalacia, Three cases of (Drei Fälle von Osteomalazia). Steckelmacher, Münch. med. Wchnschr. (Munich), 1919, **66,** 1504.

A report of three typical cases, one of which was cured by the administration of phosphorus and pituitrin; the patient had also been suffering from a goiter, treated by operation. Another case became worse after the removal of the ovaries, which leads

the author to warn against such a procedure in this disease.
—J. K.

(ENDOCRINE ORGANS) Action of tissue extracts on smooth muscle (Action des extraits de tissus animaux sur les organes a fibres musculaires lisses). Stern (L.) and Rothlin (E.), J. Physiol. Path. Gén. (Paris), 1919, **18**, 441-485.

The effects of various tissue extracts on different organs were studied by adding the extract under consideration to horse serum which was being perfused either through the isolated organ or through the entire animal. As a result of their experiments the authors conclude that all the tissue extracts studied and the body fluids in general have the power of constricting blood vessels and of influencing the tonus of various smooth muscle organs.

In the liver two substances exist. One of these increases the tonus of smooth muscle. It is destroyed by alkalis, is soluble in water and in alcohol, insoluble in ether and is dializable. It is not destroyed by boiling or by prolonged exposure to acids. The second substance causes hypotonus of smooth muscle, is soluble in water, slightly soluble in alcohol and insoluble in ether. It resists boiling and the action of alkalis. The kidney contains several substances, some of which cause hypertonus and some hypotonus of smooth muscle. Thyroid extract contains substances producing a diminution in vascular and uterine tonus. It also contains a hypertonic principle differing considerably from the hypertonic substances of the liver and kidney. The lungs contain a hypertonic substance and also an antagonistic substance, analogous to those in the liver extracts. The extract of muscle also contains hypertonic and hypotonic substances which differ physically and chemically from those of the liver. Thymus and bone medulla contain a vasoconstrictor and hypertonic substance apparently the same as that of the liver. The lymphatic ganglia contain a substance producing contraction of blood vessels, except the coronaries, and of other smooth muscle organs independent of their innervation. It exhibits the same physical and chemical properties as the hypertonic substance of liver. The suprarenals are said to contain, besides adrenalin, a substance which produces contraction of the non-pregnant uterus, acting as an antagonist to adrenalin. In the spleen there is found a hypertonic substance producing constriction of the vessels and augmentation of the tone of all smooth muscle. This substance is soluble in water, alcohol and acetone and insoluble in ether, chloroform, benzol, petroleum ether and ligroin. It is thermostable, dializable and resists the action of acids, and of enzymes. It acts as an antagonist to adrenalin when the latter produces relaxation of the tonus of smooth muscle. Bile in high concentration produces vaso-

constriction followed by a dilation and loss of excitability of the vessel walls. Defibrinated blood as well as serum contain, besides vaso-constrictors, hypertonic and hypotonic substances derived in part from the formed elements of the blood and in part for such organs as the suprarenal capsules and the hypophysis.—L. G. K.

(ENDOCRINE-SYMPATHETIC SYSTEM) Clinical study of Paget's disease and the preponderance of lues as the causative agent of the endocrine-sympathetic process (Contribucion clinica al estudio de la enfermedad ósea de James Paget y sobre la preponderancia de la lúes en la etiopatogenia endócrino-simpatico del proceso). Castex (M. R.) and Waldorf (C. P.), La Prensa Med. Argentina (Buenos Aires), 1920, **6**, 233.

A case report the authors of which promulgate the opinion that hereditary syphilis so alters the endocrine-sympathetic system that the disturbance affects osseous morphogenesis.

—B. A. H.

ENDOCRINOLOGY, General Concepts of —; clinical thyroid manifestations; hormonotherapy (Conceptos generales de endocrinología; clínica de los estados tiroideanos, Hormonoterapia). Escuder Núñez (P.), Anales Fac. Med. Univ. (Montevideo), 1919, **4**, 69-110.

Correction of reference in Endocrin. **3**, 511.

ENDOCRINOLOGY in daily practice. Garretson (W. V. P.), N. Y. Med. J., 1920, **111**, 232-235.

The present paper is of much the same trend as one previously abstracted (Endocrin., 1919, **3**, 371).

The author holds that complete extirpation of the tonsils leads to subsequent compensatory hypertrophy of appendiceal tissue and resulting chronic appendicitis. The pituitary type of headache invariably associated with tonsil or appendiceal inflammation, and following extirpation of one or both of these organs, is due to a compensatory enlargement of the hypophysis. In all so-called shock states the existing condition is vagotonia due to hypoadrenia. Relief is attained by giving atropine, or better, by administering adrenalin. The suprarenal glands bear the brunt of all toxic assaults upon the body, either of endogenous or exogenous origin. The familiar exhaustion states following infectious diseases (influenza) are classical demonstrations of vagotonia due to hypoadrenia.—H. W.

(GENERAL) The interrelationship of menstruation, hair color, and libido (Ueber Menstruation, Haärfärbung und Libido und ihre gegenseitigen Beziehungen). Heyn (A.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttgart), 1919, **82,** 136-152.

An extensive statistical study of the relations existing between the age of incidence, duration, and molimina or menstruation and social position, place of residence, color of hair, degree of hairiness and libido. The details are too intricate to be compiled in an abstract.—F. S. H.

(GENERAL) The biology of old age (Sulla biologia della vecchiaia). Scala (Guglielmo), La Riforma Medica (Naples), 1919, **35**, 813.

From an endocrine point of view Scala postulates three stages in human life, namely, childhood, puberty and old age. From 25 to 35 there is a complete balance of the "vagotonic" and sympathicotonic hormones; after this period there is vagotony for a while, then, in old age, even the "vagotonic hormones" give way. It is not only that the endocrine glands in common with other organs are approaching decay, but, according to Richter and Galdi, early senescence and physiologic old age correspond to a pluriglandular syndrome manifested by such conditions as increasing connective tissue and fat distribution resembling that in eunucoidism. Furthermore, with the dysfunction of the skin, too much strain is laid on the kidneys with consequent impairment of the same. With diminished efficiency of the cerebrospinal and sympathetic nervous systems there is a degree of failure in organic correlation, hence, as Canstatt observes, in old people the individual organs may undergo disease more or less independently, as though they were isolated from the rest of the organism.—G. V.

(GENERAL) Diagnosis of the lesions of the nervous system produced by violent explosions in close proximity without external lesions. Williams (T. A.), Boston M. and S. J., 1920, **182,** 27-34.

Refers to endocrine factors only as a means of differentiation of lesions of the nervous system.—H. W.

GIGANTISM, Notes on a case of pre-adolescent—. MacPherson (J.), N. Zealand Med. J. (Wellington), 1918, **17,** 203-207.

Report of a case of gigantism accompanied by low-grade imbecility.—F. S. H.

GLYCOSURIA, Some unusual cases of—. Brown (W. L.), Clin. J. (London), 1916, **45,** 29-36.

Several types of glycosuria are discussed with illustrative cases. These are: 1, glycosuria with hypoglycemia or renal glycosuria; 2, pancreatic glycosuria due to a deficiency of this gland; 3, pituitary glycosuria and, 4, thyroid glycosuria, the last two types being due to hypersecretion. For the treatment of diabetes the author recommends the practice of determining the carbohydrate tolerance of each case and then selecting a carefully balanced diet including the proper amount of carbohydrate. Alkalis and a small quantity of alcohol in the form of whiskey are also advised.—I. M.

GLYCOSURIA, Injury and malingering. Collie (Sir J.), Med. Press. and Circ. (London), N. S., 1916, **102,** 425.

The medico-legal aspects of glycosuria following accidents is discussed by the author, who questions the likelihood of a permanent glycosuria resulting from injury. Attention is called to the frequency with which malingering is practiced by patients following accidents in the industries. Means for its detection, such as finding cane sugar or excessive amounts of lactose in the urine, are suggested.—I. M.

GLYCOSURIA from the military point of view (Les glycuries au point de vue militaire). Derrien (E.), Montpelier Médical, 1917, **39,** 550-554.

A brief description of the various possible causes of glycosuria which points out that emotional states are to be taken into consideration before rejections for military service on the basis of sugar in the urine.—F. S. H.

(GONADS) On the cause of pseudohermaphroditism (Over de oorzaak van pseudohrmaphroditisme). van der Broek (A. J. G.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (ii), 1625.

An interesting article. When in pregnancy the child "in utero" is a girl, the hormones of the ovary of the mother come into the blood of the child. The ovary of the child itself has probably an internal secretion; so these two secretions will increase each other. If the child, however, is a boy, mother and child together form an organism that may be compared to the animals of Steinach with one ovary and one testicle. The influence of the ovary is the more important; therefore, at birth boys have some of the female characteristics (large breast, producing milk). After birth the influence of the ovary ceases and the breasts become again smaller. If in a pregnant woman the ovary shows an increased function, this will have an influence on the child, when it is a girl. When it is a boy the quantity

of ovarian hormone will be too great; the equilibrium between ovary and testis is broken, the influence of the testicle diminished and the result may be male psendohermaphroditism. A diminished function of the ovary in pregnancy will have an influence on a boy; on a girl it would be possible (but this has not yet been made probable) that when the ovary of the child is not or not enough supported by the ovary of the mother, the Wolffian duct develops. Then female pseudohermaphroditism occurs. These last statements are very theoretical; perhaps they explain why male pseudohermaphroditism is much more frequently seen than the female form.—J. K.

(GONADS) On the existence of a secretion of the epididymis of the hibernating bat and its significance (Sur l'existence d'une sécrétion épididymaire chez la chauvesouris hibernante et sa signification). Courrier (M. R.), C. R. Soc. de Biol. (Paris), 1920, **83**, 67-69.

In the bat, during hibernation and after the arrest of spermatogenesis, there exists a considerable mass of sperm contained in the tail of the epididymis, and an intense glandular secretion from the cells of the initial part of the epididymal canal. The region distal to the canal is therefore transformed into a reservoir for the sperm, while the proximal region is differentiated into a glandular organ the products of which mix with the living sperm contained in the subjacent zone of the same canal. The cells of the epididymis are described in their various stages of secretion, and Henry's opinion that this secretion serves to nourish the sperm in its passage through the canal, is confirmed. It is also suggested that the glandular activity of the epididymis is conditioned by the secretion from the interstitial (endocrine) gland. Experimental proof will be given later.—T. C. B.

(GONADS) A case of gynecomastia following unilateral traumatism of the scrotum (Un cas de gynécomastie unilatérale consécutive á un traumatisme des bourses). Decléty (J.), Thése de Paris, 1919. Abst. Presse Méd., **27**, 772.

Mammary hypertrophy in the human male is rare. It may be unilateral or bilateral. The latter, Decléty states, is always secondary to a testicular defect, inherited or acquired, and most often, to trauma. The breast hypertrophy is usually on the same side as the injured testicle. The case is described of a young man of 25 in whom unilateral right-sided gynecomastia developed following a wound of the scrotum. The breast was removed surgically. Histological examination showed a pure hypertrophy of the gland; the sections were comparable to those

from the breast of a normal young nulliparous woman with manifest activation of the epithelium (Letulle). In explanation of the phenomenon the author advances the following theory: There develops in the testicle at the time of puberty a hormone which stimulates mammary growth. The later, more complete functioning of the testicle inhibits the action of this hormone, apparently by means of reflex action originating in the gonad. Pathological conditions in the testicle may suppress this reflex function, permitting free play of the growth hormone and leading to gynecomastia. This explanation accounts for its unilateral manifestation.—R. G. H.

(GONADS) Historical remarks on experimental hermaphroditism (Historischer Beitrag zur experimenteller Hermaphroditismus). Foges (A.), Zentralbl f. Gynaek. (Leipzig), 1920, **44,** 87.

A review of the historical development of this line of experimentation. It is pointed out that Hunter as early as 1780 reported gonad transplantations.—J. K.

(GONADS HYPOPHYSIS) The effects of inanition in the young upon the ultimate size of the body and of the organs in the albino rat. Jackson (C. M.) and Stewart (C. A.), J. Exp. Zool. (Phila.), 1920, **30,** —.

Rats were underfed from birth to 3, 6, or 10 weeks and from 3 weeks of age to 20 weeks or 1 year, and were then given a full diet for a time and autopsied. Those starved a long time were permanently stunted. The hypophysis and ovaries failed to regain their normal weight but the testes were somewhat overdeveloped.—E. R. H.

(GONADS) The innervation of the gonads in the dog. Kuntz (A.), Anat. Rec. (Phila.), 1919, **17,** —.

The nerves follow the ovarian and spermatic arteries, and are derived mostly from inferior mesenteric ganglia. There is no evidence that the interstitial cells receive any innervation, especially since cutting the nerves to the testis results in overgrowth of interstitial cells as the germinal cells degenerate.
—E. R. H.

(GONADS) Case of pseudohermaphroditism. Méndez S (Martin), Repertorio de Medicina y Cirugía (Bogota), 1919, **11,** 68-71.

Mendez gives an illustrated description of another instance of blunder in sex, the androgynoid being unmistakably of male sex, although baptized and brought up as a girl.—J. Am. M. Ass.

(GONADS) Experiments on the internal secretion of the sexual glands, especially on experimental hermaphroditism. Sand (Knud), J. Physiol. (Lond.), 1919, **53**, 257-263.

Steinach's results are confirmed. Also, hermaphroditism has been produced by the formation of artificial ovario-testes by a special technique, placing the ovaries in the middle of the testes and leaving the latter in place. The ovary grows easily into the testicular tissue, and is able to develop and form corpora lutea. The testes develop to perfect spermatogenesis, the gonads of different sex thriving in intimate union, apart from traumatic injury. Sand thinks this points more to an immunity of the normal organism to the heterologous gland, rather than to an "antagonism," as suggested by Steinach.—T. C. B.

(GONADS) The specific antagonistic sex-gland action before and after puberty (Die antagonistich-geschlechtsspezifische Wirkung der Sexualhormone vor und nach der Pubertät). Steinach (E.), Kaisl. Akad. der Wissenchft. (Vienna), 1919, No. 36.

The sexual glands produce certain hormones which are antagonistic in action to the effects of the sexual glands of the opposite sex. This is shown by the apparent inhibition of the taking of the graft of implanted heterologous sex glands when the glands of the host are still present, and the prevention of the development of the secondary sexual characteristics of the host on successful implantation. The transplantation of the ovary into cats causes the feminization of the animals whether male or female. These results can be obtained either before or after puberty. Lichtenstern has observed that implantation of cryptorchic testicles into men wounded in the war or into individuals having lesions of these glands seemed to cause a reappearance of the morphological, functional, and psychic characteristics of the male sex. In one case the results lasted over three years. And in one case of transplantation after four years of eunuchism because of tuberculosis of the testicles, there was a return of the hair, musculature and virile potency. In an infantile case masculine characters developed after implantation of a graft.—B. A. H.

(GONADS) Artificial hermaphroditic glands in mammals and birds (Künstliche Zwitterdrüsen bei Säugern und Vogeln). Steinach (E.), Kaisl. Akad. der Wissenschft. (Vienna), 1919, No. 37.

In spite of the antagonism of the heterologous sexual glands it is possible to obtain hermaphroditism in rats and guinea pigs.

The result, however, depends on the amount of active tissue in each gland and on the period when the transplanation is made. The animals may take the characteristics of both sexes; e. g., females may take on the skeletal growth of the male.—B. A. H.

(GONADS) Experimental and histological proof of the presence of a causative relationship between homosexuality and hermaphroditic sex glands (Experimentelle und histologische Beweise für den ursachlichen Zusammenhang von Homosexualität und Zwitterdüse). Steinach (E.), Kaisl. Akad. der Wissenschft. (Vienna), 1919, No. 38.

The author observed that when crossed testicular implantation was done there frequently occurred in man an induced homosexuality which was usually but not always permanent. In animals, however, this perversion of sex was periodic and now one type would become evident and then the other.—B. A. H.

(GONADS) Histological properties of the generative glands in human homosexuals (Histologische Beschaffenheit der Keimdrüse bei homosexuallen Männern). Steinach (E.), Kaisl. Akad. der Wissenschft. (Vienna), 1919, No. 39.

This is a report of a study of the testicles of six men who were homosexual, the material in the majority of cases being obtained at autopsy. There was found evidence of degenerative changes regardless of age, a restricted number of the seminiferous canals, the aspect as a whole resembling that of the cryptorchic testicles. There were present large cells, having abundant protoplasm, a clear nucleus, and some chromatin, resembling corpus luteum cells.—B. A. H.

(GONADS THYROID HYPOPHYSIS) Dwarfism (Uber Zwergewuchs). Sternberg, Münch. med. Wchnschr. (Munich), 1920, **67**, 59.

Although many cases of dwarfism are of hypophyseal origin there are cases that are caused by diseases of the gonads or the thyroid. The author examined post-mortem a tubercular dwarf of 17 years in whom no secondary sexual characteristics had developed. The testicles were atrophic and the hypophysis small but apparently normal in structure.—J. K.

HORMONES and hormone therapy. Caldwell (J. E.), J. Florida M. Ass. (Jacksonville), 1916, **3**, 161-165.

A general discussion of the topic.—R. G. H.

(HYPOPHYSIS) Histamine and pituitary extract. Abel (J. J.) and Macht (D. I.), J. Phar. & Exp. Therap. (Balt.), 1919, **14**, 279-293.

Abel and Macht report that the uteri of both mice and guinea pigs respond readily to small and comparable doses of both pituitary extract and histamine salts, the uterus of the guinea pig being the more sensitive to minute doses. Both tracts of plain muscle are easily paralyzed by concentrated doses of pituitary extract and of histamine salts.—F. F.

(HYPOPHYSIS) The decomposition of the oxytocic principle of pituitary solution. Adams (H. S.), J. Biol. Chem. (Balt.), 1917, **30**, 235-242.

An extended study of the effect of heating on the stability of the uterine-contracting factor in pituitary extracts brought out the fact that this constituent is rapidly destroyed at the temperature of boiling water when the H-ion concentration of the solution is of the order of 10^{-5}. The rate of destruction indicates that a single substance is being destroyed and that the valuation of pituitary solution by the isolated uterus method consists in the measurement of a single substance. There is no evidence that this does not constitute an adequate measure of the clinical oxytocic value. It is possible, however, that the substance measured may not be concerned in the characteristic pressor effect of pituitary solution. Oxygen does not seem to be concerned in this destruction of the active principle which apparently is determined by the H-ion concentration since in an $Nx10^{-3}$ concentration there is no destruction at the temperature of boiling water.—F. S. H.

HYPOPHYSIS surgery (Chirurgia ipofisaria). Aievoli (E.), La Riforma Medica (Naples), 1919, **35**, **1080.**

The article is a review of the surgery of the hypophysis with special reference to the endonasal and the transsphenoidal methods of approach, especially the method of Hirsch.—G. V.

(HYPOPHYSIS) Entotic aural bruit, audible on oscultation of the head, due to a tumor of the pituitary region. Alexander (L. D.), Ann. Otol., Rhinol. & Laryngol. (St. Louis), 1916, **25**, 735-737.

A case report, the salient features of which are indicated in the caption. The patient had diplopia and contracted visual fields. The diagnosis of hypophyseal tumor was supported by the appearance in the roentgenogram of an enlarged and probably eroded sella turcica.—R. G. H.

(HYPOPHYSIS) Le diabéte insipide et son origine hypophysaire. Anon., Presse Méd. (Paris), 1919, **27,** 746-747.

A review of some of the literature of recent years emphasizing the value of hypophyseal extract in the treatment of diabetes insipidus.—R. G. H.

(HYPOPHYSIS) Some observations on the action of pituitary extract. Bandler (S. W.), Med. Rec. (N. Y.), 1916, **89,** 300.

The various uses to which pituitary extract is put are discussed. The author has found the drug of value in stimulating intestinal peristalsis in post-operative cases in which symptoms simulating intestinal paresis are found and as an aid to moving the bowels with catharties or by enemata. In cases of atonic bladder, the use of the catheter is said to be preferable. Cases of menorrhagia in young girls, in which currettage and other surgical procedures are not advisable for any reason, are often relieved by repeated administration of the posterior lobe extract. In addition to its ordinary use in obstetrics, it is employed with great advantage by the author to prevent excessive bleeding and to facilitate closing the uterine incision wound in caesarian section.—I. M.

(HYPOPHYSIS) A case of acromegaly. Barr (H. W.), N. Y. Med. J., 1920, **111,** 248-250.

Report of a case of acromegaly in a middle grade imbecilic male who died of hemorrhages from a neoplasm of the upper respiratory tract.—H. W.

(HYPOPHYSIS) Deficiency of the pituitary body. Barrett (Lady), Lancet (Lond.), 1919, (i), 465.

The patient, a girl of 19, had primary amenorrhoea, and on examination was found to have a very small, undeveloped uterus. She had no thyroid deficiency, and was well developed except in the size of the skull. The circumference was 19 inches, the occipito-frontal measurement, 6½ inches and the transverse, 5 inches. A skiagram showed a very small pituitary fossa, with the anterior part especially underveloped.—L. G. K.

(HYPOPHYSIS) Posterior lobe of the pituitary body and its use in obstetrics. Bear (J.), Virginia M. Semi-month. (Richmond), 1917, **22,** 65.

A brief description of the anatomy and function of the hypophysis is given, followed by a statement as to the use of extract of the posterior lobe in therapeutics and conditions in which it is contraindicated. Nothing new.—I. M.

(HYPOPHYSIS) Giant formation in larynx accompanying hypophyseal trouble. Beck (Joseph C.), Ann. Otol., Rhinol & Laryngol. (St. Louis), 1916, **25**, 790.

A brief case report of acromegaly in a man of 65. He had hemianopsia and the x-ray plate indicated destruction of the sella turcica. The "giant formation" referred to was a neoplastic mass in the larynx. It appeared to be due to hypertrophy of the mucosa. It was regarded by the author as a manifestation of an acromegalic tendency.—R. G. H.

(HYPOPHYSIS) The therapeutic future of the anterior lobe of the pituitary gland (L'avenir du lobe anterieur de la glande pituitaire en therapeutique). Barnard (A.), Rev. Internat. de med. et de chir. (Paris), 1917, **28**, 80-83.

A review of the results obtained in testing the properties of the active principle of the anterior lobe of the hypophysis and a prophecy that such extracts will be used in promoting growth at certain periods, in stimulating epidermal growth of wounds and in the treatment of exopthalmic goitre and epilepsy.

—F. S. H.

(HYPOPHYSIS) Acute suppurative hypophysitis as a complication of purulent sphenoidal sinusitis. Boggs (T. R.) and Winternitz (M. C.), Johns Hopk. Hosp. Rep. (Balt.), 1919, **18**, 56-61.

So far as the authors were able to learn, this is the first case of acute inflammation localized in the hypophysis that has been recorded. A white woman of 43 complained of intense stiffness and soreness of the neck muscles, headache, pain back of the eyes and tenderness over the scalp. She had been robust and active but had had every month dysmenorrhea accompanied by severe frontal headaches. She developed fever and continuing headache and finally coma. At the time of her death her temperature was 108.5°. Autopsy was performed shortly after death. The most striking conditions found are indicated in the caption of the article. The hypophysis was removed with difficulty on account of marked friability and extensive red granulations obscuring its demarcations. The anterior lobe was large and its engorged blood vessels contained numerous leucocytes. The cells at the periphery were not infrequently separated from their basement membrane. An infarct occupying from 1/6 to 1/2 of the anterior lobe area was found. The pars intermedia appeared to contain colloid in normal amount, but the cells were not well preserved. Large portions of the posterior lobe were necrotic. In the pancreas the Langerhans islands were made out with difficulty. The adrenals appeared

to be normal. The condition of other endocrine organs was not reported. That there may have been other endocrine disturbances, however, is indicated by the fact that both hyperglycemia and glycosuria were observed in the symptomatology.
—R. G. H.

(HYPOPHYSIS) Club fingers as acromegalic manifestations (Ueber Trommelschlagelfinger als akromegalische Veränderungen). Braum (L.), Med. Klin. (Berl.), 1918, **14**, 3-37; Abst., La Pediatria, 1920, —, 101.

These fingers are found whenever there are long lasting lesions of the lungs; the osteoartropathy of P. Marie shows the same symptoms, but referable to osseous formation, while the lung cases, where other acromegalic symptoms co-exist, can be referred to a hypophyseal dysfunction, secondary to the lung trouble.—G. V.

(HYPOPHYSIS) The development of the glandular portion of the human hypophysis (Sullo sviluppo della porzione ghiandolare dell'ipofisi nell' uomo). Bruni (A. C.), Arch. Ital. Anat. e Embryol. (Firenze), 1917, **15**, 139-192.

The hypophysis is described in embryos of 7, 11, 14, 15, 16, 17, 20, and 28 mm. It arises from four parts of the pharyngo-oral epithelium (ectoderm and entoderm), namely, the anterior cavity of Woerdeman, the pouch of Rathke, the median diverticulum and the pouch of Seessel. These four regions together form the pharyngo-hypophyseal diverticulum from which the glandular portion of the hypophysis arises. This ultimately forms the intermediate lobe and the principal lobe which is subdivided into the body, the chiasmatic lobule and the medial and lateral processes. The pharyngo-hypophyseal diverticulum also forms the pharyngeal (vestigeal) hypophysis. It is now rather generally believed that the entoderm (Bruni to the contrary) does not enter into the formation of the human hypophysis.
—E. R. H.

(HYPOPHYSIS) Dystrophia adiposogenitalis of hypophyseal origin (Distrofia adiposo-genital hipofisaria). Casas (A.), La Semana Medica (Buenos Aires), 1919, —, 728.

A typical case is reported. On surgical interference a glioma of the pituitary was found. Pluriglandular therapy gave some slight degree of relief.—B. A. H.

HYPOPHYSIS, Two cases of tumor of the—with acromegalic syndrome treated with X-rays (Due casi di tumore dell'ipofisi

con sindrome acromegalica, curati con i raggi X). Cavazzeni-Bergamo (S.), La Riforma Medica, 1920, —, 162.

Two cases are reported, a man and a woman; both had depressed vision, hemianopsia, headaches, vertigo, acromegalic facies and physical and psychic weakness. The sella turcica was enlarged in both cases. With X-ray treatments both were very much benefited as regards vision and physical strength. The A. employed Beclere's method,—deep radiotherapy through the two temporal and frontal regions, first every week, later less frequently.—G. V.

(HYPOPHYSIS) The hypophysis cerebri of the California ground-squirrel Citellus beechii (Richardson). Cooper (H. J.), Am. J. Anat. (Phila.), 1919, **26,** 185-208.

The cytology of the gland indicates to the author that the various cells in the glandular part of the hypophysis represent different stages of the same type of cell, as has been reported previously by other authors.—E. R. H.

(HYPOPHYSIS) Diabetes insipidus and its hypophyseal origin (Il diabete inspido e la sua origine ipofisaria). Costagli, Rivista critica di Clin. Med. (Firenze), 1919, **20,** 571.

Costagli subscribes to the causative effect, in diabetes insipidus, of lesions of the hypophysis and to the benefit secured by hypophyseal treatment. The mechanism of the syndrome, he believes, however, has not yet been demonstrated. Camus and Roussy found that after removal of the hypophysis in dogs, pituitary treatment did not improve the syndrome of diabetes insipidus and it was inferred that the essential factor might be a lesion of the adjacent zone of the brain. No proof has yet been offered. In the author's opinion, pituitrin constitutes a genuine hormone. It is possible that merely by reducing the size of the hypophysis it seems to improve conditions brought about by compression. In this connection, it is known that lumbar puncture can temporarily diminish the polyuria.

—G. V.

(HYPOPHYSIS) Histamine and pituitary extract. Cow (Douglas), J. Pharm. & Exp. Therap. (Balt.), 1919, **14,** 275-277.

Cow found that while pituitary extract greatly stimulated the mouse uterus, histamine produced paralysis. These observations led him to conclude that histamine and the plain-muscle-stimulating principle of the posterior lobe are not identical.

—F. F.

(HYPOPHYSIS) Some observations on the active principles of the pituitary gland. Dudley (H. W.), J. Pharm. & Exp. Therap. (Balt.), 1919, **14**, 295-312.

By extraction of powdered, desiccated, fat-free posterior lobes of the pituitary body with acidulated water, treatment of the solution with collodial ferric hydro-oxide and subsequent continuous extraction of the filtrate with butyl alcohol at reduced pressure and final evaporation of the alcohol, Dudley obtained a crystalline residue containing all the uterine stimulant of the posterior lobe together with some of the pressor principle and impurities ("contaminating substances") such as amino acids, etc. The comparison between the behavior of this residue and of histamine toward solubility in butyl alcohol and chloroform, alkalies, and tryptic hydrolysis leads the author to conclude that the uterine stimulant of the posterior lobe and histamine are not identical, but are two distinct chemical substances. No description of the crystals or analytical data to establish their constitution, are furnished.—F. F.

(HYPOPHYSIS) Concerning the U. S. P. standard for pituitary extract (Liquor Hypophysis). Eckler (C. R.), Am. J. Pharm. (Phila.), 1917, **89**, 195-202.

A general description of the writer's method of testing the strength of liquor hypophysis and a plea for the raising of the U. S. P. requirement so that it will coincide with the strength of the ordinary commercial product, which he usually found to be ten times as strong as the U. S. P. standard.—F. S. H.

(HYPOPHYSIS) Influence of pituitary extracts on the genital tract. Frank (R. T.), J. Am. M. Assn. (Chgo.), 1919, **73**, 1764.

Six litters of three weeks' old white rats, were fed for 35 days with extracts of anterior lobe of the pituitary gland. At necropsy all animals showed increase in size or weight or in the genital organs. Certain rats, some of them the controls, showed greater increase in weight, the presence of corpora lutea in the ovaries and enlargement of the internal genitals. However, Frank does not believe this growth was due to the pituitary feeding and believes that more extended experimentation is necessary before the extracts of anterior lobe of pituitary gland can be used with assurance of efficacy.—F. C. P.

(HYPOPHYSIS THYROID) Metastatic deposits in the pituitary body from carcinoma of the thyroid, causing bilateral opthalmoplegia. Haman (C. A.), Cleveland Med. J., 1916, **15**, 225-226.

A report of a case diagnosed as pituitary lesion because of corneal anesthesia, opthalmoplegia and hemianopsia accompanying carcinoma of the thyroid. At autopsy the sella turcica was found to be filled with a tumor mass seemingly continuous with, and inseparable from, the pituitary body. Histologically, the growth was a cuboidal-celled carcinoma. There were no other metastases in the cranial cavity.—F. S. H.

(HYPOPHYSIS) Multiple hemangiomas of the skin associated with dyspituitarism. Head (G. D.), Arch. Int. Med. (Chgo.), 1917, **20**, 24-31.

An extensive report accompanied by color photographs of two cases of multiple hemangiomas of the skin associated with clinical manifestations of pituitary gland changes. In case 1, the skin of the scrotum, penis, inside of the thighs, arms, back and abdomen was affected. In case 2, the skin of the scrotum and the mucous membranes of the lips and mouth were involved.—F. S. H.

HYPOPHYSIS substance, Treatment of amenorrhea with—(Über die Verwendung von Hypophysensubstanzen bei der Behandlung der Amennorrhoe). Hofstätter (R.), Zentralbl f. Gynaek. (Leipzig), 1920, **44**, 68.

Good results are here reported from the administration of pituitary preparations in cases of amenorrhea accompanied by uterine and ovarian hypoplasia.—J. K.

(HYPOPHYSIS) Functional diagnosis of polyglandular disease in acromegaly and other disturbances of the hypophysis. Howard (C. P.), Am. J. Med. Soc. (Phila.), 1919, **158**, 830-839.

A brief summary of three cases of acromegaly, two cases of dystrophia adiposo-genitalis, and one of brain tumor with flattening of the pituitary body from increased intracranial pressure. The author reports in detail the results of tests for sugar tolerance, conjunctival and subcutaneous adrenalin tests and conjunctival and subcutaneous pituitrin tests. He concludes that a secondary hyperpituitarism may result from a greatly increased or rapidly increasing intracranial pressure; that a decrease in sugar tolerance in the presence of other symptoms of pituitary disturbance justifies a diagnosis of increased activity of the pars intermedia; the conjunctival adrenalin test may be of positive value in certain cases of dyspituitarism in demonstrating hypofunction of the chromaffin system; the subcutaneous adrenalin test is of doubtful value in both normal and pathological cases; the conjuntival and subcutaneous

pituitrin tests are of doubtful value in studying the functional activity of the hypophysis. The internal administration of pituitary extract, either the whole gland or the anterior or the posterior lobes, appears to exert no definite influence.—F. C. P.

(HYPOPHYSIS) Roentgen-ray treatment of pituitary tumors (Contribution nouvelle a la radiothérapie des tumeurs hypophysaires).. Jaugeas (M.), Journal de Radiologie et d'Electrologie (Paris), 1919, **3**, 508-516.

The death of Jaugeas was reported recently. He said in this article that the action of the roentgen rays can be estimated with greater precision in the effect on a tumor in the hypophysis region than in any other field of application of deep irradiation. The changes in the visual field parallel the benefit otherwise, and form a gage for the efficacy of the treatment. He describes a case of tumor in the pituitary with acromegaly in a woman of 25. The history of the case is shown by the charts of the field of vision at one and two-year intervals, the visual acuteness finally approximating normal. Similar findings in another case rayed in 1914 show that the benefit has been permanent, so that the term "cure" is not out of place applied to such cases. The visual acuity is even better now, five years later, than when the patient was first dismissed. The acromegaly has not retrogressed, but it was arrested. Roentgen-ray treatment in these cases has to be applied early, when symptoms of hyperactivity become manifest, before the elements of the gland are destroyed. The raying must be cautious, to refrain from destroying the functional elements, as otherwise symptoms of deficiency would follow, analogous to experiences with the thyroid. The pulse in exophthalmic goiter and the visual field with pituitary tumors should be the guide to treatment. It should be suspended when these findings enter a stationary phase. It can be resumed if headache and impairment of vision indicate a new "poussée évolutive." The exposures should thus be given and suspended according to the individual findings from week to week, without any arbitrary regularity.

—J. Am. M. Assn.

(HYPOPHYSIS) The pharmacology of drugs used in parturition (Die Pharmakologie der Wehenmittel). Joachimoglu (G.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1919, **50**, 453-460.

A review of the pharmacology of the various preparations used in parturition.—F. S. H.

(HYPOPHYSIS) Clinical and surgical remarks on tumors of the hypophysis (Consideraciones cliníco-quirúrgicas sobre

tumores de la hipófisis). Jorge (J. M.) and Natale (A.), Comm. del Hosp. oftalmól. (Buenos Aires), 1919, **2,** 45.

Six clinical reports of tumors of the hypophysis, three of which were operated upon with improvement of the sight. Relapse occurred in one case.—B. A. H.

HYPOPHYSIS, On the pathogenesis of acromegaly and the relation between this disease and anomaly of the—. Kamo (K.), Bull. Nav. Med. Assn. (Tokyo), 1916, **No. 13,** 6-8.

A case of typical acromegaly investigated pathologically is described. An adenomatous tumor, consisting chiefly of peculiar eosinophilic cells which differ morphologically from the normal eosinophiles of the hyhophysis, is described in connection with a small pit. The latter corresponds to the remains of the embryological canalis craniopharyngeus. The author believes that the tumor had sprung from the germs of the hyhophysis, remaining with the canalis rest, and that acromegaly is due to hyperfunction of the special eosinophilic cells. The intact normal testicles in this case contradict the hypogenital theory of the development of hypophyseal adenoma as the cause of acromegaly.—I. M.

(HYPOPHYSIS ADRENAL) The pathogenesis of deficiency disease. II. The effects of deprivation of "B" accessory food factors. McCarrison (Robert), Indian J. Med Res. (Calcutta), 1919, **6,** 550-556.

Food-deficiency experiments were carried out on pigeons in which the "B" factor only was withdrawn. The diet consisted of autoclaved rice plus butter and onions. It was found that the morbid state resulting from deprivation of this class of food resembled very closely that resulting from complete vitamine starvation but was less often associated with oedema. Unmilled rice, like butter and onions, appears to contain some factor which tends to prevent the onset of edema. Avian beriberi seems to depend upon the absence of two food factors: (a) the so-called antineuritic factor, and, (b) the anti-edema factor. The brain, the adrenals and the hyhophysis are very sensitive to vitamine influences in the food. These increase, whereas most of the other organs diminish in size.—I. M.

(HYPOPHYSIS TESTES) Akromegalie kombiniert mit Diabetes. Machwitz, Münchener med. Wchnschr., 1920,**67,** 198.

Report of a man of 46 years; his acromegaly began when he was 22. Gradually symptoms of diabetes developed; glycosuria showed some relation to the amount of carbohydrates in

the food. There developed marked atrophy of the gonads. The patient has a son of 18 years with acromegaly.—J. K .

(HYPOPHYSIS) Pituitary extract in obstetrics and other cases. Measham (J. E.), Univ. Durham Coll. Gaz. (Newcastle), 1916-17, **17,** 42-44.

Fourteen cases are reported in which the use of pituitrin was followed by gratifying results. These included post-partum hemorrhage, uterine inertia and delayed retraction of the uterus. In a man pituitrin was used after a hemorrhoid operation to avoid the necessity of painful catheterization. Free micturition was established. Similar results occurred after an operation for anal fissure, followed by atony of the bladder. In another case a gun-shot lesion of the spinal cord was followed by atony of the bowel, leading to stubborn constipation. This was promptly and completely relieved by pituitrin. In a second, less severe case, pituitrin proved useless. In nine cases of collapse following trauma, saline solution containing 1 cc. of pituitrin to the pint was administered intravenously. The author was convinced that the restorative effect was materially greater than could have been expected from the saline solution alone.—R. G. H.

(HYPOPHYSIS) Cure of hypophyseal form of congenital lues by combined antisyphilitic and organotherapeutic treatment [Ueber Heilung der hypophysären Form der Lues congenita (Lues congenita pituitaria) durch kombinierte antisyphilitische und Organ-Therapie]. Nonne (M.), Neurol. Centralbl. (Leipzig), 1918, **37,** 194-197.

Nonne reports a case of a boy of 16 years with infantilism, physical and psychic, and with feminism and polyuria. The treatment with mercury and iodides and hypophysin tablets produced development of the genitalia and pubic hair and checked the polyuria.—G. V .

(HYPOPHYSIS) Zur Lehre vom Diabetes insipidus. Oehme, Med. Klin. (Berl.), 1918, **14,** 749; Berl. klin. Wchnschr. 1918, **55,** 798; Deutsche Med. Wchnschr. (Berl.), 1918, **44,** 1037.

See Endocrin. **2,** 496.

HYPOPHYSIS, A case of sarcoma in the region of the—. Owen (S. A.), West. Lond. M. J. (London), 1916, **21,** 138-140.

A case of sarcoma of the hyphophysis cerebri with post-mortem findings is reported.—I. M.

(HYPOPHYSIS) A case of dwarfism of Paltauf's type (Dwerggroli van Paltauf). de Monchy (L. B.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64** (i), 605.

A case is reported the symptoms of which are the opposite of acromegaly, the parts usually exhibiting the acromegalic enlargement being small in this form of dwarfism. The injection of 0.1 mgm. of adrenalin caused glycosuria. The disorder is attributed to a probable diminution of hypophyseal function.
—J. K.

(HYPOPHYSIS) The development of the hypophysis cerebri pre-oral gut, and related structures in the Marsupialia. Parker (K. M.), J. Anat. (Lond.), 1917, **51**, 181.

Several species are described. The notochord does not aid in the formation of the hypophysis. In most cases Seessel's pouch degenerates early, but in some it forms a small part of the hypophysis. Rathke's pouch develops from ectoderm. It grows up over the entoderm of the oral cavity and comes to lie under the diencephalon where it gives rise to the glandular part of the hypophysis in contact with the neural lobe. The glandular portion is subdivided into pars juxtaneuralis and pars distalis or anterior. The former is again subdivided into a pars tuberalis surrounding the stalk and a pars infundibularis in contact with the neural lobe and separated from the rest of the glandular portion of the hypophysis by the lumen.

The histological differentiation of the anterior lobe occurred in the later stages studied (9 to 13 mm.) where there were seen chromophobic and chromophilic cells. These both develop from ectoderm and not one from entoderm and the other from ectoderm as claimed by Miller.

The pars neuralis is formed by a simple down-pouching in the floor of the diencephalon.—E. R. H.

(HYPOPHYSIS) Hypophyseal adiposity in children (Kinder mit hypophysärer Adipositas). Peritz, Münch. med. Wchnschr. (Munich), 1920, 67, 141.

It is the opinion of the author that many cases of hypophyseal adiposity in children are caused by a syphilitic hydrocephalus. An increase in the blood sugar can always be demonstrated.—J. K.

(HYPOPHYSIS) Diagnosis of pituitary tumor. Potts (J. B.), Nebraska M. J. (Omaha), 1916, **1**, 52-54.

A brief article discussing the physiology and functional pathology of the hypophysis and reporting four cases in which the gland was surgically removed.—R. G. H.

(HYPOPHYSIS) Raynaud's disease (Rainaudsche Krankheit). Pribram, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 87; Münch. med. Wchnschr. (Vienna), 1920, **67,** 27.

A case report of a classical example of Raynaud's disease accompanied by no evidence of acromegaly but showing an enlarged sella turcica on X-ray examination.—J. K.

(HYPOPHYSIS) Hypophyseal dwarfism (Über hypophysärem Zwergwuchs). Priesel, Münch. med. Wchnschr. (Munich), 1920, **67,** 59.

There are two forms of hypophyseal dwarfism, the primordial form in which the individual is subnormal at birth and develops symmetrically, though remaining a dwarf, and the infantile form in which the birth size is normal as is the growth during the first years. In this latter form, however, the growth becomes retarded between the fifth and fifteenth years. The case reported is one of a dwarf of 90 years with an "abnormal" neurohypophysis and sphenoidal sinus.—J. K.

(HYPOPHYSIS THYMUS) Diabetes insipidus. Richter (G.), J. Missouri Med. Assn. (St. Louis), 1916, **13,** 308-313.

An interesting report of a case of diabetes insipidus in a girl of fourteen, presenting general adiposity, well developed breasts, and a persistent thymus. Her character was infantile though not stupid, and she was subject to attacks similar to petit-mal. The X-ray examination showed no enlargement of the sella turcica. Her urine elimination amounted to about a gallon in 24 hours. Experimentally she showed a sugar tolerance of over 400 gms. The author concludes that the case is one of diabetes insipidus due to hypopituitarism.—F. S. H.

(HYPOPHYSIS) The influence of tethelin and of other alcohol soluble extractives from the anterior lobe of the pituitary body, upon the growth of carcinomata in rats. Robertson (T. B.) and Burnett (T. C.), J. Exper. Med. (N. Y.), 1916, **23,** 631-639.

The results of these experiments are best summarized in the author's own words: "The hypodermic administration of tethelin increased markedly the rate of growth of the primary tumor and the tendency to form metasteses in rats inoculated with carcinoma in this, as in other respects, reproducing the alcohol soluble extractives of the anterior lobe of the pituitary action of the whole anterior lobe of the pituitary body. Other body, with the exception of the lecithin fraction, exert no appreciable effect upon the growth of carcinomata in rats. The leci-

thin fraction, as in previously reported experiments in which we employed lecithin obtained from eggs, causes evident retardation of the growth of carcinomata in rats."—F. S. H.

(HYPOPHYSIS) Dystrophia adiposo-genitalis durch hochgradige Hypoplasia und Atrophie der Hypophyse. Rössle, Naturwiss. med. Gesellsch. (Jena), 1916, —, —. (Abstract in Folia neuro-biol. (Haarlem), 1918, **11**, 570.) (Wolffensperger).

A man of 27 who had been weak since childhood and who died following an operation for "coxa vara," was autopsied. The data obtained were: body-length 1.62, body-weight 50 kg., adiposity, hypoplasia of the thyreoid ((11 gm.), thymus (3 gm.), adrenals (5 gm.) and especially of the hypophysis which was separate from the infundibulum. After fixation the hypophysis weighed only 180 mgm. Microscopically there were found in the hypophysis a small posterior lobe and a cystic anterior lobe, but no stalk. The testes were the size of those of a 3 year old child. The other genital organs were much under-developed.

Another man of 68 had a large tumor in the region of the hypophysis, and at autopsy no hypophysis could be found. The tumor was a pure psammoma. The body form was that of a fat female, the adrenals and thyreoid were of normal weight, but the testes weighed only 8 gm. and the other genital organs were small. The seminiferous tubules were degenerated and there was no growth of interstitial cells.—E. R. H.

(HYPOPHYSIS) Present status of the definite treatment of the pneumonias. Solis Cohen (S.), J. Am. M. Assn. (Chgo.), 1919, **73**, 1741-1743.

Solis Cohen advocates the use of posterior pituitary lobe extract to sustain blood pressure and prevent gastro-enteric paralysis. Pituitrin should be given in 1 cc. doses at 3 hour intervals until the systolic blood pressure in mm. of Hg exceeds by five points or more the pulse rate per minute.—F. C. P.

(HYPOPHYSIS GONADS) A case of traumatic hypophyseal adiposity (Ein Fall von traummatischer hypophysärer Fettsucht). Schünemann, Münchener med. Wchnschr., 1920, **67**, 198.

After a fall from a carriage the patient developed an enormous adiposity. Glucose in 200 gram doses failed to cause glucosuria, as did also injections of adrenalin. The testes and the prostate were atrophic. There was noted polyphagia, polydipsia and polyuria.—J. K.

(HYPOPHYSIS THYROID) Acromegaly and goiter (Acromegaly et goitre). Sicard and Roger, Marseille med., 1917, **53,** 381.

A case is described in which goitre and typical acromegaly (enlarged, protruding lower jaw, enlarged extremities, etc.) occurred simultaneously in a man 49 years of age, who had lived in the Basses-Alpes where goitre occurs so frequently. Examination showed the presence of a large indurated thyroid and the sella turcica was shown by radiography to be greatly enlarged. The only symptom complained of was lumbar pain. There was no glycosuria and no ocular disturbances were found. The cerebrospinal fluid showed only an insignificant increase in globulin.—I. M.

HYPOPHYSIS, Report of a case of congenital syphilis of the—. Simonds (J. P.), Tr. Chicago Path. Soc., 1915-18, **10,** 30-34.

Simonds was able to find recorded in the literature only ten previous cases of congenital syphilis of the hypophysis. In his case the examination of the new born child showed diffuse proliferation of the connective tissue throughout the hypophysis. This was mostly perivascular. The cells of the anterior lobe were mostly of the "chromophobe" variety. The mid-cleft was large, dilated and contained masses of large cells with pale and, in some cases mutinuclear nuclei. In case of the adrenals, a deformity was present which, so far as could be determined, had not previously been recorded. The right and left glands were united across the mid-line. They were slightly hemorrhagic but otherwise apparently normal. Some degree of connective tissue proliferation was observed also in the thyroid and parathyroid glands and in the testes. No colloid was present in the thyroid. The islands of Langerhans in the pancreas were frequently also invaded by fibrosis.—R. G. H.

(HYPOPHYSIS) Standardization of pituitary extracts. Spaeth (R. A.), U. S. P. H. Hygienic Lab. Bull. 115 (Washington), 1918.

Several theoretical and practical objections are advanced against the use of beta-iminazolylethylamine hydrochloride as a standard for assaying pituitary extracts of unknown strength. The theoretical and practical advantages of using potassium chloride to produce qualitative effects upon the isolated virgin guinea pig uterus, which are comparable to the effects of pituitary extracts, have been studied. It is suggested that a Locke solution containing 0.14 per cent KCl in place of the normal 0.042 per cent KCl be employed as a new standard for determining the physiological activity of pituitary solutions of unknown

strength. Seven commercial pituitary preparations have been comparatively studied. Variations between the strongest and weakest solutions have been found to be in the ratio of 5:1. No positive correlation has been found between the relative acidity of the commercial preparations and their physiological activity. It is suggested that in order to maintain their physiological potency commercial pituitary preparations should contain hydrogen ion in a concentration of the order $N \times 10^{-3}$ (Ph=3). In order to make the proposed new standard conform as far as possible with the present U. S. P. IX recommendation, it is suggested that the effect of commercial pituitary extracts in a concentration of 1:4,000 should be equal to the effect of the potassium standard solution when the isolated uterus of a virgin guinea pig is used as a test organ.—Author's abst.

(HYPOPHYSIS) Zur Organotherapie bei Diabetes insipidus. Strauss (H.), Therapie der Gegenwart, 1916, —, —. Abstract by Lubowski in Fol. neuro-biol. (Haarlem), 1917, **10,** 477.

This author decreased the output of urine by one-fourth and raised the specific gravity, by treatment with "Pituglandol" (post. lobe extract). "Glandulen" (anterior lobe) had no effect on diabetes insipidus, but in true diabetes there was some suggestion that it tended to decrease glycemia.—E. R. H.

HYPOPHYSIS and THYROIDECTOMY (Hypophyse und Thyreoidektomie). Trautmann (A.), Frankf. Ztsch. f. Pathol. (Wiesbaden), 1916, **18,** 173-304.

This lengthy communication contains an almost exhaustive summary of the literature concerned with the problem investigated. Complete and detailed protocols are given of the macroscopic and microscopic changes occurring as the result of thyroidectomy, particular reference being made to a study of the hypophysis, in all a total of 30 goats being used for the purposes of the investigation. It was found that in goats, the removal of the thyroid gland resulted in marked alterations in all of the three parts of the pituitary gland. A complete extract of the work is impossible because of its length and detail; it deserves direct study by those particularly interested. The main conclusion to be drawn is that there exists an inner physiological relationship between the hypophysis and the thyroid. The complete or partial elimination of the thyroid function causes an actual pathological alteration in the properties of the blood which acts in a harmful manner on the different parts of the pituitary. The alterations that occur are mainly of a degenerative type. There was no evidence produced supporting the idea that the hypophy-

sis might serve vicariously for the thyroid. The author is of the opinion that none of the parts of the pituitary should be considered as insignificant in function, but that they should all be looked upon as integral and necessary parts of a whole.—F. S. H.

(HYPOPHYSIS) Roentgen-ray treatment of case of early acromegaly. Webster (J. H. D.), Arch. Radiol. and Electrotherapy (Lond.), 1920, **24**, 261-264.

In acromegaly, roentgen-ray treatment at present rests almost entirely on a theoretic basis. Webster contends that it should be eminently a disease suitable for roentgen-therapy, especially in its early stages, when the anterior lobe of the pituitary would show merely a simple chromophil hyperplasia, and before secondary tumor-like formation, local pressure damage, and much skeletal change has been produced. In his case so treated the disease had been of almost four years' duration. She had sixteen treatments with hard filtered rays from temporal and frontotemporal areas, the first eleven at weekly intervals, then fortnightly, latterly at monthly or longer periods. The effect was remarkable. The severe headache was rapidly relieved, and soon entirely disappeared. The "queer feelings" almost entirely left her: from two or three weekly they dropped to about one a month. The irritability and depression almost completely left her. She lost about seven pounds in weight. The most striking changes were in the eyes; the optic discs returned practically to the normal, while the fields of vision (especially for red) greatly enlarged. The right eye still presented some irregular contraction, chiefly inferior temporal. Apart from one or two bromid powders there was no treatment beyond irradiation. The patient was lost sight of for nearly two years; her condition, subjectively and objectively, had become aggravated again. She was then operated on successfully by the nasosphenoidal route.
—J. Am. M. Assn.

INFANTILISM (Infantilismo genuino). Bufalini (Emilio), Riv. critica di clin. med, 1919, **20**, 517.

Bufalini reports a case of true infantilism, which does not show any connection with the different forms of endocrine infantilisms. He advances the hypothesis that in such cases there might be an inherited, latent morphologic dystrophy, a congenital lack of developmental tendency. A complete arrest of development may result whenever there appears an intervening (toxico-infective) cause of dystrophy.—G. V.

The glands of INTERNAL SECRETION (Las glandulas de secrecion internas). Crispin (A. M.), Rev. del Circulo med.

y Centro Estudiantes de Med. (Buenos Aires), 1919, **19**, 1204-1209.

A general discussion containing no new points of interest. —B. A. H.

INTERNAL SECRETIONS, The significance of the doctrine of—and their utilization for gynecological practice (Die Bedeutung der Lehre von der inneren Sekretion und ihre Nutzanwendung für die praktische Gynäkologie). Fehling (H.), Monatschr. f. Geburtsch. u. Gynäk. (Berlin), 1919, **50**, 143-162.

A polemical discussion of Aschner's book and of such a nature as not to be satisfactorily abstracted.—F. S. H.

(LYMPH GLANDS AUTONOMIC N. S.) Sistema linfático y sistema nervioso vegetativo. Estudios experimentales acerca de la función hormonopoiética de los ganglios linfáticos. Nóvoa Santos (R.), El Eco de Santiago, 1919, pp. 37.

The author has investigated the possibility that the symptomatology of status thymo-lymphaticus may be due in whole or in part to the action of hormone factors originating in the lymphatic gland tissues. The investigation follows the general line developed by Eppinger and Hess in their well known studies of "Vagotonia and Sympathicotonia." As criteria of overactivity of the parasympathetic system are considered: Dilatation of the pupils, relaxation of the bladder, dilatation of the heart and stomach, tachycardia, vascular hypotension, glycosuria and hypochlorhydria. The pertinent literature is discussed at some length,—including the evidence adduced by Vincent and others pointing toward a lack of specificity of extracts of such tissues as those of the lymphatic glands (See Endocrin. **2**, 421).

The observations are recorded that in 599 cases of infants and children giving evidence of status lymphaticus, the cardio-ocular reflex was usually positive, indicating hypertonic condition of the vagus. The injection of extracts of lymphoid tissue provoked in human subjects a lymphocytosis as well as lowered blood pressure and diminished frequency of the pulse. A similar hypotensive effect was noted in dogs and rabbits. In the frog's eye a marked mydriasis was produced. These effects are antagonistic to those of adrenin. Similarly, the glycosuric effect of adrenin was depressed by lymphoid extracts. (The experiments were apparently not controlled by the use of indifferent organ extracts.) The final conclusion was that the lymphatic gland cells elaborate a specific substance with pharmacodynamic influence precisely the opposite to that of adrenin and correspondingly related to the parasympathetic system as is adrenin to the sympathetic.—R. G. H.

MYASTHENIA (Over myasthenie). Schermers (D.), Medisch Weekblad (Amsterdam), 1920, **26,** 566-577

A general review. The author does not believe that there exist any relations between this disease and the endocrine organs.—J. K.

The MYOMETRIAL endocrine GLAND in the uterus of the pregnant rat (Glande myométriale dans l'utérus de la rate gestante). Weill (Paul), C. R. Soc. de Biol. (Paris), 1919, **82,** 1433-1435.

Ancel and Bouin have found in the uterus of pregnant rabbits "myometrial cells" which in structure resemble an endocrine gland. Frankel has confirmed these observations. Weill gives a histological description of similar cells found in the uterine wall of pregnant white rats. The capillary vessels at the site of the placenta are surrounded by a great number of large cells filled with granules, clearly acidophilic, with the nucleus displaced toward the periphery. Weill thinks this mass of cells, which forms a true perivascular gland, must have a well determined function, but it is impossible to elucidate it at present.
—T. C. B.

(ORGANOTHERAPY) Indications for internal gland therapy. Timme (W.), N. Y. Med. J., 1920, **111,** 226-229.

The tissue manifestations of endocrine disturbances are manifold, hence we have come to regard some of these tissue changes as fairly pathognomonic of certain states. In the large proportion of cases showing characteristic evidence of disturbances, there are also evidences of compensation, hence not all are suitable for glandular therapy. Terminal types, such as Addison's disease, exophthalmic goiter and others, are largely beyond the reach of treatment. However, such conditions as fatigability, headache, structural abnormalities, gonadal and secondary sex changes and vasomotor and neurological disturbances yield readily to organotherapy. The necessity of detecting beginning endocrine disturbances and treating them is graphically emphasized.—H. W.

(ORGANOTHERAPY) Urological problems. Vecki (Victor G.), Cal. State J. Med. (San Francisco), 1917, **15,** 495. (Dec.), Reprint, pp. 7.

In the course of a general address the author remarks that after a very unfortunate history, organotherapy is gradually being re-established in the esteem of the medical profession. To the genito-urinary specialist endocrine advancement is particu-

larly significant. Many cases of so-called sexual neurasthenia intractable to local treatment will yield rapidly to judicious use of thyroid or pituitary preparations, but careful discrimination in regard to the preparation itself, in regard to the various indications and in regard to dosage are indispensable conditions of success. Thyroid medication is frequently indicated in enuresis. In any case the patient should be carefully watched and gland medication controlled by blood-pressure studies.—R. G. H.

(MUSCULAR DYSTROPHY) Biological study of a case of progressive myopathy (Recherches biologiques sur un cas de myopathie progressive). Adraid (Ch) and Binet (Leon), Arch med. exp. d'anat. pathol. (Paris), 1919, **28,** 549-562.

A rather complete study of a case of progressive muscular dystrophy giving no evidence of any disturbance in the functions of the endocrine glands.—F. S. H.

OSTEOMALACIA, Two cases of— (Zwei Fälle von Osteomalazie). Edelmann (M.), Wiener klin. Wchnschr., 1919, **32,** 82.

No new data. Disturbed function of the endocrine system plays an important part in the etiology of such cases. Adrenalin therapy has a good effect.—J. K.

(OSTEOMALACIA). Undernourishment and disease of the bones in Munich (Hungerknochenerkrankungen in München). Heyer, Münch. med. Wchnschr. (Munich), 1920, **67,** 98.

A study of nine cases of osteomalacia in which nothing new is reported.—J. K.

(OSTEOMALACIA) Über Osteomalazie. Strümpell, Münch. med. Wchnschr., 1919, **66,** 1304.

A general review without new facts.—J. K.

(OVARY) Uterine contractions and ovarian extract. Barry (D. T.), J. Physiol. (Lond.), 1916, **50,** 259-264.

Barry studied the effects of ovarian extract on the contractions of the pregnant uterus in three cats at about the middle of pregnancy. The extract was given intravenously in some cases, locally in others. It was found that the normal contractions were increased in both frequency and force in all cases and that the increase in tone persisted for a comparatively long period. Increasing the pressure within the sac was found to increase the tendency to contraction, whereas decreasing the tension diminished it appreciably.—I. M.

(OVARY) Resume of a series of cases of ectopic gestation and ruptured graffian follicles. Brooks (C. D.) and Clinton (W. R.), J. Michigan State M. Soc., 1920, **19**, 22-23.

There are many cases of rupture in ectopic pregnancy without a history of missed menstrual period and in many cases there is a history of normal amount, scanty flow and "spotting." Along with the characteristic symptoms of rupture there is pain in the rectum and referred pains down the thigh on the affected side.—H. W.

(OVARY) Sulla struttura dell'ovario nei Teleostei. De Castro (E.), Arch. ital. Anat. e Embryol. (Firenze), 1918, **16**, 1.

A cytological study of fish eggs and one of endocrine interest.—E. R. H.

(OVARY ENDOCRINE ORGANS) Genital findings in dementia praecox and physiological observations on genital infantilism (Der Genitalbefund bei Dementia Praecox nebst physiologischen Betrachtungen über den Infantilismus genitalium). Fraenkel (L.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1919, **50**, 433-440.

The studies of F. on cases of dementia praecox occurring in women have given a new proof of the endocrine nature of this disorder and show the presence of a marked hyperfunction of the ovary. Two explanations are possible: either the basis of the disease is general "infantilismus, praecipue cerebri et ovariorum," or the disease is founded on a pathological property or function of the glands of internal secretion accompanied by a marked hypofunction of the sexual glands.—F. S. H.

(OVARY) Innere Sekretion des Eierstocks. von Franqué (O.), Biol. Zentrabl. (Leipzig), 1919, **39**, 193.

A review of the German literature on the subject with especial reference to the work of Steinach. No new data are added. —E. R. H.

(OVARY) Hydatidiform mole associated with pernicious vomiting. Geist (S. H.), Trans. N. Y. Obs. Soc., Am. J. Obs. (N. Y.), 1919, **80**, 215-216.

Report of a case of pernicious vomiting associated with a uterine fibroid. The uterus was the size of that of a four months' pregnancy. No luteal cysts were present in the ovaries.—H. W.

(OVARY THYROID) An explanation of the action of iodine in dysmenorrhea (Versuch einer Erklärung des Weges der Jodwirkung bei Dysmenorrhoe). Grumme, Berl. klin. Wchnschr., 1919, **56**, 1188.

It is pointed out that there is a well established relationship between the thyroid and the ovaries and that the administration of iodine in dysmenorrhea would act on the thyroid and the improved function of this gland would then influence the ovaries.
—J. K.

OVARIES, Sterilization by roentgen exposures of the—. Guillermin (R.), Revue Médical de la Suisse Romande (Geneva), 1919, **39**, 326-336.

Guillermin declares that exposures to the roentgen rays form the simplest and least harmful means for arresting ovarian functioning in women with pulmonary tuberculosis. Even menstruation may have a decidedly unfavorable action on tuberculosis, including congestion and whipping up hemoptysis, so that there is every reason to suspend the functioning of the ovaries in such cases, to say nothing of the menace from a pregnancy. Bezanzon long ago called attention to "these tuberculous women killed by their menstrual periods." In two cases he suppressed menstruation by fourteen and by four exposures. In the first case the menopause was complete; in the other there was merely arrest of menstruation, but this put an end to the monthly periods of fever and the recurring congestion, and this patient soon considered herself completely cured. The condition of the lungs in the other case also has materially improved.—J. Am. M. Assn., 1920, **74**, 426.

(OVARY CORPUS LUTEUM) The relation between the corpus luteum and menstruation (Über das Verhalten des corpus luteum zur Menstruation). Labhardt (A.), Zentralbl. f. Gynäk. (Leipzig), 1920, **44**, 185.

The changes in the mucous membrane of the uterus before menstruation depend upon the corpus lutem. At the time the function of the corpus luteum ceases, menstruation begins. The ovary has no influence whatever on the intensity of menstruation. Seitz has prepared from the corpus luteum a substance which he called lipamine. Probably this, according to the author, is the hormone of the corpus luteum. It is possible that some abnormalities of the mucous membrane of the uterus depend upon the ovary; for instance menorrhagia may be caused by the ovary. When, however, the uterus is normal the ovary never has an influence on menstruation.—J. K.

(OVARY) Nervous and mental disturbance after ovariectomy. Mendoza M (R.), Revista de Psiquiatria (Lima), 1919, **2**, 97-107.

Mendoza summarizes nine cases in which artificial menopause induced unusually severe nervous disturbances and change in character. No benefit was realized from organotherapy in most of the women. In the most refractory cases an element of hysteria or neurasthenia was manifest. One woman of 40 had attacks of unconsciousness, besides the usual phenomena of the menopause; no benefit was obtained from ovarian treatment, but under ergot for a time conditions gradually returned to normal. Headache, insomnia, neuralgias and pain in the lumbar region were common.—J. Am. Assn., **74**, 430.

(OVARY) The maturation of the human ovum. Thompson (A.), J. Anat. (London), 1919, **53**, 172.

The specimens were obtained from the ovaries of women who died suddenly or were accidentally killed, and not subjected to prolonged illness. This is the first time that the maturation stages of the human egg have ever been published. The human egg is shown by the author to be ovoid in shape about 0.11 x 0.95 x 0.10 mm. The zona pellucida is but loosely held to the corona radiata and hence easily separated at ovulation. There seems to be a true vitelline membrane, and a perivitelline space. The first and second polar bodies are both expelled within the ovary and the former undergoes division. Contrary to the rule for vertebrates in general, the human egg, then, is fully mature before the spermatozoa encounter it. There is evidence to show that the polar bodies are not really polar in position. It could not be determined whether or not the two polar bodies are extruded from the same point.—E. R. H.

(OVARY) Three cases of reappearance of ovarian peritoneal sacculation. Reynolds (E.), J. Anat. (London), 1916, **50**, 308.

A morphological discussion of the relation of the ovary to its endometrium in vertebrates in general and three human cases in particular, in which it was found that the ovary lay within a definite sac in the broad ligament corresponding to the condition existing normally in many of the lower animals. These are evidently cases of degressive mutation (de Vries).—E. R. H.

(OVARY) Embryology of coccids with especial reference to the formation of the ovary, origin and differentiation of the germ cells, germ layers, rudiments of the mid-gut and the intracellular symbiotic organisms. Shinji (G. O.), J. Morph. (Phila.), 1919, **33**, —.

Of technical interest.—E. R. H.

(PANCREAS) War and Diabetes (Krieg und Diabetes). Albu. Münch. med. Wchnschr., 1917, **64**, 422; Berl. klin. Wchnschr., 1917, **54**, 470.

The diabetics form but one per cent of the sick list of internal medical wards, more than half of which patients had been previously shown to be diabetic. The tolerance lost by exposure and continued field diet was usually quickly restored under hygienic dietary regulation. Albu considers that a tolerance of 100 g. of glucose is sufficiently high for acceptance for military service.—F. S. H.

(PANCREAS) Principles and possibilities in the dietetic treatment of diabetes. Allen (F. M.), Wisconsin Med. J. (Milwaukee), 1917, **16**, 231-239.

Diabetes mellitus is defined as a disturbance in metabolism in which there is an inability on the part of the body to assimilate all classes of food. The author's principle of treatment is then stated, followed by a consideration of its practical application. The methods of recognizing diabetes and of determining its severity and progress are outlined, emphasis being laid upon the value of blood sugar determinations from time to time. Management of the cases with various complications such as metabolic disturbances and infections is outlined. In the case of coma, the author places the patient under fasting, if coma comes on while a diet is being given, and gives a diet if the patient is fasting at the time it appears. Diabetics with tuberculosis are given the fasting treatment like others, often with improvement in both conditions. To prevent starvation in these patients, when some food must be given, protein is superior to other food elements. In all cases after the urine is sugar-free the diet is gradually built up by giving on the first day 10 grams of carbohydrate, with gradual addition of 10 gms. for each successive day until the limit of tolerance is reached and the blood sugar kept within normal limits. Mild cases are not necessarily treated like the more severe but require some restriction and careful watching. The author does not claim the treatment to be curative but palliative.—I. M.

(PANCREAS) Diabetes mellitus. Blodgett (S. H.), Boston M. & S. J., 1919, **181**, 422-427.

No new data.—H. W.

(PANCREAS) Acidosis in diabetes mellitus; its significance and treatment. Bridges (W. O.), Med. Herald (St. Joseph), 1916, n.s. **35**, 40-44.

A general, brief discussion of the subject.—F. S. H.

(PANCREAS) A consideration of diabetes. Brooke (Banner R.), Med. Sentinel (Portland, Ore.), 1916, **24,** 3214-3218.

A readable discussion of the principles and methods of diagnosing and treating diabetes. Emphasis is laid upon the inadequacy of quantitative determinations of urinary sugar without controlling the diet. A small quantity of sugar upon a restricted diet might be much more significant than a large quantity upon a carbohydrate-rich diet. It is recommended that the patient be kept for three days upon a diet totaling 80 gms. of protein, 200 gms. of fat and 100 gms. of carbohydrate. A quantitative determination of urinary sugar can then be made and to a considerable extent relied upon as indicating the degree of severity of the disease. The value of quantitative ammonium determinations as routine procedure in every day practice is lauded. These can be made quickly and accurately without special equipment. They afford a valuable criterion as to the rate of depletion of the alkaline reserve, and may often give warning of impending "acidosis." The formalin titration method of ammonium determinations is described and recommended.—R. G. H.

(PANCREAS DIABETES) Edgar serum treatment of diabetes mellitus. Edgar (T. W.), West. M. Times (Denver), 1920, **39,** 299-302.

Edgar bases the justification of his serum treatment of diabetes mellitus upon the following: True diabetes mellitus is not hereditary, but dietary, fostered through the medium of environment; Diabetic glycosuria is always preceded by a "preglycosuria" stage characterized by intestinal stasis and toxemia which may manifest itself either subjectively or objectively, this latter being the predisposing cause of the symptoms; we are dealing with a cycle of endocrine or pluriglandular events, and not specifically with pancreatic insufficiency; pluriglandular therapy is indicated and is of distinct benefit in all uncomplicated cases. Three cases reported.—H. W.

(PANCREAS) The relation of glycogen to the pathologic changes in pancreatic diabetes. Ervin (D. M.), J. Lab. and Clin. Med. (St. Louis), 1919, **5,** 146-153.

A theoretical deduction is offered that glycogen is greatly diminished in the cells in pancreatic diabetes, based upon the fact of the stabilizing power of glycogen in experimental emulsions. Glycogen is a stabilizing colloid in the cell and as such prevents the breaking of the emulsion or fatty degeneration by its resistance to acids, salts, etc. Glycogen is hydrolized by acids, and when hydrolized, there is left a protein-fat emulsion that is but poorly resistant toward acids. In diabetes, no gly-

cogen is formed and the fat is only slightly emulsified, permitting a high concentration of the fats or soaps to reach the cell and a consequent limited oxidation, with production of acetone bodies. The equilibrium of glycogen with glucose is shifted towards the glucose side by the presence of the hydrogen ion; this is the explanation of the high blood sugar in fever, mercury and phosphorus poisoning and nephritis.—B. T. S.

(PANCREAS) Xanthoma diabetica (Zur Frage des diabetischen Xanthoma). Fahr, Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1373.

The diabetic xanthomas generally contain large quantities of cholesterin, but in the case described only traces of this compound were found, the mass consisting almost entirely of neutral fat. The opinion is expressed that diabetic xanthoma is caused by lipaemia with diminished lipolytic activity of the blood. —J. K.

(PANCREAS DIABETES) A case of galloping diabetes in a child of fifteen years (Un cas de diabetes a marche rapide chez une enfant de quinze ans). Gautiere (P.) and Saloz (C.), Arch. de med. des enf. (Paris), 1917, **20**, 314-317.

An extensive report of a rapidly fatal case of diabetes occurring in a child of 15 who gave a positive Wassermann reaction. The striking facts were the rapid course of the disease, which is exceptional in a child of this age; the short coma, lasting hardly a day; the inefficiency of the intravenous administration of sodium bicarbonate which had no action whatever on the acetone bodies of the urine; the leucocytosis; the high sugar content of the cerebro-spinal fluid; and, finally, the histological normality of the liver and pancreas on misroscopic examination. —F. S. H.

(PANCREAS) Importance and interpretation of urinary analyses in the diabetic (L'importance et l'interpretation des analyses des urines chez le diabetique). Gulpa, Bull. gen. therap. (Paris), 1919, **170**, 808-815.

A resume of the importance of, and reasons for, frequent analyses of the urines of diabetics, illustrated by a single case report.—F. S. H.

(PANCREAS DIABETES) Retinal changes in glycosuria. Hawthorne (C. O.), Opthalmoscope (Lond.), 1916, **14**, 365-367; Tr. Ophth. Soc. U. Kingdom (Lond.), 1916, **36**, 338-344.

A presentation of three summarized case-records of glycosuria accompanied by retinitis and retinal hemorrhages; from these it is argued that such phenomena may be utilized as a help in the diagnosis of early diabetes.—F. S. H.

(PANCREAS) The starvation treatment and fasting cure in diabetes (Hongerdagen en vastkuur bij diabetes). Hoogslag (W.), Nederl. Tijdschrft. v. Geneesk. (Haarlem), 1919, **63** (ii), 1770.

A report of excellent results in the Allen treatment of diabetes.—J. K.

(PANCREAS) Treatment of diabetes (De strijd tegen de suikerziekte). Hoogslag (W.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64**, 295.

A recommendation of the Allen treatment, which is described.—J. K.

(PANCREAS) The treatment of diabetes mellitus by alimentary rest. Hume (J.), Practitioner (Lond.), 1916, **97**, 430-434; See also: Brit. M. J. (Lond.), 1916, (i), 587 and (ii) 160.

A theory is developed that diabetes is essentially an acid autointoxication, the toxin originating from stasis or other abnormal conditions in the alimentary canal. This toxin formation can be prevented by purging and fasting. Checking of the toxin formation is regarded as the significant factor in the "Allen" treatment. Hume regards detailed metabolic studies and "caloric feeding" as unnecessary refinements in the treatment of ordinary diabetes.—R. G. H.

(PANCREAS) Diabetes mellitus in the Japanese, compared with its occurrence in Europe and America (Le diabete sucré "tônô byô" chez les Japonaise et son étude comparative avec le diabete observé en Europe et an Amerique, étude clinique et expermentale). Iwai, (T.), Arch. de med. exper. (Paris), 1916-17, **27**, 1-54.

It is a rare thing to find among the Japanese diabetes presenting the fundamental symptoms of polydipsia, polyuria, and emaciation; almost always the disease is found associated with some other disorder. The malady is benign and rarely fatal. The author is of the opinion that the Japanese have a higher sugar tolerance than other races, and that this is presumably a racial characteristic rather than a dietary one.—F. S. H.

(PANCREAS) Protein-sparing by glucose in experimental diabetes. Janney (N. W.) and Isaacson (V. I.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1917, **15**, 69-70.

The surgical removal of about 90 per cent of the pancreas of several dogs did not cause any diminution of the protein-sparing action of glucose in any of the animals. It appears that pancreatic tissue is provided far in excess of actual requirements or that this gland is not solely responsible for the protein-sparing action of carbohydrates.—F. S. H.

(PANCREAS) Glucose formation from protein in diabetes. Janney (N. W.), Arch. Int. Med. (Chgo.), 1916, **18**, 584-605; Tr. Coll. Physicians (Phila.), 1916, 3.s., **38**, 168-194; Med. Rec. (N. Y.), 1916, **90**, 346.

A series of pure isolated proteins was found to yield 48-80% glucose when fed to a diabetic subject. Whether from animal or vegetable sources made no apparent difference in the yield. Beef, rabbit, fish, chicken and egg, when similarly tested yielded 36-48% glucose. For this reason Janney regards the well known food tables of Van Noorden as inadequate as a guide in framing diabetes dietaries, since no cognizance is taken of such protein foods as sources of sugar. Egg was found to be the most satisfactory of the protein foods tested, since, weight for weight, it yielded only about 1/6 as much sugar as did bread. Various proprietary "diabetic foods" were found to be so high in protein as to be quite unsuited for the use of diabetics. From the foregoing data the conclusion is drawn that a mixed diet rather low in protein is no more injurious than is the high protein and fat diet often prescribed and it has the advantage of being more palatable.—R. G. H.

(PANCREAS) Diabetes, The causes of death in—. Joslin (E. P.), Am. J. Med. Sc. (Phila.), 1916, **151**, 313-321.

The author believes that death following coma in diabetes is avoidable and that all diabetics have a certain carbohydrate tolerance which should be determined. Out of 475 deaths, 147 have been without coma and due to other causes than diabetes. Death with coma was responsible for 273 cases and many of these could have been forestalled by earlier treatment. Some added burdens that should be prevented are: ether anesthesia, impaired kidneys, infections, mental excitement, fat poisoning and loss of body fluid. Salt should never be left out of even the starvation treatment.—F. S. C.

(PANCREAS) Effect of intravenous injection of pancreas emulsion upon the hyperglycemia due to depancreatization.

Kleiner (I. S.), Scientific Proceedings, Am. Soc. biol. chem. XIII. J. Biol Chem. (Baltimore), 1920, **41**, xviii.

If fresh dog's pancreas be hashed and mixed with three or four times its weight of sterile distilled water, allowed to stand in the refrigerator for from 1 to 20 hours and then strained through muslin a solution is obtained which, when diluted with five volumes of 0.9 per cent sodium chloride solution and injected slowly into depancreatized dogs during the course of an hour, causes a marked reduction in the blood sugar and a reduction of the glycosuria . Reduced glycosuria was also produced by similar injections with extracts of other organs but this was not accompanied by reduction in the blood sugar.—F. S. H.

(PANCREAS) War diet in diabetes (Kriegskost in Diabetes). Falta (W.), Wiener klin. Wchnschr., 1919, **32**, 398-400. Elias (H.), and Singer (R.), (ibid., 503-4).

The author of the first paper has long held that reduction in protein intake is an important factor in diet for diabetes. The war has proved it. The second paper is the third of a series, and is largely polemical against Falta.—Physiol. Abst. **4**, 218.

(PANCREAS) Surgery in diabetics. Labbé (Marcel). Am. J. Surg. (N. Y.), 1919, **33**, 257-259.

The author outlines the results of his surgical experience with diabetic subjects, discussing the special features of importance in this class of patients. These he considers under the following topical headings: (1) hyperglycemia, (2) acidosis, (3) the anesthetic and (4) pre-operative and post-operative treatment. He finds that in the less severe cases, various operations may be performed with impunity, if proper precautions in technique and treatment are taken. He recommends pre-operative anti-diabetic treatment to reduce hyperglycemia and acidosis and favors the administration of bicarbonate of soda both before and after operation to prevent the development of acidosis. Local anesthesia with cocaine, if possible, or, if not, spinal anesthesia is recommended. When general anesthesia is necessary ethyl chloride is preferable to ether. Chloroform is to be avoided. —I. M.

(PANCREAS) A preliminary report of a case of diabetes mellitus at the present time under treatment, with short review of the recent literature. Larsson (B. Hjalmar). Detroit M. J., 1916, **16**, 163-165.

A modification of the Allen treatment was employed. Instead of maintaining absolute starvation, 800 calories was administered daily in the form of whiskey in black coffee.—R. G. H.

(PANCREAS) The cause of pancreatic diabetes (Das Wesen des Pancreasdiabetes). Lesser, Münchener med. Wchnschr., 1920, **67**, 307.

When the surviving liver of a frog is fed with Praeger's solution and adrenalin is added, sugar for a short time is formed in the liver. It might be thought that diastase is formed in the liver, but this is not true, for the solution leaving the liver has no increased amount of diastase. When, however, from a frog the pancreas is removed and then the liver is brought into Ringer's solution, addition of adrenaline causes the formation of diastase. It is probable that in the normal liver there is a separation of the glycogen and diastase. Removal of the pancreas brings the glycogen and diastase together.—J. K.

(PANCREAS) The recognition and management of threatening diabetic coma. Levison (Louis A.), Ohio M. J. (Columbus), 1916, **12**, 11-17.

Greatest care should be taken to recognize the signs of threatening diabetic coma. The usual symptoms of this are somnolence, gastro-intestinal disturbances,—vomiting, diarrhea or constipation,—increased irritability and muscular cramps in various parts of the body. Treatment should be begun early and pushed vigorously. In severe cases not only should alkalis be used, but also alcohol by mouth and rectum. Heart weakness should be looked for and appropriately treated, since it may lead to death from unexpected sources.—R. G. H.

(PANCREAS) The treatment of diabetes mellitus in children and adolescents. Leyton (O.), The Practitioner (Lond.), 1919, **103**, 370-380.

Diabetes mellitus is defined in some detail and means of recognizing it and of measuring its severity are discussed. Methods of treatment and control of the disease are likewise outlined. Infections, general anaesthesia and any other conditions that will disturb the metabolic processes are strictly to be avoided in diabetes. The Allen starvation treatment is strongly praised. Children are said to do exceptionally well on it if removed from sympathetic relatives and friends. After the urine is sugar-free the tolerance for the carbohydrates, fats and proteins is separately determined. The fact that intolerance for fat or protein frequently gives rise to sugar in the urine more easily than does carbohydrate food is pointed out. The optimum diet given to the diabetic when sugar-free is two-thirds of the limit of carbohydrate tolerance plus 2 gms. of protein per Kg. body weight per diem, plus sufficient fat to make the energy of the diet equal to 60 calories per Kg. body weight per 24 hours.—I. M.

(PANCREAS) Über Diabetes mellitus. Lichtwitz (L.), Ztschr. f. ärztliche Fortbildung (Jena), 1919, **16**, 601.

A general discussion without new facts.—J. K.

(PANCREAS) Lowering of the freezing point of the blood in diabetes (Blutgefrierpunkterniedrigung bei Diabetes mellitus). Lippmann (A.), Zentralbl. inn. Med. (Leipzig), 1920, **41**, 41.

A number of patients having diabetes, though with normal kidney function, showed a very marked depression of the freezing point of the blood. This depression did not run parallel with the amount of blood sugar and it is presumed that the blood sugar is not the only substance that is increased in these cases. There is evidence of the presence in the blood of diabetics of other reducing substances, for the amount of glucose determined by the reduction of Fehling's solution is always higher than when it is determined by other methods. In the author's opinion (as in that of Stepp) the increased glucose in the blood is accompanied by the occurrence of other substances.—J. K.

(PANCREAS PROSTATE) Diabetes and prostatectomy (Diabète et prostatectomie). Loumeau, Gaz. hebd. de sc. med. de Bordeaux, 1916, **37**, 71-72.

A report of the nature and the effects of removal of the prostate from a diabetic. Apparently both these prostatic disorder and the diabetes were cured. The author considers diabetes no contra-indication to surgical procedures under anesthesia.—F. S. H.

(PANCREAS) Diabetes treated by the Allen starvation method, with report of seven cases. Love (Tracy R.), Colorado Med. (Denver), 1916, **36**, 205-209.

Of seven severe cases of glycosuria all showed marked improvement following Allen's starvation treatment. Two cases did not show sugar-free urine owing to complications, but the treatment allowed the relief needed for operation. The author believes that the amounts of acetone, diacetic acid and ammonia in the urine are not a safe guide to the degree of acidosis, due to the fact that the oxybutyric acid is so combined with the tissues that it is not liberated until cases are well advanced.—F. S. C.

(PANCREAS DIABETES) Intermediary metabolism in diabetes. Lusk (G.), Trans. Coll. Phys. (Phila.), 1916, **38**, 244-248.

A brief statement of the simpler chemical changes that the carbohydrates may undergo during their metabolism in the tissues. F. S. H.

(PANCREAS) A case of fatal diabetic coma without diacetic or betaoxybutyric acid. McCaskey (G. W.), J. Am. M. Assn. (Chgo.), 1916, **66**, 350-351.

A fairly typical case of diabetes ending in coma in a woman of 53 is reported. The case is recorded as showing that coma may develop in the absence of the acetone bodies mentioned and as a warning that a negative Gerhardt reaction does not necessarily exclude impending coma.—R. G. H.

(PANCREAS) Observations on the sugar of the blood and the sugar in the urine in varying conditions of health in the Bengali. McCay (D.), et al., Indian J. Med. Res. (Calcutta), 1919, **6**, 485-507.

This is Section II of a paper describing the extensive studies made by McCay and his co-workers on the sugar of the blood and urine. A general discussion of the relationship of the sugar of the blood to that of the urine and the factors concerned in regulating the excretion of sugar is entered into. The method employed was to determine the reducing power of the blood and urine by a special method in normal individuals, in glycosurics with normal kidneys and in individuals with nephritis. It was found that the threshold stimulus of the kidney for sugar excretion varies widely in different individuals and in the same person under different circumstances. Glycosurics are met with in whom: (1) the threshold is high—usually the condition seen in the fat, over-fed classes; (2) the threshold is low—as in (a) the later stages of the above; (b) those who have lost the power of storing sugar, oxidizing it or of converting it into fat; (c) those who present an excessive permeability of the kidney to sugar as a result of oxaluria, gout, or stone. The limits of the normal variations of the sugar of the urine of Bengalis are from 0.015 per cent to 0.15 per cent, the average being 0.065 per cent.

No parallelism or arithmetic proportions exist between the concentration of the sugar of the blood and that of the urine in any of the following conditions: (1) normal health, (2) aglycosuric diabetes, (3) varying degrees of glycosuria in different individuals; (4) varying degrees of glycosuria in the same individual. The ingestion of glucose is always followed by an increase in the sugar of the urine, whether the sugar concentration of the blood increases or not, i. e., in the healthy, potential diabetics, and diabetics. Kidney disease may prevent glycosuria even when very marked hyperglycemia is present—up to 0.86 per cent.—I. M.

(PANCREAS) Observations on sugar of the blood and the sugar in the urine in varying conditions of health in the Bengali. McCay (D.) et al., Indian J. Med. Res. (Calcutta), 1919, **6**, 508-549.

The present is the third paper on this general subject by McCay and his co-workers. Their studies consisted of observations on the onset and progress of glycosuria with reference to the cause of the prevalence of diabetes in India. A large number of the natives from the various classes were examined. The authors believe that they have established the following points: (1) The fat, flabby, indolent individual who is over-fed with carbohydrates possesses a lower tolerance for carbohydrates than the lean, energetic, hard-working individual. (2) In the preglycosuric stage of diabetes, the fat and sugar of the blood are much above normal and are both increased still more by the ingestion of sugar. (3) As the ability of the tissues to convert sugar into fat is gradually diminished, sugar begins to appear in the urine and is found to increase as the fat content of the blood decreases. (4) A tendency to glycosuria occurs in normal persons when excessive amounts of sugar are ingested over long periods, hence the difference in the normal and the diabetic individuals is not a qualitative but a quantitative one. (5) The obesity so common in the preglycosuric or early glycosuric is associated with the hyperglycemia and is due to a physiological storing-up of reserve material, the excess sugar of the blood being synthesized into fat. (6) The subsequent wasting is probably pathological and may be explained as due to loss of the power of the tissues to convert sugar into fat and the actual breaking down of fat to furnish energy to the body. (7) There is a strong hereditary factor in diabetes. (8) The over-feeding with carbohydrates is said to be sufficient in itself to account for the onset of hyperglycemia, lipemia, obesity and glycosuria. (9) Excessive carbohydrate also is thought to lessen the secretion of the HCl of the gastric juice, which leads to gastrointestinal inflammation. This inflammatory process is said to spread in turn to the pancreas, causing a depression in the internal secretion, which condition interferes with the oxidation of sugar.

—I. M.

(PANCREAS) Diabetic therapy. MacLeod (J. J. R.), J. Lab. & Clin. Med. (St. Louis), 1916, **1**, 780-781.

A general discussion. The points especially emphasized are that fasting will lower acidosis either in health or diabetes if it has the effect of stopping a one-sided metabolism and throwing the tissues onto a more nearly balanced ration of fatty acids and glucose. Other things being equal, there is more danger of

serious acidosis developing in fat than in lean diabetics.—R. G. H.

(PANCREAS) Diabetes mellitus. McMillan (D. W.), J. Florida M. Assn. (Jacksonville), 1916, **3,** 238-243

A general discussion of the cause, prevention and treatment of diabetes.—R. G. H.

(PANCREAS) Diabetes during the war (Über den Diabetes im Kriege). Magnus-Levy (A.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1379; Berlin. klin. Wchnschr., 1919, **56,** 1150.

In Germany in 1914 the number of deaths caused by diabetes was double that of 1900, while in 1919 the number of fatal cases of this disease was the same as in the year 1900. During the war acidosis and diabetic coma were extremely rare, the coma that did occur failing to show the classical Kussmaul respiration. It is probable that under-feeding has played a part in the diminished number of fatal cases of diabetes.—J. K.

(PANCREAS) Diabetes during the war (Über Diabetes im Kriege). Magnus-Levy, Münch. med. Wchnschr., 1919, **66,** 1303.

During the war the number of cases of diabetes has diminished in Germany. Coma diabeticum became very rare. It may be a lesson to be careful with fat in the treatment of diabetes since fat was very rare in Germany during the war.—J. K.

(PANCREAS) Diabetes mellitus. Mettam (A. E.) and Craig (M. A.), J. Comp. Path. & Therap. (Edinburgh and London), 1916, **29,** 1-26.

An interesting case of spontaneous diabetes in a dog is described. The owner had noted the first evidence of disease three months before. The animal was thin and "skraggy" and had cataract. Appetite and thirst were normal. The sp. g. of the urine was 1.050. Glucose was noted as varying from 4.8 to 10%. The dog was killed and post-mortem examination made immediately. The blood plasma contained .39% glucose. The liver cells gave a positive glycogen test. The pancreas appeared normal in the gross; but careful search, using a variety of technical methods, failed to reveal any islands of Langerhans. The technique was controlled upon other pancreas material in which the structures were readily demonstrated. The thyroid was apparently normal. In the adrenals the cortex was somewhat hemorrhagic. Many of the medulary cells were vacuolated and showed

appearances suggestive of colloid degeneration. The nervous elements appeared normal. Many other details of the examination, not of endocrine interest, are omitted in this abstract.—R. G. H.

(PANCREAS) The treatment of diabetes mellitus. Mosenthal (H. O.), J. Med. Soc. N. Jersey (Orange), 1916, **13,** 339-355.

A valuable article for any one desiring a brief but comprehensive and readable discussion of the salient features of present day management of diabetes. The article includes useful food tables, diet and urine chart, methods of freeing the urine from sugar and acids and quantitative tests for "acidosis."—R. G. H.

(PANCREAS) Urinary output of nitrogen, chlorine, calcium, and magnesium in diabetes mellitus. Nelson (C. F.), Scientific Proceedings, Am. soc. biol. chem. XIII., J. Biol. Chem. (Baltimore), 1920, **41,** xiv.

Determinations of calcium, magnesium, and sodium chloride in nineteen cases of diabetes mellitus showed marked variations, as did the values obtained for the total nitrogen. In 26 per cent of the cases magnesium was excreted in larger amounts than was calcium. Eleven determinations, made from 5 to 21 days after six of the cases had been rendered free from sugar in the urine, showed a striking change in the urinary calcium magnesium ratio, magnesium appearing in larger amounts than calcium in 72 per cent of the determinations. The total nitrogen in each of the latter cases was from 1 to 6 grams higher than in the former.—F. S. H.

(PANCREAS) Accessory pancreas (Over het accessoire pancreas. Nieuwenhuyse (P.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (ii), 2106.

During a post-mortem examination there was found a small tumor in the stomach which proved to be an adenoma, the center of which showed typical pancreas cells, but no islets of Langerhans.—J. K.

(PANCREAS) Diabetesstudien. Petrén (K.), Arkiv för inre medicin (Nord. Med. Arkiv, Avd. II), 1918, **51,** 107-173.

Petrén records (in German) the results of a detailed study of 21 cases of diabetes. The study was undertaken to learn the conditions under which the carbohydrate tolerance could be augmented and the degree of improvement that, by dietary control, could be attained. The data on each case are tabulated. It ap-

peared that the shorter the duration of the disease, the better is the prognosis. The author agrees with Naunyn that those cases only can be regarded as mild in which glycosuria can be overcome by the reduction of carbohydrate to 60 gms. of bread a day. In any case the diet should be adjusted, if possible, to maintain an unbroken aglycosuric condition and gradually to build up tolerance. The age of the patient is regarded as the most important factor in the determination of results, but the data available did not permit any final conclusion as to the operation of this factor. The duration of treatment is also an important factor. By careful systematic attention to the diet it was found possible to increase the carbohydrate tolerance within a few weeks from 33 to 118% and as much as 128% by longer treatment. The improvement seemed to be progressive. The higher the initial tolerance the greater was the possibility of improvment. When the tolerance was 40 gms. at first, it could be raised from 50 to 100 gms. higher. It is held that dietotherapy is indicated, not alone on account of symptomatic improvement but as rationally directed toward modifying the underlying etiologic factors. For numerous details the original should be consulted.—R. G. H.

(PANCREAS) The treatment of diabetes. Robin (A.), Monde med. (Eng. Ed.) (Paris), 1916, **26,** 129-146.

The author defines four forms of diabetes and discusses the effect of treatment in the various forms. The first type is the true pancreatic diabetes not amenable to functional therapy, being benefited in but a few cases. The second form, hepatic or hepatogenous diabetes, is that in which the soil is already prepared by acquired or inherited arthritism and is precipitated by overfeeding or nervous wear and tear. These cases are claimed to be attenuated by treatment. The next type is the mild diabetes or gouty type, which is in most cases curable. Fourth in the classification are the cases of grave or complicated diabetes which call for special intervention and medication not admissible in ordinary diabetes. The necessity of educating the diabetic subject is pointed out. The habits of life with respect to general hygiene, diet and exercise must be carefully supervised. The various schools on dietary treatment are discussed and specific details as regards the various elements of the diabetic's diet are given. The diet is drawn up in each case on the basis of 30 calories per Kg. body weight per 24 hours as the minimum requirement of the diabetic, and after determining the 24-hour nitrogen output, to learn the nitrogen needs of the individual. The results of hydrotherapeutic and special hygienic measures and of various sorts of medication and electrotherapy are considered in some detail.—I. M.

(PANCREAS) Conservative treatment of diabetic gangrene; two cases, patient. Sammis (G. Frank), Long Island M. J. (Brooklyn), 1916, **10**, 202-203.

Two brief case reports. Standard diabetic regime served to conserve the resistance of the patients, so that successful results were obtained in gangrene of the feet by conservative operations.—R. G. H.

(PANCREAS) The clinical control of diabetes mellitus. Schroeder, Henry, Lancet—Clin. (Cincinnati), 1916, **115**, 102-108.

The nature of diabetes mellitus as a disease and the problems involved in its control are briefly outlined. The author emphasizes the importance of studying the blood sugar as well as the urinary sugar. The studies on eight cases of diabetes on the starvation diet are tabulated; these show that hyperglycemia very frequently persists long after the urine is sugar-free. The conclusions drawn from pathologic and clinical observations are that effective supervision of the patient with respect to diet and general hygiene makes possible the raising of the sugar tolerance, whereas dietary abuses lead to a lowering of tolerance. The paper is followed by discussion from other observers.—I. M.

(PANCREAS) Diabetic retinitis. Shafer (J. J.), Am. J. Surg. (N. Y.), 1918, **32**, 67-68.

Four forms are described. (1) Central punctuate retinitis: at the posterior pole of the fundus, especially in the macular region, are found numerous ivory white points, spots and stripes which surround the macula in an irregular manner. The spots are round, oval, or irregular in outline; their margin may be serrated. Some of them cover the small blood vessels, thus showing that they are within the nerve fibre layer. Between the white areas fine blood points, stripes or little spots may be seen. (2) Hemorrhagic diabetic retinitis in four forms: (a) fine punctiform hemorrhages; (b) larger hemorrhages which may enter the vitreous humor and produce localized bluish dimness; (c) sudden large hemorrhages (often with very little sugar in the urine); (d) hemorrhagic glaucoma, with no hope of recovery. (3) Diabetic albuminuric retinitis: in addition to an opaque and slightly swollen optic nerve-head and retina with alterations of the blood vessels characteristic of albuminuric retinitis, there are groups of white spots which are peculiar to diabetic retinitis. (4) Albuminuric retinitis is wholly independent of the coincident diabetic process.—L. G. K.

(PANCREAS) The starvation treatment of diabetes mellitus. Steiner (Walter R.), Proc. Connect. M. Soc. (New Haven), 1916, **124**, 176-186.

The principles of starvation treatment are briefly explained and the histories of eight cases of diabetes mellitus are reviewed with special reference to the importance of this form of treatment. Discussion of this paper with reports of other similar cases by a number of other investigators is appended.—I. M.

(PANCREAS) The treatment of diabetes with special reference to acidosis. Stilman (Edgar), Med. Rec. (N. Y.), 1916, **89**, 390.

A very brief note on the principles of determining "acidosis."—R. G. H.

(PANCREAS) Prognosis and treatment of diabetes as influenced by recent studies. Strouse (Solomon), Illinois M. J. (Chgo.), 1916, **30**, 332-337.

A general discussion not amenable to abstracting.—R. G. H.

(PANCREAS) Diabetes in the young. Strouse (Solomon), Med. Clin. (Chgo.), 1916, **2**, 327-329.

Cases of diabetes mellitus in children are presented and discussed with special reference to the successful employment of the Allen starvation treatment in the young. The author emphasizes the importance of careful supervision of the diet after the patient leaves the hospital. A comparison of the results obtained by modern methods of treatment in diabetes with those of old shows marked improvement, making the prognosis in children decidedly more hopeful. A case of typical renal glycosuria is presented, with a warning against treating such cases of lowered sugar tolerance as true diabetes mellitus.—I. M.

(PANCREAS) Inanition in the treatment of diabetes mellitus. Strouse (Solomon), Med. Clin. (Chgo.), 1916-17, **2**, 999-1006.

A brief historical review of various methods of treatment employed in diabetes mellitus is given, followed by a short exposition of the "Allen treatment." The author does not fully agree with Allen that the weight curve should be entirely neglected for the urine chart. The general nutrition of the patient must be carefully guarded.—I. M.

(PANCREAS) Syphilis as a cause of diabetes mellitus. Williams (J. R.), J. Am. M. Assn. (Chgo.), 1918, **70**, 365-367.

Careful clinical and laboratory examinations were made on a large number of patients suffering from diabetes mellitus to discover signs of syphilitic infection. Only 4 out of 143 cases showed a positive Wassermann reaction, while the physical examination of 126 cases for lesions characteristic of syphilis did not lend support to the view that the disease is a common causal factor in diabetes. Literature corroborative of Williams' conclusion on the subject is cited. The study, therefore, does not support the view advanced by Warthin that syphilis is the chief etiologic factor in the production of pancreatic diabetes. If it proves anything it is that syphilis is rarely the provocative agent.—L. G. K.

(PANCREAS) The treatment of diabetes mellitus. Williams (John R.), Vermont Med. (Rutland, Vt.), 1916, **1**, 341-348.

Following a general discussion of the topic Williams concludes that liability to diabetes is undoubtedly transmissible from parent to offspring. Infections have a very deletarious influence on diabetes and should be sedulously guarded against. Instruction of the patient is a major part of the treatment. Unless he understands the reason for procedures undertaken, and is willing and able to co-operate, the treatment will fail. Intercurrent complications demand careful study; they may be more serious than the diabetes. Difficult cases should be sent to institutions adequately equipped to make metabolic studies.
—R. G. H.

(PANCREAS) The dietetic treatment of diabetes mellitus. Williamson (R. T.), Practitioner (Lond.), 1918, **100**, 35-40.

Three different diets are described which are said to check glycosuria if restricted or rigid diabetic diets fail. Starvation is advised only if all other methods have failed. Fast days, once a week, are said to be of service. After the glycosuria has been checked the diet is gradually changed, bacon, green vegetables and eggs being permitted. Later, diabetic bread or biscuits are allowed. Salicylate of soda and acetyl-salicylic acid are often of value when given in large enough doses, and should be tried if the dietetic treatment fails.—L. G. K.

(PANCREAS) The dietetic treatment of diabetes. Worcester (G. F.), N. Eng. Med. Gaz. (Boston), 1916, **51**, 127-139.

The historical development of various forms of dietetic treatment in diabetes mellitus is briefly reviewed with a consideration of the present systematic methods. The importance of early treatment is strongly emphasized.—I. M.

(PANCREAS) Ear affection and diabetes. Zimmerman (Chas.), Ann. Otol. Rhinol. & Laryngol. (St. Louis), 1916, **25**, 637-648.

The otologist is concerned with diabetes in that the lowered resistance characteristic of the disease may aggravate several of the conditions with which he has to deal. Furunculosis of the auditory meatus is sometimes encountered while otitis media and mastoiditis in diabetics are particularly hard to deal with. The literature is reviewed and five cases illustrative of the relationship are described.—R. G. H.

PARATHYROIDS, Transplantation of—in postoperative tetany (Epithelkörerverpflanzung bei postoperativer Tetanie). Borchers (E.), Zntralbl. f. Chir. (Leipzig), 1919, **49**, 907.

The author has described a case of post-operative tetany perfectly cured by transplantation. The patient became pregnant; in the fourth week she complained of pains in arms and legs and she lost a great part of her hair. In the fifth month very severe attacks of tetany were seen and it was necessary to produce abortion. This proves again what was already known from experiments on animals, that during pregnancy the function of the parathyroids must be increased and that, when the glands are not able to increase their function, tetany may occur. This patient is of importance as Adler and Thaler proved that animals without parathyroids never become pregnant. The author believes that in these cases of postoperative tetany, it is better to add to the transplantation sterilization of the woman. This patient was again restored to health after abortion. A second case of successful transplantation in postoperative tetany is also reported.—J. K.

(PARATHYROID THYROID) Considérations sur la paralysie agitante. Gauthier (G.), Le Méd. Français (Bourg-la-Reine), 1919, **12**, 181-183.

The author regards Parkinson's disease as due primarily to disturbance of calcium metabolism which is regulated especially by the action of the parathyroid glands. In 1902, struck by a resemblance between paralysis agitans and Graves' disease, Gauthier began treating his patients with a glycerine extract of the thyroid-parathyroid glands. His success therewith "has been incontestible."—R. G. H.

(PARATHYROID) Treatment of postoperation tetany (Zur Therapie der postoperativen Tetanie). Haas (W.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 171.

A case is reported in which the author obtained good results from the administration of tablets of parathyroids (up to 0.1 gram dried glands six times daily). In the literature are described cases of postoperative tetany cured by thyroid preparations. Many theories are given to explain this result. Haas, however, believes that such cases are instances of spontaneous amelioration and that the administration of thyroid has no effect whatever. During pregnancy, post-operative tetany is very serious. In this connection a case is described in which, during pregnancy, strumectomy had to be performed for stenosis. There was found a very marked hypertrophy of the parathyroids.—J. K.

(PARATHYROIDS) Treatment of postoperative tetany by transplantation of parathyroids (Die Behandlung der postoperativen Tetanie durch Epithelkörpertransplantation). Landois (F.), Zentralbl. f. Chir. (Leipzig), 1920, **47,** 74.

The results of animal experimentation and a clinical case have led L. to the conclusion that in general postoperative parathyroid transplantation is unsuccessful in relief of postoperative tetany unless the patient had previously shown no symptoms of latent or manifest tetany. One case is reported in which the implantation of three parathyroids gave but temporary relief, the patient later dying of tetany.—J. K.

(PARATHYROID) Studies on the relation of the human parathyroid glands to the occurrence of calcium deposition in the organism (Untersuchungen über das Verhalten der Glandulae parathyroideae des Menschen beim Vorhandensein von Kalkablagerungen im Organismus). Tomaszewski (Zdzislaus), Frankfurt. Ztschr. f. Path. (Wiesbaden), 1918, **21,** 38-56.

The post-mortem pathological findings made with a view to studying the apparent histological changes evidencing activity in the parathyroids. The occurrence of calcium depositions resulted in the author's classifying his subjects into three groups according to the intensity of the glandular function indicated in this manner.

In the first group were nine individuals in whom the histological picture of the glands showed the presence of all the elements commonly ascribed to an increased glandular functioning, such as many oxyphil cells, follicles and colloid.

The second group, although showing the presence of some activity by histological criteria, did not present a complete picture, there being usually omitted one or two of the factors going to make up a unified and active composite. There were seven subjects in this group.

In the four members of the third group there was but little evidence of glandular activity and if any had been present it was of a low order. Many of the cases were complicated by the demineralizing activities of tubercular processes, but notwithstanding this, those cases presenting histological pictures of heightened glandular activity also presented evidence of extensive calcium deposition.—F. S. H.

(PARATHYROID?) A case of osteomalacia and tetany (Ein Fall von Hungerosteomalazie und Tetanie). Sauer (H.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 45.

Description of a case which in contradistinction to those frequently observed in Vienna presented no pain when the bones were subjected to pressure.—J. K.

(PARATHYROID?) Tetany in the eunuchoid: report of case. Woltman (H. W.), J. Nerv. & Ment. Dis. (Phila.), 1919, **50,** 433-447.

The history of tetany and its relation to the parathyroids is briefly reviewed. The detailed case history may be summarized as follows: A barber, aged 36, complaining of convulsions, presented himself for examination. His family history showed some tendency toward endocrine disturbances. The patient had convulsions for one year in infancy. He married at 29, but his wife has never been pregnant. At 29 he noticed that his legs became very easily tired. This grew progressively worse. At 33 he noted marked abdominal distension, at intervals of about one week, lasting 45 minutes. One month later he noticed that his legs "jerked up," and he was able to walk only by staggering along on his toes. These spasms increased in frequency and intensity. Six months later they were accompanied by "cramping of the jaw" and lasted 30 or 40 minutes. He improved somewhat and was able to be about on crutches, but soon his legs began to swell and he noted edema of the abdominal wall and back and complained of burning pain in the legs. Soon after this he was unconscious for three days, developed contractures of the legs and some mental symptoms. The muscles were atrophied, the skin dry and scaly, and, over the abdomen, covered with brown spots. The spasms diminished in intensity and number, but any attempt to get up was followed by vomiting.

Physical examination. The hair was seen to be thin and dry; there was hypotrichosis of body hair with female distribution over the pubis. The right testicle was very small, the left absent (surgical removal). The voice was high pitched and somewhat cracked. Palpation of the thyroid was uncertain. The blood serum and spinal fluid Wassermann reaction was

negative. Roentgenograms of the sella and the hands were negative. There was slight pallor of the optic discs.

On compressing the left upper arm (testing for the Trousseau phenomenon) the fingers grew pale and cold and in one-half minute passed into a tonic spasm. The spasm extended up the arm and almost simultaneously appeared in the right arm, muscles of the floor of the mouth, tongue, lips and, to some extent, in the legs. The jaw was fixed by a tonic spasm, interrupted occasionally by painful clonic movements. The patient was conscious and able to talk. The spasm was terminated after 65 minutes by a hypodermatic injection of ½ grain of morphine. The spasm gradually disappeared, leaving the fingers last. About two weeks later the spasms involved the throat muscles, and the eye-balls were rotated upward until only the border of the cornea was visible.

Medication (thyroid gland and calcium lactate) produced no results. Death occurred about one year later. The case report is followed by an able discussion of the symptoms and their individual frequency and a list of references to medical literature.

The author states that it would seem justifiable to assume that when there appears marked evidence of polyglandular participation in which the disorder is not initiated by a disturbance of the thyroid gland the prognosis is very grave. A distinct heredofamilial tendency to glandular disturbance, especially when associated with the psychoses or certain neurasthenic states, renders the prognosis much more grave.—F. C. P.

PARATHYROID, Histological examination of—in a case of chorea (Nuovo reperto istologico delle paratirodi in un case di corea volgare). Zibordi (F.), Gazzetta degli Ospedali (Milan), 1919, **40**, 471.

In a case of goitre only two parathyroids were found and these contained very few chromophil cells.—J. K.

PINEAL innervation in teleosts (Zur Frage der Epiphysen-Innervation bei Teleostei). Holmgren (N.), Fol. neuro biol. (Haarlem), 1918, **11**, 1.

A brief description of the nerves to the pineal body of various fishes.—E. R. H.

(PINEAL) Histology and embryology of the human pineal (Histologische und embryologische Untersuchungen über die Zirbeldrüse des Menschen). Krabbe (K. G.), Anat. Hefte, 1916, **54**, — (Abstract by Lubowski in Fol. neuro-biol. (Haarlem), 1918, **11**, 68.)

The development of the pineal has already begun in the second fetal month, at which time it consists of two parts: a fold in the roof of the second vesicle and a cell mass anterior to this; later, these two parts unite. During fetal life the original type of cell differentiates into three forms from which the parenchyma of the gland develops, during infancy and adolescence. These cells are glial, neural, and parenchymatous, proper. A description of them is included. Connective tissue follows the blood-vessels. It contains mast cells, previously called acidophiles, pigment cells and, in senile individuals, plasma cells. The latter are present in children under certain pathological conditions, such as progressive paralysis. Concretions are present at 6 years and sometimes earlier. The pineal grows very little after childhood.

As to function the gland may be a sort of sense organ to regulate the pressure of the "central process" or it may have an internal secretion. The author states that, anatomically, it looks more like a gland than a sense organ.—E. R. H.

(PINEAL) Effect of feeding the pineal body upon the development of the albino rat. Sisson (W. R.) and Finney (J. M. T.), J. Exp. Med. (N. Y.), 1920, **31**, 335-346.

Pineal bodies of young calves were fed to albino rats of three weeks of age for a period of three to six weeks. Fourteen were fed powdered pineal body and ten were used for control. About half of the treated animals remained slightly smaller than the controls. The microscope revealed no differences in the pineal bodies of the treated animals when compared with those of the controls. The authors conclude that "feeding the desiccated pineal body of young calves to young albino rats fails to produce any effect upon the development of these animals."

—B. T. S.

(PINEAL) Menstruatio precox. Volhard, Münch. med. Wchnschr. (Munich), 1919, **66**, 1502.

A short note concerning a girl of 8 with regular menstruation and adiposity, in whom, at the time of menstruation, eclamptic-like seizures occurred. The diagnosis as given is a probable teratoma of the pineal.—J. K.

(PLACENTA) The placenta as a birth-promoting organ (Die Placenta als wehenförderndes Organ). Ludwig (F.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1919, **50**, 256-282.

In view of the interest taken in the endocrine aspects of the placenta L. has made a study of the effect of placental extracts on the contractability of the isolated intestinal segment of the

rabbit and guinea-pig. He found that both fresh and boiled extracts of the placenta caused contractions of such segments from both types of animal. Moreover, the extract exerted a similar type of stimulating effect on segments of a pregnant guinea-pig uterus as well as on a bit of human fallopian tube. However, liver extract and pituitary extract gave similar responses, but apparently not to the same extent. On the basis of these experiments he concludes that there must exist in the placenta a specific substance initiating and faciliatating parturition. It is the opinion of the abstractor that the evidence for this conclusion is insecure, first, because of the fact that the published curves fail to show any marked difference in action between the placental extracts and those obtained from the liver and pituitary, and in the second place, since it is distinctly stated that the extract of a freshly delivered placenta is completely inactive, the active extracts having been obtained from the so-called "ripe" material.—F. S. H.

(PROSTATE) Action of extracts of hypertrophied prostate on the bladder (Action des extraits de prostate hypertrophiée sur la vessie). DuBois (Ch.) and Boulet (L.), C. R. Soc. de Biol. (Paris), 1919, **82**, 1054-1055.

The intravenous injection of extracts of normal prostate causes a contraction of the bladder. Extracts of hypertrophied human prostate have no such effect in most cases. Positive results are occasionally obtained, but it is due to the presence of normal tissue in the hypertrophied gland. The retention of urine in subjects of hypertrophied prostate is due to the fact that the gland no longer furnishes the internal secretion which is the excitant of the vesical muscles. The return of micturition after prostatectomy is due to the removal of the growth which has obstructed the normal function of the gland, allowing it to recover its functional activity.—T. C. B.

(PROSTATE TESTES) Organotherapy in prostatism (Organotherapie des Prostatismus). Rohleder. Deutsche med. Wchnschr. (Berlin), 1920, **46**, 70.

Not only is it generally accepted that the prostate has an internal secretion, but it is usually acknowledged that there is a relationship between the secretion of this gland and the internal secretion of the testicle. This conception is derived from the fact that castration is followed by atrophy of the prostate and that hypertrophy of the prostate generally begins to appear when the sexual desires begin to diminish. It has already been shown that when dogs are castrated and extracts of the testicles injected there fails to occur any atrophy of the prostate (Walker). This affords valuable indications for treatment. In the

first and second stages of hypertrophy of the prostate the administration of testicular preparations by mouth may have a temporary good effect, but in the last stage no beneficial results are obtained. The author advises the implantation of fresh human testicles into individuals suffering from hypertrophy of the prostate, although he himself has never performed the operation.—J. K.

SCLERODERMA, Two cases of—with sclerodctylia (Due casi di sclerodermia e sclerodattilia). Capezzuoli (Cesare), Rivista critica di Clinica Medica, 1919, .., 577-593.

The A. reports two cases of scleroderma with sclerodactylia, one complicated with Raynaud syndrome. Both cases had tuberculosis in their parental anamnesis; neither of them showed any thyroid or thymus disorder, but in both slight adrenal deficiency was apparent with, in one case, marked melanoderma. There was no alimentary glycosuria and no adrenal glycosuria could be obtained.—G. V.

SCLERODERMA, The relations between—and diseases of the endoctrine organs (Über die Beziehungen der Sklerodermie zu den Erkrankungen der endokrinen Drüsen). Roesch (W.), Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1329.

Scleroderma is a symptom of polyglandular insufficiency. In the case described by the author, there were symptoms of adrenal and thyroid insufficiency. —J. K.

(SECRETIN) On the influence of atropine on the secretion of pancreatic juice. Savich (V. V.), J. russe de physiol., 1917-1918, **1**, 134-140.

The secretory effect of soap and fats on the pancreas is rapidly inhibited by atropine, if used in acute experiments, but not in animals with permanent pancreatic fistulæ; this difference is explained by the difference of method of administration of the drug in these cases, intravenously or subcutaneously—i. e., it depends upon the quantity of poison which reaches the secreting cells. The secretory effect of soap is thus under the influence, not only of a nervous mechanism, but also of a humoral one. On the other hand, the author is inclined to believe that some hormone, perhaps secretin, is produced in the duodenum, under the stimulation of the secretory nerves of the pancreas.—Physiol. Abst. 4, 391.

(SEX) Intersexuality and hermaphroditism in man (Die biologischen Grundlage der konträren Sexualität und des Her-

maphroditismus beim Menschen). Goldschmidt (R.), Arch. f. Rassen-u-Gesell. Biol. (Berlin), 1916, **12,** 1.

The author discusses the biological foundation for the existence of individuals who are neither truly males nor females, but have certain primary and secondary characters of either sex.

He has shown by his studies in genetics on certain insects, that it is possible to produce, experimentally, every grade of intersexuality from the male to the female, not only in external body form but also in the internal organs. (See Endocrinology 1917, **1,** 433.) The experimental animals showed also, all grades of instincts and habits between the extremes of the two sexes. He points out that no animal, including the human, is either purely male or female, but each has the potentialities of both. Usually, of course, the one sex or the other predominates, but either sex may normally show secondary characters of the other. Animals of either sex will take on characters of the other following castration or transplantation of gonads (Steinach).

Hermaphrodites, pseudohermaphrodites and many persons considered sexually abnormal are simply sexual intergrades, and therefore not pathological, but simply natural variations, the result of the chromosome complex, and perhaps partly of abnormal internal secretions of the gonads. (Lillie has shown that the free-martin is a sex intergrade caused by male hormones, acting through the placental circulation, on a female fetus. J. Exp. Zool., 1917, 23, 371.)

Goldschmidt believes that these human sex intergrades are not degenerates, since 50 per cent of them are found in sound families, but that they are the natural result of crossed matings of people of different genetic constitution. The number of "contrary sexuals" is much greater in these peoples than where the race is pure.

There are psychic as well as physical sex intergrades.

The author suggests that intersexuals (individuals with characters of both sexes) be treated with gonad extracts or transplants.

This paper affords a possible answer to those who blame the thymus for the appearance of secondary sex characters of the opposite sex in cases of so-called "status thymicus," and especially in the "recessive" cases of Symmers wherein, so far as can be demonstrated microscopically or otherwise, the thymus is perfectly normal or even atrophic, and probably entirely blameless of the condition obtaining.—E. R. H.

SEX, The determination of—. McConnel (Mrs. D.), Med. Press (Lond.), 1918, n. s. **106,** 27-29.

Not of endocrine interest.—L. G. K.

(SKIN) On a protective function of the skin (Ueber eine nach innen gerichtete Schutzfunktion der Hant). Hoffmann (E.), Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1233.

The author does not believe that the function of the skin is only a mechanical one. It is known that the skin is able to produce an enzyme ("dop-aoxydase") that is required for the formation of pigment. It is also generally accepted that infectious diseases with well developed symptoms of the skin (syphilis, scarlatina, typhus exanthematicus) have a better prognosis than when the eruption is not well developed. The irritation of the skin seems to have a favorable influence on the resistance of the body. Therefore the author thinks that it may be possible that the skin has an internal secretion. Stimulation of the production of this internal secretion may have an influence on other diseases of the organism. In this way it is perhaps possible to explain the splendid effect of light-therapy, of artificial "sunlight," and other therapeutic procedures directed toward internal diseases in patients who have skin affections.—J. K.

SPLEEN, Effects of the removal of the—upon the metabolism in dogs. Preliminary report. King (J. H.), Johns Hopk. Hosp. Rep. (Balt.), 1919, **18**, 7-9. For abstract of earlier report see Endocrin. **3**, 226.

Metabolic studies were made on dogs before and after splenectomy. Metabolic processes were in general little affected. After the operation, however, there was observed an increase in the fat and cholestrin of the blood, together with increased absorption of fats and increased elimination of fatty acids. The blood thereby acquired an increased efficiency against hemolytic agents, a fact which probably explains to some extent the efficacy of splenectomy in the treatment of hemolytic types of anemia. An increased elimination of calcium was noted which, it is suggested, may stand in some causal relation to the clinical tendency of these cases to hemorrhage. The calcium disturbance, however, can hardly be considered of moment because it was found that it was not sufficient to interfere with the skeletal development of puppies after the operation. The studies as a whole fail to bring to light any group of findings which can be correlated into a clinical symptom complex dependent upon a loss of function of the spleen. A detailed report is promised at an early date.—R. G. H.

SPLEEN, The importance of the—in resistance to infection. Morris (D. H.) and Bullock (F. D.), Annals of Surgery, 1919, **70**, 513.

An experimental study of the problem, which is more of immunological than endocrine interest. The experiments involved 392 rats. One-half of these were splenectomized and one-half were subjected to a laparotomy and the removal of one testicle. This operation was selected as furnishing a fair basis of comparison. The operations were done under ether and every precaution taken to guard against operative complications. The animals were all exposed to chance laboratory contagion and kept under observation for several months. The results show in a very definite manner that, while the animals may get on fairly well without a spleen in the absence of any infection, the reverse is true when the organism is put to the strain of resisting acute bacterial invasion. The death rate among the splenectomized rats was 80.5% as compared with 38.9% among the controls during the time they were under observation.—J. F.

STATUS LYMPHATICUS, Its occurrence and significance in war neurosis. Davis (T. K.), Arch. Neurol. & Psych. (Chgo.), 1919, **2**, 414-418.

The author studied two groups of soldiers (114 psychoneurotics, and 119 surgical cases) all of whom had seen front line duty. The term status lymphaticus was applied in this series of cases to the soldiers showing bodily hypotrichosis in contrast to abundant scalp hair, feminine type of pubic hair, a velvety skin, a tendency toward abnormal length and narrowness of the thorax, and slenderness of the long bones. Of the 114 psychoneurotic cases 23.68% were of this status type, and among the surgical cases only 12.6% showed this syndrome. Davis concludes that an endocrine abnormality (status lymphaticus) increases the susceptibility to the neurosis. (See Endocrin. 3, 209.)—F. C. P.

(SYMPATHETIC N. S.) "Trichotonia" and "trichographism": a new sign of hyperirritability of the sympathetic (Tricotonia e tricografismo: un nuovo segno d'ipereccitabilitá sympatica). Pende (N.), Gazz. Ospedali Clin. (Milan), 1917, —, — (No. 60). Abst. Riv. Patol, Nerv. e ment, **22**, 998.

Pende has applied the term "Trichographism," to the phenomenon commonly known as "goose-flesh," when it is caused, not by cold, but by mechanical irritation. The phenomenon is due to the contraction of the musculi arrectores pilorum which are under control of the sympathetic nervous system. When the sympathetic system is hyperirritable, stroking the skin along the sternum or mammary region with a blunt point sets up local reflexes and causes the "goose-flesh" to appear as a zone of closely placed elevations in the path of the stroke. The re-

action signifies a condition of augmented activity of the muscles concerned, hence "trichotonia." The phenomenon is seen especially in conditions of hyperthyroidism and may be regarded as a special manifestation of "sypathicotonia."—R. G. H.

(TESTES) Operation for cryptorchism (Zur Operation der Kryptorchismus). Frangenheim (G.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 173.

Of technical surgical interest.—J. K.

(TESTES) Demonstration of the appearance after castration of chick feathering in a hen feathered cockerel. Morgan (T. H.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1916, **13**, 31.

In Seabright fowls the cocks normally have "hen feathering," i. e., the hackles and saddle feathers are similar to those of the female. If the male adult is castrated and the saddle feathers removed those which grow in are more nearly of the masculine type. There is reason to believe that cock feathering is the fundamental tendency of both sexes but that normally this is inhibited in females by hormones from the ovaries. Morgan suggests that in the Seabright variety a similar inhibitory influence emanates to some extent from the testes, also.
—R. G. H.

(TESTES, ADRENAL) Normal and morbid conditions of the testes from birth to old age in one hundred asylum and hospital cases. Mott (F. W.), Brit. Med. J. (Lond.), 1919, (ii), 655-659, 696-700, and 737-742.

The testes were examined in 100 subjects who had died in asylums and hospitals at all ages from birth to 86 years. The contents of the vesiculae seminales were examined in a majority of the cases and in a few, the thyroid, suprarenal and pituitary glands also.

The study showed that at birth there is a large amount of interstitial tissue between the seminiferous tubules; the interstitial cells of Leydig are numerous and have the appearance of a gland; these cells contain a lipochrome substance like lutein and lipoid granules. At four months the tubules have doubled in size, the interstitial cells are hardly visible and no lipoid granules are seen. At eleven years there is little change in the size of the tubules and the interstitial cells are only discernible with an oil-immersion lens. Little or no interstitial lipoid is seen. There is commencing evidence of nuclear activity and karyokinetic figures, but no spermatids nor spermatozoa. At 15 (puberty) the tubules are closely approximated and all stages of active spermatogenesis are observable. There is abundant in-

terstitial lipoid and lipoid granules are seen in the cells of Sertoli, though not so abundant as in the adult.

Cases dying before puberty of chronic diseases (tuberculosis, congenital syphilis and morbus cordis) show complete arrest of development of the seminiferous tubules. This seems to confirm Kyrle's view that arrested development of the seminiferous tubules is a sign of deficient vital resistance to disease.

Normal spermatogenesis was studied in cases of death following injury. Active spermatogenesis is seen in all stages; the interstitial cells contain much lipoid, and the spermatogonia, and especially the Sertoli cells, are filled with fine lipoid granules. Where there are sheaves of spermatozoa these granules in the Sertoli cells are fewer. The immature sperms dive into the Sertoli cells and there acquire their tails, which consist almost entirely of lipoid, lecithin and some cholesterin.

Evidence is given to show that the lipoid granules seen in the interstitial tissue and in the cells lining the basement membrane of the tubules constitute the raw material from which the nucleic acid, necessary for active nuclear proliferation and spermatogenesis, is formed. These lipoid granules give the oxidase reaction owing to the presence of traces of unsaturated fatty acid. Decomposition and recomposition processes are brought about by catalytic action of the iron of the cell nucleus upon the oxidase, causing molecular oxygen (O_2) to be converted into free atomic oxygen O-O on the surface of the granules.

Reasons are given for supposing that these lipoid granules are derived from the lipoid store in the adrenal cortex. Elliot's work, showing that the lipoid content of the cells of the adrenal cortex is diminished in microbial intoxication, is confirmed. However much it is diminished on this account, the lipoid granules in the testes are not appreciably so. This may explain the fact that prolonged microbial toxemia does not arrest spermatogenesis. It seems as if the lipoid substance in the testes acted not only as the phosphorized raw material of nuclear activity, but as a protective barrier against the effects of circulating microbial poisons.

The remainder of this series of papers deals with changes in the testes in cases of general paralysis, dementia precox and other forms of insanity. In general no correlation between psychoses and testicular conditions could be determined.—L. G. K.

(TESTES) Growth of testicular grafts in the goat (Evolution des greffes testiculaires sur le bouc). Growth of testicular grafts in the ram (Evolution des greffes testiculaires du belier). The testicles in the aged (Testicules des vieillards). The conditions which cause variations in the growth of the testicular epithelium (Des conditions qui font varier l'evolution de l'epithelium testiculaire). Retterer (Ed.), C. R. Soc.

Biol. (Paris), 1919, **82**, 1022-1025, 1099-1102, 1123-1126, 1153-1156.

These papers deal with the histological changes in the testes and testicular grafts under various conditions. The general conclusion seems to be that when the epithelial cells of the tubules are transformed into connective tissue, they lose a plasma, which, when resorbed determines the secondary sex characters. —T. C. B.

(TESTICLE) Geroderma genito-dystrophico (lean type) with delayed hereditary lues [Geroderma (Senilismo) génito distrófico de Rummo y Ferrarini (tipo magro), por lues hereditaria tardía]. Castex (M. R.) and Waldorf (C. P.), Rev. Assoc. Med. Argentina, 1919, —, 177-178 (Aug.-Sept.).

A typical case is described to which the authors attribute a syphilitic origin (hereditary). A bit of testicle removed for examination showed marked sclerosis with disappearance of the glandular elements.—B. A. H.

(TESTIS) Transplantation of testicle in man (Über Hodenimplantation beim Menschen). Kreuter (E.), Zentralbl. f. Chir. (Leipzig), 1919, **46**, 954.

The removal of tubercular testicles was followed by a loss of sexual desire which reappeared after the implantation of a normal testicle. The desire was accompanied by the ability to have erections.—J. K.

TESTICLE Implantation. Voncken (S.), Archives Médicales Belges (Brussels), 1919, **72**, 64.

Voncken reviews what has been accomplished in this line, citing Lydston's work and Steinach's experimental research, the clinical case reported by Steinach and Lichtenstern and Rohleder's experimental and clinical experiences with treatment of homosexual perversions. He then describes Voronoff's "painstaking experimental research carried on for more than a year at the College de France. He studied on sheep and goats the influence of transplantation of testicle tissue. He found it easy to follow by the external manifestations the changes in the functioning of the internal secretion of the testicles." Castration of a young goat arrested the development of the horns. He conducted three series of experiments: In the first series, testicle implantation in the young castrated animals restored in a short time their normal vigor. The growth of the horns, arrested by the castration, began anew as soon as the implant had grown into intimate connection with the adjacent tissues. In his sec-

ond series of experiments implantation of testicle tissue in females transformed their character: Gravid goats were delivered normally, but they exhibited marked repulsion for suckling their young and other maternal cares. The testicle implant seemed to stifle all the instincts of maternal affection. In his third set of experiments, he implanted the testicle tissue in rams and goats 14 to 15 years old. This age in these animals corresponds to the human age of 65 to 70. The senile animals, with sluggish reactions, underwent a radical transformation within periods ranging from a few days to three weeks after the implantation of the testicle graft. Voncken emphasizes that the photographs which Voronoff exhibited with his report at the recent Congrès de chirurgie at Paris testified most significantly to the truth of his statements. One of the goat bucks impregnated a female.

"Counter experiences were equally significant," he adds, "removal of the graft reducing the animal to his former senile condition. A new implantation restored anew les avantages de la jeunesse." In view of such an ensemble of facts," Voncken comments, "can one doubt further the preponderant influence of the internal secretions of the testicle on senile phenomena?" He adds that Voronoff's histologic study of the grafts showed that the vessels growing into the graft do not reach the center in time to perpetuate its vitality. The center dies and is resorbed; only the periphery retains its vitality. Hence small grafts take better than large ones. He only succeeded in keeping two alive out of thirty whole testicles implanted, while the partial grafts were constantly successful. A number of small grafts can be implanted under the skin in any part of the body, or in the peritoneal cavity, or under the vaginalis in the scrotum. He found this latter technic the most reliable. Voncken adds that Lydston's experience has given a practical confirmation of the experimental results thus realized in the laboratory. "Organotherapy is invading more and more the different chapters of pathology, and this surgical opotherapy seems to augur a fruitful future which is only the natural sequence of the marvelous results already realized with transfusion of blood." He suggests the possibility that grafts of thyroid tissue might be used in treatment of cretinism. "With any endocrine insufficiency, some harmless surgical intervention might definitely restore the organic balance." (Voronoff's report of improvement in a case of myxedema after implantation of monkey thyroid tissue was summarized in J. Am. M. Assn., 1914, **63**, 810. (Abst. J. Am. M. Ass., **74**, 62.

(TESTIS) Mitoses of seminal epithelium in the cat (Les mitoses de l'épithélium séminal du chat). de Winiwarter (H.), Arch. de Biol., 1919, **30**, 1.

A cytological study of spermatogenesis in the cat, together with a short description of the interstitial cells. These latter are said to resemble those of the ovary in the cat. They contain lipoid droplets and some small bodies which stain readily with safranine, the number of two kinds of bodies varying inversely with each other in different cells, and hence the author believes it possible that the lipoid is formed from the other body as has been described for sebaceous cells. He found a few examples of mitoses among these interstitial cells, the number of chromosomes being about 35. These mitoses prove that the interstitial cells are able to multiply as in the ovary, but the rarity of mitoses indicates that some of the cells are transformed from the stroma.—E. R. H.

(TESTIS) Orchidopexy for inguinal testicle (Zur Orchidopexie bei Leistenhoden). Glass (E.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 174.

Of technical surgical interest.—J. K.

(TETANY) Edema in children with tetany (Oedembildung bei tetaniekranken Kindern). Bossert, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 45.

Evidence is presented tending to show that in tetany a low salt diet may produce edema. The eating of porridge with an egg gave rise to tetanic contractions and edema.—J. K.

(THYMUS) Certain peculiarities of thymus development (A proposito di alcune particolaritá di svilluppo del timo, in Amia calva e Lepidosteus osseus). Castellaneta (V.), Arch. ital. Anat. e. Embryol. (Firenze), 1917, **15**, 218.

A discussion of the development of the thymus in these bony fishes. In the case of Amia, Castellaneta agrees with Hammar that the original epithelium forms a reticulum not spontaneously, as Hammar says, but as the result of mechanical forces, as stated by Maximow. At the time of the early reticulum transformation there are present a few lymphocytes and large numbers come into the gland coincident with its later formation.

It is decided that some of the small lymphocytes are formed in the thymus from larger cells, but that most of them come in from the mesenchyma. The thymus of ganoids is regarded as a phylogenetic descendent of several primitive thymic anlagen fused together.—M. M. H.

(THYMUS) Les réversions épithéliales dans le thymus humain. Dustin (A. P.), Arch. Zool. expér. et gén. (Paris), 1917, **56**, 73-87.

The author describes some small bodies of cells often found in the thymus of mammals, birds, reptiles and amphibians, and which represent a reversion to the original epithelial type. These bodies sometimes are cystic and lined with ciliated epithelium, and sometimes are compacted, resembling parathyroid tissue.

In many they become more numerous in older persons in whom the thymus has undergone involution.

As regards the various cells found, the author disagrees with Hammar, who believes that the original embryonic thymus (epithelium) forms the reticular cells of the adult which in turn give rise to all the atypical thymus elements,—epithelial nodules, ciliated cysts, Hassl's corpuscles, epithelioid cells, myoid cells and mucous cells,—and that the small thymus cells which are true lymphocytes enter the thymus from the outside. Dustin believes that the small thymic cells are derived directly from the original epithelium (stem cells) and that the epithelioid cells and Hassl's corpuscles are mesenchymal in origin. He holds that the thymus is in some manner associated with nuclein metabolism, acting as a sort of storehouse for nuclein substance.

—E. R. H.

THYMUS and tetany. Honeyman (J. T.), J. Physiol. (Lond.), 1919, **53**, 207-210.

Observations on young guinea pigs in which the thymus is functionally active, show that when the thymus and parathyroids are both removed, typical parathyreoprival tetany develops, with increased electrical excitability. The author believes that this disproves Uhlenhuth's claim that the thymus secretes a substance capable of producing tetany.—T. C. B.

(THYMUS) Pathology of Graves' disease (Die pathologischen Grundlagen der Basedowschen Krankheit. Nach vergleichende pathologischen und klinischen Studien). Klose (H.), Bruns. Beitr. z. Anat. Phys. Path. usw., 1916, **102**, —. (Abstract in Folia Hematol. by Müller.)

The author says that in Basedow's disease the thymus is next to the thyroid in importance, in that it undergoes morphological changes ("epithelization"). The thymus can "thymusize" the thyroid. The two glands can cause a general hyperplasia of the lymphoid system.—E. R. H.

THYMUS, Involution of the—in birds. McCarrison (Robert), Indian J. Med. Res. (Calcutta), 1919, **6**, 557-559.

McCarrison studied the thymus in a large number of pigeons, varying in age from sixty-one days to two years, to determine the relationship of the size of the gland to the age and sex

of the bird and also to the body weight under different conditions. The following facts were elicited: The thymus is twice as large in the male as in the female. In the pigeon the involution of the thymus is dependent upon factors other than the maturation of the sexual functions. These factors are mainly nutritional. Starvation causes thymic atrophy out of all proportion to loss of body weight. Deprivation of "B" accessory food factors causes a like atrophy which is marked. Excessive feeding with grains and butter causes no increase in size in the thymus as it does in most of the other organs.—I. M.

(THYMUS) Case of enlarged thymus gland and some remarks on status lymphaticus. Newton (R. C.), Am. J. Med. Sc. (Phila.), 1919, **158**, 534-544.

A man of 20 years complained of lassitude and dyspnea beginning two weeks after a cold plunge when overheated. Muscular weakness progressed, soft edema of the neck, chest and shoulders developed. Examination revealed a double cardiac murmur. A skiagram showed the presence of a thymic shadow nearly covering the pericardium. Six X-ray treatments at weekly intervals resulted in the patient's return to work and in his resuming his active athletic life. One year later a run of about one mile resulted in the return of his former symptoms and the development of an aortic aneurysm. A rupture of the aneurysm about a year after this time caused his death. No autopsy could be obtained. The case report is followed by a brief summary of the literature on the anatomy, the growth and involution, the physiology, and the pathology of the thymus gland and status lymphaticus.—F. C. P.

(THYMUS THYROID) Extirpation of the thymus in Graves' disease (Thymusexstirpation bei Basedowscher Krankheit). Nordmann, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 109.

The partial resection of the thyroid and the removal of the thymus in a girl of 20 years having suffered for 3 years from Graves' disease, resulted in a general improvement, although the tachycardia remained. The author believes that it is necessary in every operation for Graves' disease to look for the thymus. In cases with symptoms of status lymphaticus or hypoplasia of the sex organs the thymus should first be removed before anything is done with the thyroid. In 11 fatal cases of thyroidectomy there was found a persistent and enlarged thymus. In one other case in which thyroidectomy only was performed, the symptoms of the disorder did not subside and the patient died some time later. At autopsy the thymus was found present.

—J. K.

(THYMUS) Thymusectomy and its relationship to rickets. Renton (J. Mill) and Robertson (Madge E.), J. Path & Bact. (Cambridge), 1916-17, **21,** 1-13.

The claims of Klose and Vogt and of Matti that extirpation of the thymus gland in puppies leads to a sydrome somewhat resembling rickets, but associated also with other growth and psychic abnormalities, have had wide publicity. That these claims have failed of confirmation at the hands of various competent observers seems less generally known. The authors report an attempt to confirm the earlier findings. The thymus was completely removed from 8 puppies from 13 to 25 days old. These were kept for varying periods up to several months. The experiments were controlled by keeping other dogs under the same environmental conditions. It was found that there was not the slightest effect ascribable to the loss of the thymus. Unfavorable environmental conditions alone were found to produce ricketslike changes such as were described by the earlier investigators, and it was concluded that such was the probable source of these changes.—R. G. H.

(THYMUS) Myasthenia gravis pseudoparalytica. Steckelmacher, Münch. med. Wchnschr. (Munich), 1919, **66,** 1504.

In the case described no persistent thymus was found. —J. K.

THYMUS gland in infants, Normal and pathological anatomy of the—. Vasyutochkin (A. M.), Kharkov Med. J., 1916, **22,** 160, 215.

V. summarizes his extensive data on the weight of the thymus glands of infants in health and disease. During the first year of post-natal life the thymus increases in weight uninterruptedly from 7 to 12 grams. The weight of the thymus of males is greater than that of females. The weight of the thymus of well nourished infants exceeds by 1½ times the weight of the gland of emaciated infants. Inherited syphilis in most cases produces a sharp atrophy of the thymus. Gastro-intestinal diseases produce a hyperplasia of the thymus. Diseases of the respiratory system (non-tuberculous) produce no change in the weight of the thymus other than a decrease corresponding to the disturbance in nutrition. Similarly there is no effect on the thymus in septic cases. In tuberculosis and diphtheria the weight of the thymus is diminished; but only a few of these cases were investigated.—S. H.

The THYMUS; a summary. Wooley (P. G.), J. Lab. & Clin. Med. (St. Louis), 1916-17, **2,** 632-637.

A general article giving an interesting review of the literature on the physiology and functional pathology of the thymus. —R. G. H.

(THYROID) Considerations in the medical treatment of goitre. Anders (J. M.), Trans. Am. Therap. Soc. (N. Y.), 1916, **16,** 85-90.

A brief summary of the kind of treatment best suited to the various types and stages of thyroid disorder. Emphasis is laid upon the necessity for differentiating these factors. For definite hypothyroidism sodium iodide in gradually ascending doses, beginning with five grains three times a day, up to a maximum of ten grain doses is recommended. When gastro-intestinal fermentation is an accompaniment, thyroid extract is indicated in beginning doses of one grain, three times a day, to be slowly increased if the pulse reaction is not noticeably affected, up to a maximum of five grains daily. In general this treatment is contraindicated in Graves' disease. In the latter, the problem is to remove, as far as possible, the recognizable causes, such as emotional excitement, shocks, tuberculosis, rheumatism, syphilis and intoxication from the intestinal canal. Quinine hydrobromide and antithyroidin have given good results in the author's hands.—F. S. H.

(THYROID) Blepharochalasis with goiter and doubling of the mucous membrane of the upper lip (Blepharochalasis mit Struma und Schleimhautduplicatur der Überlippe). Ascher, Münch. med. Wchnschr. (Munich), 1919, **66,** 1365; Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1400; Wiener klin. Wchnschr. (Vienna), 1920, **33,** 73.

The author reports having sometimes seen the combination of the three conditions mentioned in the title. This combination has never previously been described and he considers it a sign of an abnormally functioning thyroid.—J. K.

(THYROID) The treatment of toxic goiter. Batchelor (F. S.), N. Zealand Med. J. (Wellington), 1918, **17,** 214-218.

Surgical treatment, either ligation or excision, is recommended for these cases.—F. S. H.

(THYROID) The development of Basedow's disease as an increasing cause of post-war female sterility (L'accroisement d'une cause de sterilité feminine depuis la guerre par la developpement de la maladie de Basedow). Blondel (R.), Bull. gen. therap. (Paris), 1919, **170,** 816-823.

The text of the argument lies in the author's observations that Basedow's disease is commonly accompanied by a marked diminution in the size of the uterus which he considers clearly attributable to disordered thyroid and that such atrophic uteri tend toward sterility. Therefore, since emotional shock or stress is admitted as one of the possible causes of thyroid disorder, and since women are notably emotionally unstable, the sequence of war, emotions, Basedow's disease and small uteri will tend to result in an increased sterility among the females of France.
—F. S. H.

(THYROID) Long-standing case of goitre cured by inunctions. Bazett (Henry), The Practitioner (Lond.), 1919, **103**, 389-390.

A typical case of exophthalmic goitre with advanced symptoms was apparently cured by inunctions of the following fomula:

Glyc. Belladonnae	1 part
Ung. Iodi	2 parts
Ung. Hydrarg. Co.	4 parts
Ung. Plumbi Subacet.	6 parts

15 m. Donovan's solution were given internally over part of the period of treatment. One lobe of a large firm goitre had been removed at a previous operation which had caused only a temporary relief from the tachycardia, tremor and exophthalmos. Twenty days of the above treatment caused a marked improvement in the symptoms and a very noticeable dimunition in the size of the tumor. One year later there were remaining no signs or symptoms of the disease. The author claims several other cures on less difficult cases.—I. M.

(THYROID) The treatment of goitre by radiation. Boggs (R. H.), Am. J. Roentgenol., 1919, **6**, 613-624.

A restatement of the indications and contraindications for the roentgen or radium treatment of goitre.—J. F.

(THYROID) An address on goitre. Boyd (H. J.), Brit. Med. J. (Lond.), 1919 (ii), 169-170.

According to the author's observations goitre was almost unknown 25 years ago in the section of Ireland in which he is practicing, but at present is extremely common. The water supply apparently had some connection with a number of the cases, since a change caused a decrease in size or disappearance of the goitres. Also when several people in one house were affected, the one who drank the most water was observed generally to possess the largest goitre. Some who drank nothing but boiled

water in the form of tea, etc., were also affected. Water from one well was found to be infested with micro-organisms similar to those described by McCarrison as a cause of goitre.—L. G. K.

(THYROID) Suppurating thyroid: complication of blenorrhagia. (Thyroidite suppurée: complication de la blenorragie). Buscarlet (F.), Bull. mem. Soc. de Chir. (Paris), 1917, **43**, 2286-2288.

A detailed clinical report of progress and treatment of a case of septicemia of blenorrhagic origin which terminated in recovery after discharge of contents of a thyroidal abscess. —F. S. H.

(THYROID) Further course of an interesting case of Flajani-Basedow's disease (Ulteriore decorso di un interessante caso di morbo di Flajani-Basedow). Capezzuoli (Cesare), Riv. Critica di Clin. Med., 1919, **20**, 469.

The author reports a case which he has followed since 1913, when the patient was 35. After a partial thyroidectomy in 1915, she improved and was almost well until the fall of 1916, when a psychic trauma started the syndrome again with considerable swelling of the residual thyroid. Besides nervous and digestive symptoms, tetany developed. Improved, yet not cured, she went back home and married. After the marriage there was a considerable improvement of all her symptoms, which remained favorable despite a confinement in August, 1917. She then lost her husband, and felt very low in spirit, yet there was no recrudescence of the Basedow symptoms, and the thyroid remained small.

The author emphasizes the fact that in this case marriage, pregnancy and nursing, instead of bringing back the symptoms seem to have favored recovery. Even her character, which had been, during the sickness, changeable and intolerant, underwent a complete modification, becoming calm and steady.—G. V.

(THYROID) The facilitation of difficult strumectomy (Erleichterung schwieriger Strumectomien). Claessen (M.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 9.

Of technical surgical interest.—J. K.

(THYROID) Consideration of the surgical treatment of exophthalmic goiter. Clark (P. S.), Clinique (Chgo.), 1917, **38**, 227-231.

A brief review in which because of the low mortality of 4% or less, and the high percentage of cures or improvement after

operation, the author strongly advocates surgical interference in cases of exophthalmic goiter.—F. S. H.

(THYROID) A case of exophthalmic goitre and anoci-association. Corner (Edred), Brit. J. Surg. (Bristol), 1916, **3**, 568-569.

The operation for removal of a hyperplastic thyroid was modified by Corner by the introduction of Crile's principle of anoci-association. As a preparatory measure the skin surface over the gland was painted with picric acid solution. Three days later thyroidectomy was performed under nitrous oxide anesthesia. Quinine-urea hydrochloride solution was injected into the subcutaneous tissues before these were incised and then into the tissues surrounding the thyroid itself before it was removed. Recovery with marked improvement in the symptoms was very prompt and satisfactory.—I. M.

(THYROID) Medical treatment of exophthalmic goitre (Tratamiento médico del bocio exoftálmico). Dominguez (C.), Rev. Assoc. Méd. Argentina (Buenos Aires), 1919, **31**, 370-374.

A general discussion of the dietary, medical, and surgical treatment of exophthalmic goitre. Although medication produces amelioration in the majority of cases it is rare that a cure is obtained.—B. A. H.

(THYROID) The medico-legal significance of trauma as an etiologic factor in Basedow's disease (Graves' disease, exophthalmic goiter). Drysdale (H. H.), Ohio State Med. J. (Columbus), 1917, **13**, 310-316.

This paper presents the case reports of four litigants out of a total of thirteen, all of whom were seeking financial recompense for disabilities and ill health alleged to have resulted from trauma, who were found to be afflicted with exophthalmic goiter. The author is of the opinion that although the disease was alleged to have been caused by trauma, there is conclusive evidence that there was in these cases an inherent predisposition to the malady. It is Drysdale's opinion that the degree of physical violence had little, if any, significance, and whatever harm was done in this respect arose from shock and emotional stress acting through an unstable nervous and psychic constitution. Trauma then becomes only an exciting factor in the etiology.
—F. S. H.

(THYROID) The constitutional disturbances which come with chronic goiter. Dowd (C. N.), J. Am. Assn. (Chgo.), 1917, **69**, 614-619.

The paper is a report of 37 cases of chronic goiter selected from a total of 181. The average duration of the goiter in the patients studied was ten years; the average duration of the more disturbing symptoms was one and one-tenth years. The surgical interference consisted in removing about two-thirds of the enlarged glands, the posterior capsules and adjacent gland tissue being regularly left in position. In one instance boiling water was injected with excellent results. In studying the later histories of this group of patients one has been observed fourteen years; one has been followed into the fifth year; five into the fourth; six into the third; twelve have been followed into the second year, and seven into the first. All made good recoveries from the operation. Twenty-seven are reported free from symptoms and in excellent health; eight are greatly improved; two, respectively, eleven and four months after their operation, are far from well. The constitutional disturbances have accordingly been largely relieved.—F. S. H.

(THYROID ADRENAL) Lymphatic tissue in the thyroid in Addison's disease (Über das Vorkommen lymphatischer Herde in der Schildrüse bei Morbus Addisonii). Dubois (M.), Berlin. klin. Wchnschr., 1919, **56,** 1178.

Large centers of lymphatic tissue may be observed in the thyroid in cases of Addison's disease. Apparently they are not caused by inflammation but by a chronic irritation of the thyroid gland following abnormal adrenal function. It is also possible that they are a manifestation of the status thymo-lymphaticus which is often present in this disorder.—J. K.

(THYROID) Skin complications in Graves' disease (Complications cutanees di la maladie de Basedow). du Castel (J.), Paris Médical, 1919, **31,** 382-385; Abst. from La Riforma medica, 1919, **35,** 509.

Numerous cutaneous complications are found in this syndrome, part of which the author claims to be common to all neuropathic conditions, some exclusively from dysfunction of the thyroid, and some from secondary endocrino-sympathetic conditions. He differentiates them into vasomotor, trophic, toxic and microbic. To the first division belong flushing, edema, and purpura; among the trophic manifestations are melanoderma, seldom vitilligo and scleroderma and alopecia. Burney Yeo has reported the case of a patient in whom, after hypertrophy of the right lobe of the thyroid, left exophthalmos and fall of the hair of the left eye-brow occurred and in whom, when the left lobe started to hypertrophy, analogous symptoms referable to the right eye appeared. Toxic erythema—especially urticaria—

is frequent; and according to some authors, furunculosis, pyodermatitis and eczema are connected with dysfunction of the thyroid, as is indicated by subsequent development of exophthalmic goitre in some patients with a tendency to recurring attacks of these maladies.—G. V.

(THYROID) Papilloma of the larynx. Report of a case treated with radium, with resultant chronic diffuse thyroditis. Duffy (Wm. C.), Johns Hopk. Hosp. Rep. (Balt.), 1919, **18**, 417-438.

A Negro boy, 3 years of age, was treated with radium for papilloma of the larynx. At autopsy there was found, among other pathologic conditions, a chronic diffuse thyroiditis of wide extent. The connective tissue was overgrown and had encircled the acini and even invaded them, causing involution. The fibrosis had spread through the gland capsule also and invaded surrounding parts. The acini were small for the most part and the epithelium mostly columnar or flat. Colloid was scanty. In many acini was seen faintly staining granular material regarded as representing much attenuated colloid. In acini of various sizes were seen groups of lining cells with both nucleus and cytoplasm poorly stained. In the thickened stroma were found occasional clumps of epithelial cells apparently residuals of destroyed acini. In numerous acini were seen groups of exfolliated epithelial cells the cytoplasm of which exhibited eosinophilic tendencies greater than normal. Red blood cells also were seen, but were regarded as normal. The resulting histologic picture was closely similar to that of "thyroiditis" as first described by Riedl in 1896.—R. G. H.

(THYROID) Experimental studies of Basedow's disease (Experimentelle Untersuchung der Basedow'schen Krankheit). Eiger, Cor.-Bl. f. Schweiz. Aerzte. (Basel), 1916, **46**, 1567-1568.

The author found that the feeding to rats of preparations of the thyroid gland caused flooding of the blood with the glandular products, which phenomenon can be utilized as a clinical-biological method of testing thyroidal activity. Correlated with this is the fact that the blood plasma of six cases of Basedow's disease enhanced the action of adrenalin, while the plasma from two cases of struma gave negative results. E. claims to have objectively proven the presence of the specific thyroid secretion in the blood of the vena thyroidea in man and animals, and is convinced that thyroid extracts enhance the automatic contraction and movement of the isolated intestine. Very strong doses of the extract inhibit the movements and bring the peristalsis to a standstill.—F. S. H.

(THYROID) Clinical forms of Basedow's disease (Formas clínicas de la enfemedad de Basedow). Escudero (P.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31**, 278-309.

Delimination and classification of the various clinical types of Basedow's disease.—B. A. H.

(THYROID) Surgical treatment of exopthalmic goiter (Tratamiento quirúrgico del bocio exoftálmico). Finochietto (R.), Rev. Assoc. Méd. Argentina (Buenos Aires) ,1919, **31**, 342-352.

A general discussion of the subject in which early surgical procedures are advocated.—B. A. H.

(THYROID) The surgery of thyrotoxicosis. Frank (L. W.), Kentucky Med. J. (Bowling Green), 1920, **18**, 10-15.

Toxic goiters should be immediately removed.—H. W.

(THYROID) The importance of the Basedow symptoms in the early diagnosis and treatment of pulmonary tuberculosis (L'importanza dei segni di Basedow nella diagnosi precoce e nella cura della tubercolosi polomonare). Gallotti (A.), Riforma medica (Naples), 1920, —, 88-92.

The author reports six cases of symptomatology of Basedow in incipient tuberculosis, where the first symptom, sometimes contemporary with and sometimes preceding the tuberculous symptoms, is enlargement of the thyroid. Such enlargement he considers as of toxic origin. Basedow symptoms may be regarded in many instances, as probable symptoms of latent pulmonary tuberculosis. Enlargement of the thyroid often appears as a complication in tuberculosis and gives to the disease a typical character with benign evolution. In cases of pulmonary tuberculosis with Basedowian complication the treatment of the thyroid gland may favorably influence the course of the pulmonary lesion, even to a full recovery.—G. V.

THYROID and acquired immunity. The influence of thyroidectomy (in the rabbit) upon the formation of heterohemolitic sensitizing substances [Thyroide et immunité acquise. Sur l'influence de la thyroidectomie (chez le lapin) sur la formation de sensibilisatrices hétérohemolytiques d'immunisation]. Garibaldi (A.), C. R. Soc. de Biol. (Paris), 1920, **83**, 15-16.

As the experimental results of Fjelstad, Launay and Levy-Bruhl and Frouin do not agree, the problem has been reinvestigated. This first note gives the results of thyroidectomy on the formation of hemolytic immune bodies. Rabbits were used: 4 thyroidectomised, and 3 controls in which the gland was laid

bare, but not touched. Protocols are given and the conclusion arrived at that the serum shows a hemolytic titer superior to that of the controls. Thyroidectomy seems to favor the formation of antibodies.—T. C. B.

(THYROID) Iodine action in goiter (Zur Joddarreichung bei Kropf). Grumme (D.), Cor. Bl. f. Schweiz. Aerzte (Basel), 1916, **46,** 494-499.

A review of the literature concerned with the mode of action and form of administration of iodine in goitrous conditions. —F. S. H.

THYROID, Observations on the—. Hagerty (J. F.), J. Med. Soc. New Jersey (Orange), 1917, **14,** 341-348.

A general review of the known data concerned with the diseases of the thyroid and their treatment.—F. S. H.

(THYROID) Etiology of Basedow's disease (Etiología de la enfermedad de Basedow). Hardoy (P. J.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31,** 228-236.

It is the opinion of the author that Basedow's disease arises in individuals constitutionally predisposed to the disorder. Among the etiological causes he has observed the presence of syphilis in 55 per cent of the cases and tuberculosis in 18 per cent.—B. A. H.

(THYROID) Operation for intrathoracic goiter (Zur Operation der intrathoracale Struma). Hartert (W.), Zentralbl. f. Chir. (Leipzig), 1919, **46,** 929.

Of technical surgical interest.—J. K.

The THYROID-PARATHYROID mechanism, The significance of—with special reference to its metabolic function. Hewitson (W. A.), Univ. Durham Coll. Med. Gaz. (Newcastle), 1916, **16,** 45-51.

A general review of the physiology and functional pathology of the glands mentioned.—R. G. H.

(THYROID) The treatment of thyrotoxicosis by means of roentgen ray. Holmes (G. W.) and Merrill (A. S.), J. Am. M. Assn. (Chgo.), 1919, **73,** 1693.

A report of a series of 152 toxic thyroid cases treated by x-ray. The authors believe that it is possible to decrease the

activity of the thyroid gland and probably to destroy its glandular structure by such treatment.—F. C. P.

(THYROID) Pathogenesis of Basedow's disease (Patogenia de la enfermedad de Basedow). Houssay (B. A.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31,** 237-277.

Detailed discussion of the present status of this problem.—B. A. H.

(THYROID) Chemical identification of the thyroid hormone. Kendall (E. C.), Scientific Proceedings, Am. Soc. Biol. Chem. XIII. J. Biol. Chem. (Baltimore), 1920, **41,** xxii.

A brief resume of the chemical nature of the iodine-containing compound of the thyroid which has been reported elsewhere in Endocrinology.—F. S. H.

(THYROID) "Funnel breast" in Graves' disease (Einzeihung des Brustkorbes bei Basedow). Just, Deutsche med. Wchnschr. (Berlin), 1919, **45,** 1373.

The author describes this as the second case he has seen of a retraction of the thorax in the region of the apex of the heart accompanying Graves' disease in a girl of 13. He suggests that this condition may perhaps be found somewhat frequently in this disease when occurring in children.—J. K.

(THYROID) The prevention of simple goiter in man. Kimball (O. P.), Rogoff (J. M.) and Marine (D.), J. Am. M. Assn. (Chgo.), 1919, **73,** 1873.

A report of the re-examination of girls (5th to 12th grade) in the public schools of Akron, Ohio, 19 months after the beginning of the prophylactic use of iodine. Tabulated reference is made to reports published in 1917 and 1918. The treatment consisted in giving 2 gms. of sodium iodide, in 0.2 gm. doses, for ten consecutive school days, repeated each autumn and spring in those taking the iodine. No enlargements, in previously normal cases, were seen, while 15.9% of those not taking the prophylactic treatment are reported as showing definite enlargement. A distinct decrease in size of the slightly enlarged glands was noted in 38.1% of the pupils using the iodine, while only 27.8% of those listed as not taking treatment showed this decrease in size. Similar therapeutic effects were noted in the cases classed as having moderate or marked enlargements of the thyroid gland.
—F. C. P.

(THYROID) The problem of the etiology and pathogenesis of endemic goiter and cretinism (El problema de la etiología

y patogenesis del bocio y cretinismo endémico). Kraus (R.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31**, 206-227. Rev. del Inst. Bact. del Dep. Nacional de Higiene (Buenos Aires), 1919, **2**, 309-323.

A discussion of the theory of the infectious origin of goiter. Goiter exists in the Argentine in the mountainous regions while the "Vinchuca" or triatoma infestans occurs on the plains. There is thus no relation between endemic goiter and Trypanosomiasis crusi.—B. A. H.

(THYROID) Dominant sex-linked inheritance and heredity of the Basedow's diathesis (Über dominant—geschlechtsbegrenzte Vererbung und die Erblichkeit der Basedowdiathesis). Lenz (F.), Arch. f. Rass. u. Gesellsch. Biol. (Berlin), 1918, **13**, 1.

The author points out the fact that many inherited defects such as color blindness, progressive muscular atrophy, inherited optic atrophy, some near-sightedness, some nystagmus, albinism of the eyes, etc., are sex linked characters dominant in males (heterozygotic), recessive in their daughters (homozygotic) and appear again in their grandsons, following the laws of genetics and easily explained. There are also sex-linked defects which appear dominant in females.

In his study Lenz included as of Basedow's diathesis (tendency toward goitre) patients with any or all of the following symptoms: classical syndrome (exophthalmos, tachycardia and struma), fine tremors of the fingers, temperature easily raised, moist glistening eyes, enlarged heart, dyspnoea, anxiety, insomnia, night sweats, troubled dreams, and general debility. He describes several families, following one for eight generations, in which there seems to be some evidence of hereditary tendency to goitre.—E. R. H.

THYROID, A consideration of the treatment of the disease of the—with special reference to so-called hyperthyroidism. Lichty (J. A.), Am. J. Roentgenol., 1919, **6**, 608-611.

This paper by an internist is a plea for the prompt employment of the proper treatment be it medical, surgical, or X-ray. The author has evolved a classification of goitre patients which has been very helpful to him as a working basis for the determination of the proper treatment in the individual. According to this plan, patients having diseases of the thyroid gland are divided into four groups:

I. Those patients with thyroid disturbances without any apparent pathological change in the gland. A study of the basal metabolism and possibly the ap-

plication of the Goetsch test may be necessary to confirm the diagnosis in the more doubtful cases. These are strictly medical cases.

II. Those patients having an enlargement of the thyroid, but in whom, from the age of the patient and the absence of certain symptoms, the diagnosis of adolescent goitre may be made. Such patients need only prophylactic care; if more than this is required they belong in the next group.

III. Those patients having an enlarged thyroid with definite hyperthyroidism active or at times potential. This enlargement may be due to Graves' disease, colloid goitre, cyst, adenoma, or any combination. This group may be medical for a while and later require surgical or x-ray treatment.

IV. Those patients having definite pathology of the gland with disturbances in function. This group includes neoplasms, simple colloid goitre, tuberculosis, lues, and other chronic infections of the gland. This group is always surgical, but presents an enticing field for investigation with the x-ray.

From the author's experience, he concludes that surgery has the larger field of application. It also has the advantage of furnishing definite information in that tissue removed may be studied. The earlier that hyperthyroidism is recognized, the more likely is medical treatment to be sufficient and give permanent results. In hyperthyroidism the roentgenologist and the surgeon can at best only break through a vicious circle for which the internist may or may not be responsible.—J. F.

(THYROID) Goiter and cretinism in the Argentine Republic (El bocio y el cretinismo en la Republica Argentina). Lozano (N.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31,** 169-205.

A general consideration of the distribution of this disorder in the Argentine Republic, following the various censuses. —B. A. H.

(THYROID) Goiter, Some surgical aspects of. Mann (A. T.), Journal-Lancet (Minneapolis), 1916, **36,** 703-706.

Thyroidectomy should not take place until the patient has given no response to medical treatment. This does not apply to a diseased tissue which causes constant autoactivation of the whole gland or marked pressure. As treatment, rest, the judicious use of iodine, antithyroid serum, the ligation of the blood vessels and nerves of the thyroid, and partial thyroidectomy,

each has its place according to the case in question. The author gives the technic of the larger operation, in which he puts emphasis on the care needed to prevent injury to nerves, to prevent the removal of the parathyroid and of the entire thyroid. —F. S. C.

(THYROID) The absorption of potassium iodide by perfused thyroid glands and some of the factors modifying it. Marine (David) and Feiss (H. O.), J. Pharm. & Exper. Therap. (Balt.), 1916, **7,** 557-576.

Experiments were conducted to determine whether the thyroid cells exhibit a specific affinity for iodine or not and to compare their activity along this line with that of other tissues. The thyroid gland, the spleen and the kidney were separately perfused both in vivo and in vitro with Ringer's solution containing KI. Hyperplastic glands of otherwise normal dogs were used in all cases. From their studies the authors draw the following conclusions: Artificially perfused thyroids take up and retain KI to the same extent as do in vivo-perfused thyroids. KI is not absorbed by the cells of the spleen, kidneys, liver or muscles. The amount of KI absorbed by the thyroid is independent of the concentration of KI in the perfusate. Only surviving glands exhibit the ability to take up the KI. KCN inhibits this activity. Small amounts of iodothyreoglobulin wash out during perfusion with defibrimated blood. Autolysing glands do not take up KI, but give up what was previously stored. The KI stored in surviving cells is pharmacologically inactive.—I. M.

(THYROID) Physio-therapeutic treatment of exopthalmic goiter (Tratamiento fisioterápico del bocio exoftálmico). Marque (A. M.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31,** 333-341.

A general discussion of the subject.—B. A. H.

(THYROID) Pathology and treatment of exophthalmic goiter (Le goitre exophthalmicque. Sa pathogénie. Son tratement). Masson (Guy), These, Geneva, 1918, pp. 172. Abst., J. Physiol. et de Pathol. Gén. (Paris), 1919, **18,** 638.

Masson treats in order the theories of the pathogenesis of exophthalmic goitre and various forms of therapy and follows this with a critique on both. He favors the dysthyroidism theory of pathogenesis. As to treatment, he recommends the serum of thyroidectomised animals, and even the milk of such has been found useful. In either case, however, adequate dosage and continuation for some time is needed. Such therapeutic measures

directed toward neutralization of circulating toxins might well be supplemented by radiotherapy to depress the activity of the thyroid. Surgery is reserved as a last resort for rebellious cases in which prompt measures are essential.—R. G. H.

(THYROID) The pathological physiology of human body temperature (Zur pathologische Physiologie der menschlichen Körperwärms). Mayer (A.), Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1382.

During the war the author observed a number of men with slightly enlarged thyroid glands and a slightly increased temperature, not caused by organic disease. The injection of milk raised the temperature of these patients, a reaction which does not occur in normal persons. The injection of antithyroidin caused the temperature to become normal. Apparently the endocrine organs play a most important part in the regulation of the temperature, since in normal persons the injection of adrenalin or thyroidin raises the temperature and antithyroidin diminishes it. These things are considered as important in the treatment of fever.—J. K.

(THYROID) The basal metabolism in exopthalmic goitre. Means (J. H.) and Aub (J. C.), Arch. Int. Med. (Chgo.), 1919, **24**, 645-677.

The results of the present work substantiate conclusions drawn in a previous paper (J. Am. M. Assn., 1917, **69**, 33). The discussion is based upon 345 observations on 130 patients. The degree of elevation of gas exchange above normal is used as a measurement of thyroid intoxication. Normal and pathological cases were used for controls. The studies were made upon cases of exophthalmic goitre treated either surgically or by exposure to roentgen-rays. The authors believe determinations of basal metabolism very important and valuable for purpose of differential diagnosis of obscure thyroid disease. The results are tabulated. The object of the experiments has been to determine the exact effect of roentgen-ray therapy and partial thyroidectomy in exophthalmic goitre, using the basal metabolism as an index of toxicity. Studies were made of the effect of rest, quinine hydrobromid, roentgen rays and of surgery.

It is the opinion of the authors that treatment by roentgen-rays is first indicated, the result being controlled by metabolic studies; when relief cannot be had by this method, operation is then recommended. It was concluded that in the majority of cases, results after two or three years are equally as good with roentgen-ray as with surgery. With surgery, a rapid fall of metabolism and with roentgen-ray, a gradual progressive fall is noted. There is no mortality with roentgen-rays. Surgical

patients do best who have been previously rayed. Surgical risk is greater in cases of very high metabolism. Routine radiation of exophthalmic goitre with surgery held in reserve is recommended. Surgery is contraindicated in patients whose metabolism is rising in spite of complete rest in bed. Periodic determinations of basal metabolism should be made in management of all cases of exophthalmic goitre.—B. T. S.

(THYROID) Vasomotor symptom of hyperthyroidism. Marañón (G.), Revista Española de med. y. Chir. (Barcelona), 1919, **2,** 598-600.

Marañón found in ninety-two of 100 cases of hyperthyroidism that rubbing the skin in the neck lightly with the fingers made it turn very red in the region of the thyroid, a much brighter red than could be elicited by rubbing the skin in the same way elsewhere. This vasomotor reaction may be more pronounced in the milder cases, and is more distinct in the nervous, in women, in the young, at the menopause, and in persons inclined to sympatheticotony rather than vagotony. He has not seen any mention in the literature of this induced localized erythema in the thyroid region; it may be a uniform or irregular redness, and there may be slight swelling of the red patches.
—J. Am. M. Assn., **74,** 429.

(THYROID) The cause of exophthalmos in Graves' disease. Murray (G. R.), Brit. Med. J. (Lond.), 1916, (ii), 540.

Murray expresses a belief that exophthalmos in Graves' disease is due to an excessive increase in the amount of retro-orbital fat, which mechanically causes protrusion of the eye-ball. Post-mortem findings in a human case and experiments on animals in which melted parafin was injected retro-orbitally led him to this conclusion.—I. M.

(THYROID) Sporadic cretinism caused by a thyreoaplasia of specific origin (Cretinismo esporádico por tireoaplasia de origen específico). Novaro (Raul) and Gonzalez (J. Ortuño), Anales del Inst. Mod. de Clín. Méd. (Buenos Aires), 1919, **4,** 173.

A description of a myxoedematous cretin fifteen years of age and 1.40 m. in height. The parents gave a positive Wassermann reaction, but the patient herself gave a negative reaction.
—B. A. H.

(THYROID HYPOPHYSIS ADRENAL) Interdependence of the function of the ductless glands. O'Day (J. C.), N. Y. Med. J., 1920, **111,** 250-251.

From a brief consideration of the function of the thyroid, adrenal and pituitary the author concluded that no part is played which in any way might make one gland's function dependent upon the functions of others.—H. W.

(THYROID) Three hundred goitre operations (Klinische Erfahrungen bei 300 Kropfoperationen). Orth (O.), Deutsche Ztschr. f. Chir. (Leipzig), 1919, **148**, 360-384.

Orth reviews his experience with 300 goiter operations; the mortality was 0.17 per cent. A number of cases showed the close correlation between the various endocrine glands which surgeons have to bear in mind; for instance, one woman first developed goiter after splenectomy. In another woman the goiter developed at once after removal of a myoma, while Wettergreen has witnessed the subsidence of a myoma as exophthalmic goiter developed. Several have reported increase in the size of the thyroid after removal of both ovaries, and Orth had a case in which the woman aborted three days after resection of the thyroid. Such happenings show the necessity for investigation of the genital organs before operating for goiter. In three cases a moderate form of tuberculosis seemed to be whipped up by removal of a goiter which had been compressing the trachea, and the patients soon died. Clairmont has reported some similar experiences with tuberculosis patients. The blood pressure was high in 70 per cent of Orth's cases, and after the thyroidectomy it dropped below normal, but gradually righted itself in a few weeks. No change in the coagulation of the blood was apparent. Transient albuminuria was evident in ten cases after the operation, not before. One patient had a spontaneous fracture of the femur a year after resection of the thyroid, and she died in six weeks. Orth is inclined to ascribe this fragility of the bones to abnormal conditions such as are observed in the bones of thyroidectomized dogs. The displacement of the trachea should be determined with radioscopy before the intervention, as a guide to the operation. His only recurrences were in the four cases in which radioscopy had been neglected, and the protrusion of the goiter in the depths was not fully appreciated. He had fatal hemorrhage or embolism in two malignant cases, and in one case the esophagus was injured during the operation, as also the trachea in another, but both healed without mishap after suture. Anomalies in the vessels were not infrequent, and this possibility should never be forgotten. In conclusion he warns of the necessity for caution in using disinfectants in this region; some have witnessed the flaring up of latent hyperthyroidism after application of iodized dressings, etc. Another danger from them is the effect on the vocal cords, similar to Cisler's experience with dogs; the vocal cords kept in the cadaver position when their

innervation had been cauterized with silver nitrate. After thyroidectomy the vocal cords are liable to keep in the median position for a long time before they resume normal movements, and any chemicals in the vicinity might exaggerate this.—J. Am. M. Assn.

(THYROID) Exophthalmic goiter and pregnancy (Bocio exoftálmico y embarazo). Peralta Ramos (A.), Rev. Asoc. Méd. Argentina (Buenos Aires), 1919, **31,** 289-309.

The coexistence of the two conditions is rare and in the majority of cases pregnancy does not aggravate the goiter; when such does occur it is necessary to operate.—B. A. H.

(THYROID) Congenital goitre. Peterson (Edward W.), Med. Rec. (N. Y.), 1916, **90,** 789.

A case of congenital goitre is described in which a large adenomatous thyroid was found displaced to the right side of the neck. The removal of the tumor was followed within a short time by tetany, which, however, disappeared after administration of thyroid extract. The extract was employed until the child was four years of age, when its use was discontinued. Mental and physical development remained normal.—I. M.

(THYROID) Goitre and psychoses. Phillips (N. R.), J. Ment. Sci. (Lond.), 1919, **65,** 235-248.

That the role played by goiter in the psychoses is more extended than is indicated, is the theme of Phillips' paper. Of 200 patients examined by him, the actual proportion of goiter was 12 per cent. No less than seventeen of these patients suffered from manic-depressive insanity or from the melancholia of involution, i. e., 70 per cent of the whole number. Of the remaining seven, four were cases of dementia precox and three were cases of paranoia. Phillips believes that those cases show that the nature of the psychosis is, in some degree, determined by the form of the functional disturbance of the thyroid gland, e. g., hyperthyroidism is usually associated with states of excitement, agitation, etc. (manic-depressive insanity), whereas hypothyroidism is more often associated with states of apathy and indifference (dementia precox).—J. Am. M. Ass. 74, 423.

(THYROID PARATHYROID) Concerning the surgical anatomy of the thyroid with special reference to the parathyroid glands. Pool (Eugene) and Falk (Henry K.), Ann. Surg. (Phila.), 1916, **63,** 71-77.

A careful study was made in the human cadaver to determine the anatomical relations of the thyroid and parathyroid glands and the recurrent laryngeal nerve with a special view to learning specifically how much latitude is available in operations upon the thyroid gland. The findings are illustrated by 21 halftone plates. So far as immediate results are concerned, it was determined that a single lobe of the gland can be removed freely and completely, the recurrent laryngeal being sufficiently protected by its capsular sheath. The loss of the two parathyroid glands involved could readily be compensated by those remaining. The possibility would remain, however, that a second surgeon in a subsequent operation might repeat the same procedure upon the other lobe with consequent acute parathyroid deficiency. The authors are acquainted with two cases in which this actually occurred. It is advised, therefore, that in a primary thyroid operation the posterior part of the lobe excised should be left in situ, by way of conserving the parathyroid tissue in that locality.
—R. G. H.

(THYROID) On certain dietary factors to be considered in the treatment of cases of hyperthyroidism. Rosenbloom (Jacob), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1919, **17**, 28.

The writer has obtained clinical evidence that in formulating a diet for patients suffering from hyperthyroidism, two important factors must be considered: first, the diet should contain the minimum amount of protein; and second, foods low in iodine content should be selected.—Quoted.

(THYROID) The surgical treatment of exophthalmic goitre. Rowan (Charles J.), J. Iowa State M. Soc. (Des Moines), 1916, **6**, 199-208.

Rowan believes that while some cases of exophthalmic goiter can best be treated by medical means, the majority are surgical. Proper surgical treatment will cure approximately 70 per cent and greatly improve most of the remainder. Great harm is done when futile medical treatment is prolonged until the patient becomes a poor surgical risk or permanent damage has been done to various organs,—especially the heart. An extremist's attitude toward either method is deplored.—R. G. H.

(THYROID) Concerning the "rickets," so-called, of rabbits from thyroidectomised parents. Rusca (G. L.), La Pedriatria (Naples), 1919, **27**, — (No. 10); Abst., Presse Méd., 1920, **28**, 10.

Claude and Rouillard claimed in 1913 to have observed experimental rickets in young rabbits, the parents of which were

subjected to thyroidectomy. The principal manifestations of the disease were arrest of skeletal development and changes in the muscles, viscera and bones which both microscopically and macroscopically resembled those seen in human rickets. Rusca repeated the experiments, claiming for himself a rigorous technique. The results were completely negative. The author is convinced that these results cannot be ascribed to failure to remove all the thyroid tissue, since in all cases they were consistently negative. It is concluded, therefore, that the results of the previous investigators were merely examples of "spontaneous" rickets such as have been noted by various other observers.—R. G. H.

(THYROID) Congenital thyroid atrophy (Angeborene Schilddrüsenatrophie). Schultze, Deutsche med. Wchnschr. (Berlin and Leipzig), 1916, **42,** 1211.

A clinical report, in which nothing new is given, of a case of partial myxœdema in a mentally and physically retarded girl of 15.—F. S. H.

(THYROID) The non-surgical treatment of Graves' disease—a counter-blast. Scott (T. B.), Practitioner (Lond.), 1918, **100,** 442-450.

The author contends that in Graves' disease we have "a pluriglandular disturbance, not only as to quantity of secretion, but as to quality also, and that this disturbance is in the great majority of cases caused by bacterial poisons from within." He believes that shock, grief and fright are only emergencies stirring up partly latent trouble. "The glandular disturbances act partly by direct action on certain organs, such as the heart, and sympathetic, but chiefly, perhaps, by producing discord in the glandular system of the whole body."

Intestinal antiseptics such as beta-naphthol and salicylate of bismuth are recommended, since there is frequently a gastric or intestinal dyspepsia and often colitis. In addition to these, duodenal extract is said to act "like a charm on duodenal catarrh and on colitis that has not gone too far." The following formula is advised:

Duodenal extract .....grs. 2
Ext. Cannabis Ind.....grs. 1/6

In tablets; one, three times a day, an hour after food.

Parathyroid is also advocated to help control the tremors and other nervous manifestations of the disease.

The observation that thyroid hypofunction ending in a form of myxœdema occurs at the end of a fair number of cases of Graves' disease causes the author strenuously to object to the

surgical removal of any thyroid tissue whatever, since in old age the patient is likely to require all the thyroid he can get. X-ray treatment is also condemned because of probable destruction of thyroid tissue.

"That brilliant craftsman, the thyroidectomist, should become an anachronism, a tradition only of the dark days that are gone; and medicine, strong in physiological and philosophical faith, should resume her peaceful sway."—L. G. K.

(THYROID) Fatality under roentgen treatment of exophthalmic goiter. Secher (K.), Nordiskt Medicinskt Archiv (Stockholm), 1918, **51,** 63-70.

Secher reports the case of a previously healthy woman of 39, who had developed exophthalmic goiter in the course of a year. He gave eight roentgen exposures in two days, each a one-half Sabouraud-Noire dose, with a 2 mm. filter, exposing three fields on the thyroid gland and one on the thymus. The condition became aggravated even during the roentgen treatment, and the condition grew rapidly worse till death the fifth day. He reviews the three cases on record in which roentgen exposures of simple goiter were followed by symptoms of exophthalmic goiter. In Rieder's and Verning's cases the aggravation proved speedily fatal, as in the case here described. (See also Endocrin. **3,** 573.)—J. Am. M. Assn.

(THYROID) Treatment of goiter with injections of phenol, tincture of iodin and glycerin. Sheehan (J. E.) and Newcomb (W. H.), J. Am. M. Assn. (Chgo.), 1920, **74,** 81-82.

In an attempt to produce a local inflammation, which would eventually cause a fibrosis in the gland, these authors injected 80 cases of goiter (55 parenchymatous, 14 exophthalmic, 8 cystic, 2 colloid, and 1 adenomatous) with five drops of equal parts of pure phenol, tincture of iodin, and glycerin, at five days intervals. The number of injections varied from five to fifty-five. They report cures in 76.4% of the parenchymatous goiters, and improvement in 80% of the toxic cases. In the cystic, colloid and adenomatous group they found no improvement.—F. C. P.

(THYROID) Studies on hyperthyroidism. Smith (F. M.), J. Am. M. Assn. (Chgo.), 1919, **73,** 1828-1832.

Thirty men who were convalescing from influenzal pneumonia and showed rapid pulse, enlargement of the thyroid gland, fine tremors of the hands, moist, clammy skin and some of the eye signs usually associated with exophthalmic goiter, were examined to determine, if possible, whether the thyroid gland was the basis of these symptoms. In addition to the usual physical

examination and laboratory work, blood sugar determinations, following the administration of glucose by mouth, were made. The response to epinephrin and the effect of thyroid feeding were also noted.

Seventeen of the cases were diagnosed as simple tachycardia, and seven as irritable heart; none of these cases responded to 5 grain doses of desiccated thyroid, nor gave any evidence of disturbed carbohydrate metabolism. Six cases were finally diagnosed as hyperthyroidism, the diagnosis being based on the response to thyroid feeding, a positive response to epinephrin and a suggestive disturbed carbohydrate metabolism.—F. C. P.

(THYROID ENDOCRINE ORGANS) Angioneurotic edema. Staffieri (D.), Revista Médica del Rosario, 1919, **9**, 293-298.

Staffieri summarizes the prevailing views in regard to Quincke's edema, in the statement that it is characterized by abnormally exaggerated excitability of certain nerves which have control of the secretion and circulation of lymph. This hyperexcitability is almost always constitutional, the result of "dysendocrina" (defective functioning of the endocrine glands), with thyroid insufficiency predominating. This excitability is rendered manifest by influences of different kinds, including some which behave like antigens, inducing anaphylaxis. In the first of his two cases, one side of the throat was affected but there was no inflammation. The young man showed signs of thyroid insufficiency and hypogenitalism, and under thyroid treatment there has been no recurrence of the acute edema of the throat. Atropin and a saline purge relieved the immediate symptoms; it was the first and only attack to date. In the other case there had been fleeting edema at various points during seven years. In this latest attack the face alone was involved, and the edema was so extreme that the eyelids could not be closed. As usual, the edema subsided completely in a few days. The patient was a healthy married woman of 35 with two healthy children and negative Wassermann reaction, and there are no signs of derangement of any of the glands of internal secretion.

—J. Am. M. Assn.

(THYROID THYMUS) Thyroidectomy for vagotonic type of Basedow's disease. Stettin (W.), Med. Rec. (N. Y.), 1916, **89**, 580.

A brief case report. A patient was operated upon for Graves' disease, part of the thyroid being removed. A relapse was experienced. At a second operation another portion of the thyroid was removed, together with a small retrosternal mass which, upon microscopic examination, proved to be atrophic thymus tissue. Recovery was satisfactory.—R. G. H.

(THYROID) The etiology of mongolism (Zur Aetiologie des Mongolismus). Stoeltzer (W.), Münch. med. Wchnschr. (Munich), 1919, **66,** 1493.

The author observed ten children with Mongolian idiocy. No noteworthy features were presented, but in three the mother had complained during pregnancy of a loss of appetite and constipation; she became fat, did not perspire, lost hair and became dull. It is suggested that these cases of mongolism were due to hypofunction of the thyroid of the mother.—J. K.

THYROID treatment, The results of—in nine cases of alopecia areata maligna. Strandberg (J.), Acta Med. Scand., 1919, **52,** 165-175.

Five cases out of 9 showed marked improvement upon administration of thyroid. However, results do not warrant conclusion that the etiology of the disease is found in the disturbances of the endocrine glands.—Chem. Abst.

(THYROID) Method and results of a study of the distribution of iodine between cells and colloid of thyroid glands. Tatum (Arthur L.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1919, **17,** 28.

Method: Use was made of the fact that from frozen sections, as prepared for histological study of fresh, unfixed tissues, the colloid of the thyroid gland completely disappears out of the acini when the sections are floated in physiological salt solution. The sections were picked out by means of a needle, washed in another salt solution, dried at 105° C., weighed and analyzed for iodine by the technique of Kendall. The iodine in the colloid portion was sometimes determined by evaporation of the salt solution—and at other times differentially by analysis of the whole dried gland.

Results: In a series of about 30 experiments on dogs' thyroids the iodine was found in the majority of cases to be wholly in the colloid. In a smaller number the cell mass gave only qualitative tests for iodine, which, at the present stage of this investigation might be considered due to small unopened acini. The physiological significance of these findings is being investigated.—Quoted.

(THYROID) Some blood pressure phenomena in exophthalmic goiter. Taussig (A. E.), Tr. Assn. Am. Physicians (Phila.), 1916, **31,** 121-127.

The blood pressure in exophthalmic goitre shows the same sort of anomalies, but to lesser degree than those seen in aortic

regurgitation. The pulse pressure is high as compared with the diastolic. Both systolic and pulse pressures are higher in the leg than in the arm. Non-toxic goitres, on the other hand, do not give rise to this difference, the pressures in both upper and lower limbs being equal. This differential arm and leg pressure, although characteristic of exophthalmic goitre, is by no means pathognomonic. Identical pressures in arm and leg are regarded, however, as of considerable value in ruling out this type of goitre.—R. G. H.

THYROID and PANCREAS, Giant-cell sarcoma of—(Reus cellensarcom van de schildklier en het pancreas). van Rijssel (E. C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63** (ii), 2914.

A pathological-anatomical description of two cases, the first of which was a sarcoma of the thyroid with metastases in the lungs and the second, a sarcoma of the pancreas associated with gastric ulcers. The article contains some good microphotographs, but no clinical details.—J. K.

(THYROID) The "hydro-telluric" theory of Bircher and its application to the regions of endemic goiter in Argentina (La "Teoria hidrotelúrica" de Bircher y su aplicacion a las regiones de bocio endémico en la Argentina). Wernicke (R.), Rev. del Inst. Bact. del Dep. Nacional de Higiene (Buenos Aires), 1919, **2**, 325-332.

The drinking waters from Rosario de Lerma and Chicona (Province de Salta) which are regions very strongly infected with endemic goiter do not have the low surface tension observed in the waters from the endemic regions of Switzerland by Bircher. The geological characters of the goiter regions in the Argentine fail to confirm Bircher's hydrotelluric theory.—B. A. H.

(THYROID AUTONOMIC N. S.) The histopathology of the autonomic system in goiter. Wilson (L. B.), Journal-Lancet (Minneapolis), 1917, **37**, 368-370.

An examination by the above writer of the nerve cells, etc., of the cervical sympathetic in all cases of goiter, revealed various degrees of degeneration. Glandular degeneration was shown in the ganglion cells of cases of exophthalmic goiter. The degree of degeneration always paralleled the intensity of the manifested toxicoses.—J. H. L.

(THYROID) Goiter, considered from the standpoint of the pathologist. Wilson (L. B.), Miss. Valley M. J. (Louisville, Ky.), 1916, **25**, 225-228.

The author divides the pathologic enlargements of goiter into four groups: (1) non-symptomatic or simple goiters, in which the primary parenchymatous hypertrophy and hyperplasia are absent. The enlargement is colloidal in nature and in the belief of the author is caused by a water-borne, chronic infection. (2) The toxic non-exophthalmic, as a rule, are associated with encapsulated adenomas. The differentiation from the pathologic standpoint between the toxic and non-toxic adenomas is not complete. (3) In toxic exophthalmic goiter there is generally found either primary hypertrophy and hyperplasia or both. The additional over-production symptoms are probably due to the irritation of the cervical sympathetic ganglia. (4) Malignant neoplasms of the thyroid are not so common nor so easily recognized. Most cases were originally encapsulated tumors containing small cells with large nuclei.—F. S. C.

(THYROID AUTONOMIC N. S.) Further study of the histopathology of the autonomic nervous system in goiter. Wilson (L. B.), J. Lab. & Clin. Med. (St. Louis), 1916-17, **2,** 295-307.

The following pathological changes were found in the cervical sympathetic ganglia (twenty ganglia) which were removed at operation from sixteen patients with hyperplastic, toxic (exophthalmic) goiter: (1) Definite change in the cells of the ganglion. (2) All showed various changes of degeneration. (3) Degeneration was also shown in some of the nerve fibers. (4) The pathologic changes in the cervical sympathetic ganglia were parallel to the stage and intensity of the symptoms of hyperthyroidism.—J. H. L.

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CLASSIFICATION OF DISORDERS OF THE HYPOPHYSIS*

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St. Louis

To have the opportunity of submitting a classification of the disorders of the hypophysis to this audience, many of whom have done original work upon this gland, is indeed a privilege. This presentation is made with the view that the many complexities encountered in correlating the clinical manifestations of these disorders, with the changes in function and histology of the hypophysis, will be clarified by its discussion. The primary essentials relative to the physiology of the pituitary body, upon which this classification is based, have been deduced almost entirely from the theoretical conclusions of pituitary function advanced by American investigators (Cushing, Goetsch, Homans, Crowe, and Bab). The application of these principles has been stimulated by our analysis† of 892 endocrine cases, of which 147 were diagnosed disorders of the pituitary gland; 350, of the thyroid; 194, of the gonads; 186, pluriglandular disorders; 10, diseases of the adrenals and 5, thymus diseases. Of the 123 hypopituitary disorders, 23 were grouped as anterior lobe; 3, as pos-

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

†From observations made in conjunction with Dr. J. L. Tierney, to whom we are indebted for the determinations on basal metabolism and carbohydrate tolerance.

terior lobe; and 86, as bilobar insufficiencies. The hyperpituitarisms totaled 24, of which 6 were anterior lobe; 2, posterior lobe, and 16, bilobar varieties. There were 11 cases of diabetes insipidus, or hypophyseal polyuria, some of which were associated with an anterior lobe or a pars nervosa syndrome. Pituitarism as a part of a pluriglandular complex (not included in the 147 primary pituitary disorders) occurred in 122, making a total of 269 cases in which clinical manifestations of pituitarism were present. Of the total number of pituitary cases, only 8, or 6 per cent, were neoplastic in origin. Conclusions, dependent upon the differentiation of the clinical manifestions determined from comparing pituitary with other endocrine disorders, have substantiated to a considerable degree the theories of the functions of the individual lobes of the pituitary gland.

Lobar Grouping. This classification separates the hypophysis into two lobes, the anterior and the posterior, with the pars intermedia as part of the latter. The clinical manifestations, due to abnormal secretions of one or both of these lobes, are taken as the chief guide for the grouping of the disorders. The clinical syndromes (exclusive of pituitary neighborhood signs and symptoms), formerly termed "glandular" symptoms, are named "hormonic" signs and symptoms, a qualification applying to all endocrine disorders. The "hormonic" signs and symptoms are defined as physical or metabolic changes associated with other endocrine symptoms due to an abnormal secretion of a ductless gland. Those pertaining to the pituitary disorders are divided into the physical, metabolic, and other endocrine symptoms. The physical "hormonic" signs are subdivided into the general and regional.

Among the general "hormonic" signs are the well-known changes in osseous development, producing classical disproportion in the measurements (torso, lower measurement, and span), unusual development of the voluntary musculature, abnormal contraction of the unstriped muscle tissue, pigmentation, and hair distribution. Among the significant regional "hormonic" signs are local changes in the head, nose, teeth, chin, hands, and genitalia, localized adiposity, pigmentation, etc. Other important pituitary endocrine symptoms are polyuria, changes in basal metabolism, carbohydrate tolerance, mentality, other endocrine secretions, temperature, pulse, and blood-pressure.

Certain combinations of the above "hormonic" signs and symptoms are taken as indicative of abnormal secretion of an individual lobe or of both lobes of the pituitary gland. These combinations or clinical syndromes were present so constantly in classical types and varieties of pituitary disorders, that they have been deemed the most valuable as a grouping system for these diseases. The neighborhood signs and symptoms, while important as diagnostic evidence of the neoplastic varieties of the disorders, were of little value for differentiating the varieties and types for the purpose of classification or diagnosis. This is true on account of the fact that pituitary tumors were found associated with all the various clinical syndromes. Furthermore, the incidence of pituitary tumor was so rare (6 per cent of the cases herewith reported) that its symptomatology was practically useless as a basis for general classification. The histopathology of the hypophysis, particularly of the a-neoplastic type, has been too poorly defined to make it a dependable basis worthy of classification.

Functions of the Lobes of the Hypophysis. In order to justify this lobar classification of these disorders, it becomes necessary to establish the function of each lobe of this gland producing these specific "hormonic" signs and symptoms. As the function of the entire pituitary body, as well as of its individual lobes, is yet a matter of controversy, this will be difficult and must remain somewhat questionable. In attempting to assign definite "hormonic" syndromes to specific disturbances in the lobes of the hypophysis, the writer has accepted, to a large extent, the early experimental work of Cushing, Goetsch, and others. Personal clinical observations, so far made upon these hormonic complexes, have seemed to substantiate their theories, in contradiction to those of Bell, Falta, Fisher, Biedl, and others.

As will be seen from the following table, the *major hormonic signs of the anterior lobe* (A and B) are those referable to the growth and function of the *osseous* and *genital* systems, and the minor signs (C, D, E, F, G and H), to the dermal system, mentality, temperature, pulse and blood-pressure. The major signs attributed to the posterior lobe (I, II, III and IV) are those resulting in disturbed metabolism, deposition of adipose tissue, polyuria and unstriped muscle contraction. Associated

TAB
HORMONIC SIGNS OF THE ANTE

	HYPOPITUITARISM	
	Preadolescent	**Post**adolescent
A. **Osseous**	A. **Undergrowth. All Bones LORAIN-LEVI** type	A. **Undergrowth. Short** and **flat bones** only. (Normal long bones)
1. Stature a. Measurements	1. Short a. Torso greater than lower. Span less than height	1. Tall, or normal a. Varies. Torso greater than lower or less than lower (eunuchoid)
2. Head a. Sinuses b. Nose	2. Small a. Small b. Pointed, straight	2. Small a. Small b. Pointed, straight
c. Superior Maxilla	c. Normal	c. Normal
d. Chin	d. Pointed, sharp	d. Pointed, sharp
e. Sella Turcica (X-ray)	e. Small, except **neoplastic** type enlarged	e. Small, except **neoplastic** type enlarged
3. Hands	3. Type "en petit," one-third smaller than normal	3. Small
a. Phalanges (X-ray)	a. Narrow, tapering, tuberosities and tufting absent	a. Narrow, tapering tuberosities and tufting absent
4. Pelvis	4. Broad, feminine type	4. Broad, feminine type
a. Genu	a. Valgum	a. Valgum
B. **Genital**	B.	B.
1. Gonads (ovary or testicle)	1. Infantile	1. Normal
2. Uterus	2. Infantile	2. Normal
3. Menses	3. Amenorrhea, metrorrhagia, and dysmenorrhea	3. Tendency to dysmenorrhea, amenorrhea, and metrorrhagia
4. Sterility and Impotence	4. Present	4. Present
5. **Secondary Sex Characters**	5. Absent	5. Present
C. **Muscular**	C. Proportionate to development	C. Normal
1. Muscle Tonus	1. Normal	1. Fatiguability frequent
D. **Mental**	D. Usually deficient or retarded	D. Average
E. **Dermal** a. Teeth b. Hair Distribution	a. Upper incisors enlarged, lateral occlusion good b. Absent	a. Occasional separation and frequent enlargement of upper incisors b. Normal
F. **Temperature**	F. Subnormal	F. Subnormal
G. **Pulse**	G. Slow	G. Slow
H. **Blood-pressure**	H. Hypotension, or normal	H. Hypotension, or normal

LE I
RIOR LOBE OF THE HYPOPHYSIS

HYPERPITUITARISM

Preadolescent	**Post**adolescent
A. **Overgrowth of all bones** — Normal giant, Eunuchoid giant, Acromegalic giant — **Gigantism**	A. **Overgrowth. Acral, short and flat bones** only. (Long bones short) **Acromegaly**
1. Abnormally tall	1. Short and stocky, or normal
a. Normal giant: torso = lower, span = height Eunuchoid giant: torso less than lower, span greater than height Acromegalic giant: torso greater than lower, span less than height	a. Acromegaly: torso greater than lower, span less than height
2. Large	2. Large
a. Large	a. Large
b. Pointed, normal (eunuchoid giant) Blunt (acromegalic giant)	b. Blunt, rounded
c. Normal, except prominent in acromegalic giant	c. Prominent
d. Pointed, except prognathism in acromegalic giant	d. Rounded, blunt. Prognathism
e. Normal, except **neoplastic** type enlarged	e. Normal, except **neoplastic** type enlarged
3. Type "en longe," one-third larger than normal. No disproportion	3. Type "en large," spade hand, wrist wide, fingers broad and clubbed. Infiltration of soft tissues over bones. Hands and head involved
a. Wide, dense, tuberosities large, terminal tufting, exosteses	a. Wide, dense, tuberosities large, terminal tufting, exostoses
4. Narrow, masculine type	4. Narrow, masculine type
a. Varum	a. Varum
B.	B.
1. Large, well developed	1. Large, well developed
2. Normal	2. Normal
3. Normal	3. Normal
4. Absent (present in a few years with transition to hypoactivity)	4. Absent (present after many years with transition to hypoactivity)
5. Present (even after hypoactivity occurs)	5. Present (even after hypoactivity occurs)
C. Normal, or overdeveloped	C. Overdeveloped
1. Loss after few years' overactivity)	1. Retained after age of 40-45
D. Apathetic (after activity changes)	D. Abnormally developed, temperamental, loquacious, unstable
a. Enlarged and separated upper incisors. Lowers separated in acromegalic giant	a. Separation of upper incisors constantly; frequently of lower, with prognathism
b. Increase on torso	b. Marked increase on extremities and chest
F. Normal	F. Normal
G. Normal	G. Normal
H. Normal. Hypotension after change to hypoactivity	H. Normal, or above normal

with these are minor signs, affecting the secretion of other endocrine glands, the nervous system, temperature and pulse.

While it is true that the secretion from the anterior lobe seems to have a definite effect upon the development and function of the osseous and genital systems, it is acknowledged that other factors, endocrinous and endogenous, undoubtedly have considerable influence upon both the growth and development of these two systems. Not all cases of retarded osseous growth and aplasia, for instance, can be attributed to hyposecretion of this lobe of the hypophysis. The French school (Brissaud, Meige, Bauer, Anton and Brammel) have many subdivisions of infantilism ("nanisme," "chetivisme," "nanisme complet"), many types of which have no relation to pituitary disorders. The above table contrasts the hormonic signs related to the anterior lobe in hypopituitarism with those of hyperpituitarism, and demonstrates the differences dependent upon the age at which this disturbed activity occurs (pre- and post-adolescent). Attention is directed particularly to the extreme opposite change noted in the osseous system in pre-adolescent hypopituitarism (first column) as compared with pre-adolescent hyperpituitarism (third column).

The effect of the secretion from the anterior lobe upon the muscular tonus is a subject which has received comparatively little attention, but which has appeared to the writer as being almost as important as the difference present in the osseous growth and development. This is particularly striking when one compares the muscular development and tone of pre-adolescent hypopituitarism (Lorain-Levi type) with those of post-adolescent hyperpituitarism (acromegaly). The extreme difference in the genital function and development is also emphasized in comparing the foregoing two types. In the first (Lorain-Levi type) the genitals are infantile and functionless, with the presence of sterility and impotence; whereas in the acromegalic, the genitals are unusually well developed and associated with hypersexuality. In pre-adolescent varieties of both over- and under-activity of this lobe, there is a tendency to decreased genital function. This is present as a cardinal sign in the hypopituitary post-adolescent subject, and is soon acquired in pre-adolescent hyperpituitarism, on account of the early transition to inactivity in this variety. Decreased genital function and muscle tonus

occurred so constantly with hypoactivity of the anterior lobe, that they established themselves as the best indicators of the state of activity of this lobe. Hence, the genital functions (menses, libido, and potency) and the muscular tonus (muscle fatigue or physical capacity), taken with the temperature, pulse, and blood-pressure, were considered, at the time of their determination, the significant signs of activity. The osseous changes, genital development, and secondary sex characters were interpreted as evidence of former activity which might have changed to the opposite state.

The intermittent enlargement and infiltration of local parts, such as the hands and face, in acromegaly, were undoubtedly due to changes in the soft tissue covering the short and flat bones involved, and not a result of osseous change. The rapid changes in these localized swellings, besides the frequently associated sweating of these parts, helped to prove this origin. While there was no nervous syndrome specific of pituitary disorder, the different mental states, as described above, were most frequently demonstrable. The most significant mental change was probably that occurring in gigantism and acromegaly, with change of activity in this lobe. Change from a hypermental state to one of depression, apathy and indifference, if associated with loss of genital function and muscle tone, was considered particularly significant of transition to hypoactivity. The orthodontial markings in anterior lobe insufficiencies varied considerably. In the pre-adolescent hypopituitary individual, there was usually a tendency to overcrowding of the lower teeth, with fairly good lateral occlusion of the upper. The frontal incisors were constantly enlarged in those cases in which there was absence of genital function and development. The separation of the upper incisors occurred in post-adolescent hypopituitarism, and was usually present in pre- and post-adolescent hyperpituitarism; whereas the separation of the lower teeth was limited to the acromegalic giant and acromegaly, being absent in other hyperpituitarisms, as well as in all deficient secretions of the anterior lobe. The blood-pressure, temperature, and pulse were important signs of activity in this, as well as in other endocrine glands, but were by no means specific for pituitarism. Hence, they are valuable as signs of activity, but not as signs of any individual ductless gland. They are respectively subnormal and slow in the

hypoactive cases, and normal or slightly above normal in the opposite state of secretion.

Basal metabolism determinations* have been made on only 32 of the cases which came under observation during the last six months. These cases have been grouped among the five varieties, so that there were too few in any one variety from which to draw satisfactory conclusions.

The basal metabolism in these few cases of disorders of the anterior lobe of the hypophysis varied considerably. This is in contradiction to the theories previously advanced, to the effect that the anterior lobe secretion has no influence upon metabolism. One would believe that either there must be some relationship between the metabolism and the function of this lobe, or the clinical diagnosis excluding the posterior lobe of the hypophysis and the other endocrine glands, as an accompaniment in these cases, was incorrect. In the simple anterior lobe dyscrasias reported herewith, 7 cases had a basal metabolism varying from the normal. In 5 cases it was decreased, varying from 2 to 30 per cent, and in 2, it was increased 14 and 15 per cent respectively. In one case in which anterior lobe extract was given therapeutically, the basal metabolism was increased from —30 to +8 per cent during six weeks' treatment. This increase in metabolism to slightly above the normal was accompanied by relief of other symptoms, such as headaches, mental disability, muscular fatigue, loss of libido, etc. In the pure hyperactivities of the anterior lobe, the same discrepancy in basal metabolism determinations occurred. In the 4 cases in which the metabolism was determined, it was found normal in 2, and increased in 2. In 5 cases originally diagnosed as simple anterior lobe hypoactivities, it was found that the basal metabolism was increased beyond 10 per cent, and the sugar tolerance markedly decreased,

*Benedict's Portable Apparatus No. 49 was used for these determinations. The linear formula of D. Du Bois and E. F. Du Bois was used for computation of the area of body surface. The following table of Aub and E. F. Du Bois was taken as the normal standard for the calories per square meter of body surface per hour:

(Height-Weight Formula)

Age, Years	Males	Females
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.0
30-40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60-70	36.5	34.0
70-80	35.5	33.0

which necessitated a change in the diagnosis and grouping to the bilobar division, under the heteroactive variety.

The *carbohydrate tolerance** was estimated in 10 cases of anterior lobe dyscrasia. Of these, 7 were decreased, and 3 were increased in activity. Of the hypopituitarism cases, 5 showed an increased, and 2, a decreased sugar tolerance; whereas, in the hyperactivities, 2 cases showed an increased, and 1, a decreased tolerance. In the 2 cases having an increased basal metabolism, the sugar tolerance curve was normal.

The hormonic signs due to increased and decreased activity of the posterior lobe are given in detail below. It will only be necessary to refer to the fact that they are exactly opposite, a statement that cannot be proved absolutely on account of the considerable difference of opinion regarding the functional effects of this lobe, as related to specific influence upon other processes and structures of the body. It will be observed that the writer is of the opinion that this lobe of the hypophysis has practically no relation to the growth or function of the osseous and genital systems. On the contrary, its function is limited directly to the regulation of the metabolism, and indirectly to effects upon other organs and tissues which deal with metabolic procedure.

The influence of the secretion of the posterior lobe upon metabolism, estimated from personal observations based upon the determination of basal metabolism and carbohydrate tolerance, was found more definite in its relationship than those changes of metabolism associated with the simple anterior lobe dyscrasias. The following is a summary report of the basal metabolism and carbohydrate tolerance determinations made upon cases of pituitary disorder in which the posterior lobe was involved independently, or was associated with an anterior lobe syndrome. Many of the cases having anterior lobe disorder had a secondary gonad disturbance, but none was of the pluriglandular syndrome having hormonic signs of the thyroid, adrenals, or other ductless glands. The *basal metabolism* determi-

*The sugar tolerance was estimated by the Janney-Isaacson method. The blood sugar was estimated first after 15 hours' fasting. Glucose, 1.59 grams per kilogram of body weight, was given, and blood sugar estimations were again made, one hour and two hours following the ingestion of this amount. A normal curve was arbitrarily established, as follows: after 15 hours' fasting, 0.10; after the first hour, 0.18; and after the second hour, 0.15. A decreased tolerance was considered one which would produce a higher curve during the two hours' estimations than the normal curve. Increased tolerance would show a curve 3 or 5 points below this curve.

TABLE II

HORMONIC SIGNS OF THE **POSTERIOR** LOBE OF THE HYPOPHYSIS

	HYPOPITUITARISM	**HYPER**PITUITARISM
I. **Metabolism**	I.	I.
a. Basal Metabolism	a. Decreased	a. Increased
b. Carbohydrate Tolerance	b. Increased	b. Decreased
c. Glycosuria and Hyperglycemia	c. Absent	c. Present
II. **Adiposity**	II. Marked girdle, mons and mammary	II. Absent, usually emaciation
III. **Polyuria**	III. Present (Pars Intermedia?)	III. Absent (or present with glycosuria)
IV. **Involuntary Muscle Contraction**	IV.	IV.
a. Intestinal	a. Absent; frequent intestinal atony	a. Present; frequent intestinal spasticity
b. Uterine	b. Absent	b. Present
V. **Endocrine Secretion**	V.	V.
a. Thyroid	a. Hypoactivity (hibernation)	a. Hyperactivity
b. Adrenals	b. Insufficiency?	b. Hyperactivity?
c. Gonads	c. Hypoactivity (with Anterior Lobe disorder)	c. Hyperactivity (with Anterior Lobe disorder)
d. Pancreas	d. Normal (increased sugar tolerance)	d. Hypoactivity (decreased sugar tolerance)
VI. **Nervous**	VI. Apathy; Somnolence frequent	VI. Psychic instability
VII. **Temperature**	VII. Subnormal	VII. Normal
VIII. **Pulse**	VIII. Slow	VIII. Rapid

nations were made in 18 cases in which the posterior lobe was involved. Of these, 14 cases were hypoactivities, and 4, hyperactivities. In the hypoactivities, this metabolism was decreased in 5 cases, normal in 5 cases, and increased in 4 cases. Of the 4 cases showing an increased metabolism, against the rule for hypoactivities of this lobe, it occurred in 2 after treatment, and in 1 associated with a polyuria. This practically left only 1 case which had an increase in metabolism, not conforming to the supposition that decreased secretion of this lobe is constantly associated with decreased metabolism. Of the 4 hyperpituitarisms, the metabolism was increased in 2, and normal in 2, all fitting perfectly into the clinical diagnosis.

In 61 cases diagnosed as posterior lobe disorders, the *carbohydrate tolerance* was determined. Of these 61, 3 were grouped with the hyperactive variety, in 2 of which the sugar tolerance was increased, and in 1, decreased. In 58 cases a diagnosis was made of hypoactivity of this lobe, which showed in 53, an increased, and in 5, a decreased sugar tolerance. A recent contribution by Rohdenburg, Bernhard and Krehbiel, upon the study of the sugar mobilization, based upon 228 cases (cancer, tuberculosis, thrombo-angiitis, cirrhosis of the liver, myocarditis, etc.), discredits to a considerable extent the value of the carbohydrate tolerance test in metabolic disturbances. They conclude that in other conditions, as widely different as diabetes, tuberculosis, epithelioma, and pregnancy, a blood sugar curve is found, similar to that in metabolic disturbances; that many of these conditions are accompanied by hyperglycemia and that concentration of the blood sugar is not the sole factor concerned in the development of glycosuria.

The classical obesity interpreted as a "hormonic" sign of posterior lobe hypopituitarism, consists of girdle- and mons-adiposity, to which, in some cases, is added mammary adiposity. There is yet considerable controversy concerning the cause of this obesity. Its character and location have suggested secondary gonad insufficiency as its origin, because this frequently accompanies the bilobar cases having anterior lobe insufficiency. An argument against this cause of the obesity is that it is absent in the pure anterior lobe insufficiency in which there is complete aplasia and absence of function of the gonads. The writer has observed cases of this kind, in the female, aged 36 and 38 years,

in which there was complete amenorrhea and infantilism of the genitalia during the entire life, without the development of this typical adiposity. The emaciation which is present in hypersecretion of this lobe is easily accounted for on the basis of increased metabolism. The rapid loss of weight and emaciation frequently accompanying hypophyseal polyuria, however, is more difficult to explain, particularly if this polyuria is attributed to decreased secretion of the posterior lobe. If both these functions (polyuria and adiposity) are attributed to hyposecretion of the posterior lobe, then we should obtain adiposity much more frequently with the diabetes insipidus syndrome, which clinical experience demonstrates is more constantly associated with emaciation. Biedl has reported some exceptional cases, however, in which this peculiar combination of adiposity and polyuria occurred. It is not uncommon to have a history of early transient polyuria, followed later by adiposity, which might be due to a change of activity of this lobe. Bab's theory that the polyuria is due to *hypo*secretion of the pars intermedia, not including the pars nervosa, seems to approach nearer to an explanation of the clinical combinations, as well as the therapeutic relief which many of these cases obtained from hypophyseal treatment. The argument that this polyuria is really due to hypersecretion, on account of the fact that it is associated with so many other symptoms of posterior lobe hypersecretion, such as increased metabolism, decreased sugar tolerance, hypophyseal glycosuria, emaciation, and bladder and intestinal tenesmus, has not been entirely disproved.

The control of the contraction of the unstriped muscles, particularly those of the intestine and uterus, as well as of the bladder and the vascular and bronchial systems, is one of the most striking and easily demonstrable effects of the secretion of the posterior lobe. The writer has used the constriction effect of this substance upon the intestinal muscle ("intestinal reaction") to define the tolerable dose of pituitary extracts in the treatment of posterior lobe insufficiency. Extracts of the posterior lobe are given in dosage to the amount producing definite intestinal cramps, followed by evacuation. This reaction occurs within ten or fifteen minutes after giving this substance hypodermically. The dosage at which this reaction occurs is taken as the normal physiologic dose, and increase above this amount for

therapy is deemed inadvisable. If a larger dose is given, that which is described as a "general reaction" occurs. This consists of tremor, tachycardia, and emotionalism. The effect of extracts of this lobe upon the nervous system is strikingly demonstrated by giving so intolerable and untoward a dose. Mental symptoms from so large an injection, consisting of emotional attacks, crying, laughing, shouting ,and, in some, definite brainstorm, simulating temporary insanity and obsessions, have been produced. The "intestinal reaction" was tested out by the writer for its diagnostic value to determine whether the amount of extract producing these intestinal symptoms might not indicate to some degree the sufficiency of the posterior lobe. It was thought originally that cases having a deficient secretion from this lobe, would require a much larger injection to produce the "intestinal reaction" than those having a normal or increased secretion. While it was found that the cases of hypopituitarism usually required a larger does for its production, this did not occur constantly, or in a sufficiently larger percentage to make it of value as a diagnostic sign.

The effect of posterior lobe secretions upon the other endocrine glands is not absolutely defined. The fact that a hypothyroid state is frequently associated with hypopituitarism, especially if it occurs in late adult life, which produces a combination that is believed necessary for the production of pituitary hibernation, has led to the conclusion that hypoactivity of the thyroid more frequently accompanies decreased function of this lobe. It has also been noted that peculiar hyperthyroid states have been frequently associated clinically with hyperpituitarism of the posterior lobe. This relationship may possibly be accountable for the increased basal metabolism and decreased sugar tolerance present in these cases, and it might help to explain the discrepancies which have existed in basal metabolism determinations made in pituitary disorders.

The adrenals are supposedly insufficient in the hypopituitary, and hyperactive in hyperpituitary disorders of this lobe. The peculiar pigmentation (chloasma) so frequently found about the hairline, angles of the mouth, eyes, lateral aspects of the neck and nipples, has been taken by the writer as a sign probably associated with the anterior lobe disorders, and not due to the adrenals. This is thought to be true on account of

TABLE III

CLASSIFICATION DISORDERS OF THE PITUITARY GLAND

I. Anterior Lobe	
A. Hypoactivity	
1. Preadolescent a. A-neoplastic b. Neoplastic	**Lorain-Levi Type**
2. Postadolescent a. A-neoplastic b. Neoplastic	**Amenorrhea, Dysmenorrhea, Metrorrhagia** reacting to Anterior Lobe treatment. No signs of Posterior Lobe disorder
B. Hyperactivity	
1. Preadolescent a. A-neoplastic b. Neoplastic	**Gigantism** (no signs of Posterior Lobe disorder)
2. Postadolescent a. A-neoplastic b. Neoplastic	**Acromegaly** (no signs of Posterior Lobe disorder)
II. Posterior Lobe*	
A. Hypoactivity	
1. Pars Intermedia (?)	**Polyuria** (Bab) (Reaction to Pituitrin. Signs of Anterior Lobe and Pars Nervosa disorder absent)
2. Pars Nervosa	Pituitary **Obesity** (Decreased metabolism, increased sugar tolerance. Polyuria and signs of Anterior Lobe disorder absent)
B. Hyperactivity	Hypophyseal **Glycosuria** (Increased metabolism, decreased sugar tolerance. Polyuria and signs of Anterior Lobe disorder absent)
III. Bilobar*	
A. Anterior and Posterior Lobes	
a. Hypoactivity	**Froelich's Type** without, or with polyuria (Biedl)
b. Hyperactivity	**Gigantism** or **Acromegaly** with **increased** metabolism and **decreased** sugar tolerance. Adiposity absent
c. Heteroactivity	
1. Anterior Lobe hyperactive Posterior Lobe hyperactive	**Gigantism** or **Acromegaly** with **Polyuria**
2. Anterior Lobe hypoactive Posterior Lobe hyperactive	**Genital Aplasia, Nanism, Amenorrhea,** etc., with **Pituitary Glycosuria** (Increased metabolism; decreased sugar tolerance)

*(1) Pre- and (2) Post-adolescent varieties and (a) A-neoplastic and (b) Neoplastic types are subdivisions under each activity (Hypo- and Hyper-) as given under I, Anterior Lobe.

its frequent presence in positive hypophyseal cases that are entirely free from other signs of adrenal disease, such as disturbed blood-pressure, marked asthenia, diarrhea, and other symptoms.

It has been stated by some authors (Fischer, Falta and others) that the hypersecretion of the posterior lobe has a marked inhibitory effect upon the gonads, as well as a stimulating effect upon the mammary gland. Personal observation in the writer's cases has led to the conclusion that Bell is probably correct in stating that this relationship does not exist. In those cases of pituitary disease in which the function of the gonads was disturbed, this was attributed to the hormone from the anterior, and not from the posterior lobe. Four cases with pure posterior lobe pituitarism, had marked changes in metabolism and carbohydrate tolerance, adiposity, etc., in which no abnormal changes, either in function or development, of the genitals could be demonstrated or were on record.

Pemberton and Sweet assign to the secretion of the posterior lobe an inhibitory influence upon the pancreatic secretion. It is known that there is a marked increase in the sugar tolerance in hypopituitarism, and yet there is an uncertainty of a hypoactivity of the pancreatic secretion in this condition. The nervous makeup of the individual is markedly affected in changes of activity of this lobe. In decreased secretion, apathy and somnolence are frequent. In hypersecretion, marked periodic psychic instability, of various degrees and moods, is very common. The temperature, pulse, and blood-pressure correspond well to the activity of any other endocrine gland, being subnormal in decreased secretion, and normal (or at times there is a slight pyrexia, hypertension, and tachycardia) in increased secretion of this lobe.

With the above physiologic effects serving as a basis for the "hormonic" signs of the secretory functions of these lobes, the accompanying classification has been evolved.

This classification, based solely upon the "hormonic" signs of hypophyseal disease, groups the disorders of this gland into three divisions, dependent upon whether one or both of the lobes were involved: (I) Anterior lobe disorders, in which this lobe alone was involved; (II) Posterior lobe disorders, in which this lobe, without clinical evidence of anterior

lobe dyscrasia, was affected; (III) Bilobar disorders, in which abnormal function of both lobes could be demonstrated. Each lobar division is subdivided into the activities prevailing, the anterior and posterior lobe disorders into the states of: (A) hypoactivity and (B) hyperactivity; the bilobar group into the states of: (A) hypoactivity, (B) hyperactivity and (C) heteroactivity. The last named (heteroactivity) comprises mixed cases, in which there were opposite secretory states of the individual lobes, such as hyperactivity of the anterior lobe, combined with hypoactivity of the posterior lobe, and vice versa. These activities are redivided into: (1) pre-adolescent and (2) post-adolescent varieties, dependent upon the age incidence of the abnormal secretory state. A final division is made of the age incidence, into: (a) a-neoplastic and (b) neoplastic varieties.

Under the pre-adolescent hypoactivity of the anterior lobe is grouped the Lorain-Levi type of pituitary insufficiency. This type has not yet received the distinction of a special group division. Others, besides Lorain and Levi (Meige, Allard, Rennie, Kunell, Falta, Bell), in fact, nearly all writers who have collected a series of cases, have described similar types, intimating that the types were due to simple and single insufficiency of the anterior lobe. These types are characterized by having a classical arrest of osseous growth, with complete aplasia of the genital system, without additional endocrine symptoms referable to the posterior lobe.

In the post-adolescent hypopituitarism of the anterior lobe, the writer has grouped those female cases which have had some osseous changes indicative of early anterior lobe disorder, and which developed, after the age of maturity, amenorrhea, metrorrhagia, or dysmenorrhea, dissociated from any local or general disease, that reacted completely to substitution treatment of anterior lobe extracts. Under the hyperactivities of this lobe are described the well-known clinical syndromes of gigantism and acromegaly. These differ from case illustrations ordinarily found in the literature, by having negative evidence of posterior lobe involvement, such as polyuria, adiposity, abnormalities of basal metabolism, carbohydrate tolerance and unstriped muscle contractions.

Under the posterior lobe dyscrasias, the differentiation between the opposite states of activity was not so clear-cut. There

is yet considerable uncertainty as to whether hypophyseal polyuria should be classified with the varieties of insufficiency or of overactivity of this lobe. These cases are most easily explained by Bab's theory, which attributes them to the pars intermedia insufficiency. The writer has observed 9 (of 11) cases of typical diabetes insipidus, reacting positively to hypophyseal extract treatment, 3 of which were free from other "hormonic" signs both of the anterior lobe and the pars nervosa disorders. This might be explained by defining a simple pars nervosa syndrome as consisting clinically, in the hypoactive state, of obesity, and in the hyperactive state, of increased basal metabolism and decreased sugar tolerance. On the contrary, it is true that the majority of the polyurias attributed to the hypophysis have other endocrine symptomatology connecting them with either the anterior lobe or the pars nervosa portion of the posterior lobe. The hypoactivity of the pars nervosa, independent of the pars intermedia, is given as pure pituitary obesity, not associated with "hormonic" signs of the anterior lobe or polyuria, but having positive evidence of a decreased basal metabolism and increased sugar tolerance. Under the hyperactive varieties of the posterior lobe is classed hypophyseal glycosuria. This is a glycosuria which can be differentiated from one due to pancreatic disorder or one associated with ductless gland dyscrasia. It has the usual increased metabolism and decreased sugar tolerance, but is free from polyuria and "hormonic" signs of anterior lobe disorder.

Under the bilobar divisions are grouped those cases in which there is a concomitant anterior and posterior lobe disorder existing in the same individual. In order to include all cases thus represented, three activities must be considered: (1) hypoactivity of both lobes; (2) hyperactivity of both lobes and (3) heteroactivity, in which the lobes have an opposite secretory function. Under hypoactivity, Froelich's disease, either with or without polyuria (the former as described by Biedl) is classed. Under hyperactivity, those cases of gigantism or acromegaly and glycosuria, with which are associated increased metabolism and decreased sugar tolerance, without adiposity, are grouped. This classification takes many of the cases of both gigantism and acromegaly out of the simple anterior lobe dyscrasia variety, for it has been well known for many years that a large percentage of

these cases have been associated with posterior lobe symptoms, such as polyuria, glycosuria, and disturbance of metabolism and sugar tolerance. Nevertheless, they have been classed by many authors either as simple anterior lobe dyscrasias, or have been grouped under the gross term "pituitary dystrophy."

The heteroactive varieties of bilobar pituitarisms should contain those cases in which the individual lobes of the hypophysis have opposite activities. For instance, gigantism or acromegaly, associated with polyuria, a not infrequent variety, should naturally be placed in this bilobar variety. Another considerable percentage of these diseases shows evidence of anterior lobe hyposecretion (such as genital aplasia and infantilism, amenorrhea, sexual impotence, muscle fatigue, and mental apathy), associated with posterior lobe hyperactivity (such as pituitary glycosuria, with increased metabolism and decreased sugar tolerance). It is the hope of the writer that this conception of a heteroactive bilobar division will be the means of disentangling many of the so-called dyspituitarisms and dystrophies, which have been so ill-defined that they add only confusion to the efforts toward diagnosis and treatment.

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HEMORRHAGIC SYNDROME CURED BY THYROIDIN*

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Although much has been written upon the subject of thyroid opotherapy, the indications for this treatment are still so indeterminate as to demand many more data. The following is a report of a case in which severe hemorrhagic manifestations were successfully controlled by the use of thyroidin.

The patient is a woman twenty years old, under-weight and whose hereditary antecedents are of no importance. Menstruation commenced at eleven years, was profuse and usually lasted twelve days, during which time severe epistaxis occasionally occurred. Using thyroidin the menstruation period was reduced to three days and the nasal hemorrhages arrested. As soon as the patient ceased taking this product the disturbances returned.

When she was about 12 years old her eyebrows began to fall out. At 14 years of age she gave birth to a child, and during childbirth acquired a puerperal infection, causing cervicitis and adnexitis. From this time until she was 19 years old the patient suffered three induced abortions and a mercurial intoxication, the latter producing a mild nephritis of which she was cured.

During the periods when opotherapy was omitted the patient suffered from otorrhagia and sub-conjunctival hemorrhage in addition to the other hemorrhagic disturbances. Owing to her negligence an acute hemorrhagic attack occurred, signalized by metrorrhagia, epistaxis, hemoptysis and purpura; this was resistant to the classic coagulative treatment. One of us then thought of using thyroid opotherapy, which was successful in arresting the hemorrhages. This once accomplished, clinical examination proved the existence of the adnexitis already mentioned.

*This paper has appeared elsewhere. It was accepted before the rule of exclusive publication was announced.

Laboratory tests disclosed the following conditions.

Urine, normal.

Wassermann reaction in the blood, negative.

Thorax, by radioscopy, normal.

Hemoglobin	85%
Coagulation and retraction of blood coagulum	Normal
Red corpuscles	4,170,000
White blood corpuscles	8,600
Neutrophiles	62%
Eosinophiles	6%
Basophiles	1%
Lymphocytes	25%
Large mononuclears	5%

DISCUSSION

Our patient had a pale, swollen face and an abnormal tendency toward vasodilatation phenomena in her cheeks. The falling of the eyebrows combined with the above was the only symptom of the minor hypothyroidal syndrome so well described by Levi and Rothschild (1).

We believe the case is probably a form of dysthyroidism, a diagnosis which, although it cannot be assured, should be considered, more especially in view of the remarkable results obtained with the thyroid therapy.

In a previous publication (2) we have insisted upon the desirability of taking much notice of those minor symptoms, so that we may finally be able to make a positive diagnosis when the aborted forms of hypothyroidism are encountered.

Without further discussion we wish merely to mention that Hertoghe (3) Werklen and Walther (4), and Max Perlsée (5) demonstrated some time ago the existence of hemorrhagic conditions in hypothyroid cases. These may result from dyscrasic alterations, or as one of us (6) has demonstrated contemporaneously with Levi (7), from congestive phenomena. Moreover, it is apparent that in some cases of hemorrhage that cannot as yet be attributed exclusively to a thyroid origin the success of thyroid therapy has been no less remarkable. This is evidenced by Sheffler's (8) observations on Werlhof's purpura, and by the studies of Taylor (9) and Marcel Labbé (10) in hemophilia.

In conclusion, although we are unable definitely to assert that the origin of this hemorrhagic complex lies in a purely thyroid dysfunctioning, it is nevertheless certain that the results secured emphasize the practical importance of thyroid therapy, whatever its form of action.

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PUBERTAS PRECOX WITH ESPECIAL ATTENTION TO MENTALITY*

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Pubertas precox is a syndrome manifested by premature maturity, anatomically, physiologically, and often mentally, as a result of faulty metabolism induced, supposedly, by endocrine disturbances.

That this condition was recognized by the ancients is beyond doubt. For the first account of the condition recognizable as a clinical entity we must go back to Craterus, the brother of King Antigonus (1), who writes: "The subject was an infant, a young man, a mature man, an old man, was married and begat children and all in the space of seven years."

Pliny the elder, who lived in the reign of Vespasian, handed down the history of certain remarkable children; he states: "It is well known that there be some that naturally are never but a foot and a half high, others again somewhat longer, and to this height they came in three years, which is the full course of their age, and then die. We read, moreover, in the chronicles, that Salams, one Euthimenes, had a son who, in three years, grew to be three cubits or four and a half feet high, but he was in his gait slow and heavy, and in his wit as dull and blockish, howbeit in the time overgrown he was, and his voice changed to be great, and at three years he died suddenly of a general cramp" (2).

In 1747 Mead (3) presented before the Royal Society of London, a patient who was "remarkable for his bulk and height," and also for the external marks of puberty, which were first observed at the age of twelve months. At the age of five he had pthisis pulmonalis and died in a few months. "He had when dead the appearance of a venerable old man."

One of the first well observed cases was recorded over a century ago by Anthony White (4). He presented "Philip Howarth in whom signs of puberty commenced at an early age."

*Read before the New York Neurological Society April 6, 1920.

The family history was negative, gestation was normal, and he was the ninth child born. At birth he had a full crop of hair; the sutures of his cranium were closed, but a slight fontenalle was palpable. At the end of the first year a change took place; his hair had grown to a great length, he grew pale and ugly in appearance. Small hairs appeared on his pubis; his testes and penis increased in size, and his voice altered. White, who was keenly interested in the lad, invited him to his home for further observation. He states: "On first view of the boy the manly character, strongly expressed, is extremely striking. His voice is like that of a young man of sixteen years and he can whistle very low tones; his laugh is loud. There was no hair on his chin, but steatomatous matter was present which usually makes its appearance preceding the growth of a beard. His teeth were spaced (how many not recorded); the nipples were prominent; no hair was visible in the axilla, but there was an odor emanating as that of an adult. His height was three feet, two inches and he weighed 47 pounds, i. e., at two years. At three years his height was three feet, four and a half inches and his weight was three stone, nine and a quarter pounds, or fifty-one and a quarter pounds." He was observed to have an understanding of a six-year-old child and, quoting this keen observer, "many of his observations and inquiries appeared to have been the result of mature reflection. It must, however, be observed that his general character was marked with a considerable mixture of childish playfulness. He was mild and not easily provoked to anger. When, however, his rage was excited, it was not expressed in the usual manner of children, but by the lowering of the eyebrows, the shaking of his head and with uplifted fist. He had a talent for music and sang with correctness."

The factor of hereditary transmission is apparent in the following two cases. Plumb (5) delivered a mature looking child whose facial appearance was feminine, and gave the impression of a delicate twelve-year-old child. Her external genitalia were developed as those of a child of seven to eight years, and her form was that of a fifteen-year-old girl. Her head was covered with thick, beautiful, brown curly hair which was three to four inches in length. There was no hair in the axilla. What was more remarkable was the beginning of menstruation when she was six weeks old. She menstruated for two and a half days

each month thereafter. At the time the case was recorded, she was ten months old and perfectly well. The child's clitoris was so long as to necessitate amputation. The parents of this child were both very vigorous sexually. Irion (6) reported a similar case in which menstruation first appeared seven days after birth; the patient showed the characteristic nervous phenomena when she skipped a period.

In the following case reported by Stone (7), there is a direct history of pubertas precox in the father. The subject when dressed gave the impression of a ten-year-old lad; he was actually four years old. When he disrobed, he looked the typical Infant Hercules, showing a fine physical development of a young man of 21. He was 4 feet, ¼ inch tall and weighed 70 pounds. His secondary sexual characteristics were fully developed. Mentally, the boy showed a lively intelligence; he was very talkative at home, but shy with strangers. His speech seemed to be imperfect. He was nearly always in good humor, but when angry settled his quarrels with old-fashioned "knock-down blows." The father, as mentioned above, was prematurely developed, and his first sexual indulgence occurred at the age of eight. He stated that between the age of ten and thirteen, "he was a better man than he has ever been since." Rogers also quoted a number of cases that showed the factor of heredity.

The direct causative factor of precocious puberty is hypersecretion of either the gonads, pineal gland or adrenal cortex, as indicated by hyperplasia or neoplastic development. That the pituitary and thyroid are also concerned, secondarily, however, is unquestionable. It will be necessary, therefore, to divide the cases of premature precocity into those that have acquired this syndrome through neoplasms and those due to hyperplastic states.

Ovarian Type. Rogers has collected 101 cases of pubertas precox; of these 81 subjects were females and 20 males. Of the 81 female cases, 73 appear to be due mostly to hyperovarianism. The cases of Krabbe (8), Wells (9), Lenz (10) and Bruno Wolff (11), were also of this type. Lenz's case was studied very carefully. He first saw the child when she was six and one-quarter years old. Menstruation had begun at 16 weeks. The secondary sex characteristics were those of a mature woman. She was shy and easily embarrassed. She went to school and was a good pupil.

She played with children of her own age and was childish in activity. She was again seen when twelve years old, when she appeared to be twenty-two. Her behavior was still childish, and extraordinarily shy. She was still playing with dolls. She cried pitifully when the other children teased her about her large breasts.

An instance of neoplasms of the ovary producing pubertas precox is recorded by Lucas (12). The little patient was seven years old and showed all the signs of genito-somatic maturity and early menses. A tumor of the ovary was diagnosed and after its removal all the signs of adolescence and menstruation disappeared. Blair Bell (13) quotes Roger Williams, who collected eleven cases of sexual precocity in female children, due to neoplasms of the ovary. However, one should not draw the conclusion from this that all ovarian tumors in young children necessarily lead to sexual precocity. There must be other factors entering into this mechanism.

To summarize the mental traits and habits in these ovarian cases, it can be said that none show mental precocity. In fact, the subjects are of a low mental type. They speak, play and act in accordance with their true age. The girl reported by Lenz (10) still played with her dolls, although she gave the physical impression of a girl of twenty-two. They learn well at school, but they show no "old-fashioned" way of thinking, as Krabbe (8) puts it. Neurath (14), who had a considerable opportunity to observe them, also comes to the conclusion that their psychic condition is not so far advanced as their physical. That some of these children put away their toys and become seclusive is to be ascribed to self-consciousness rather than to any mental maturity

Adrenal Cortex Types. The clinical picture differs here, according to whether the male or female is involved. When there occurs hyperplasia of the adrenals in the male, it tends to accentuated masculine precocity. When it occurs in the female it tends to change the female into the male type, and to give her the secondary sexual characteristics of the male.

In a case reported by Marchand (15), a girl was baptized as a male. As a result of a medico-legal examination, it was found that her body showed a spurious hermaphrodism with hair over face and body, and a clitoris as large as a penis. At autopsy

she showed hypertrophy of the adrenals, and particularly of the cortex.

Tumors of the Adrenal Cortex. Pitman (16) reported a girl of three who showed nothing child-like in either voice or manner. She often seemed idiotic, but aggressive. She showed bushy eyebrows and a moustache in addition to other male characteristics. A tumor of the adrenal cortex was found.

Bulloch and Sequeira (15) collected 12 cases of adrenal tumors. Ten were found in the female and two in the male. Orth (15) reported the case of a girl of 4½ years, who had so much hair on her face that she had to be shaved. The clitoris was the size of a small penis. She had a neoplasm of the right adrenal. In Dobbertson's (15) case, a girl had a mass of hair on her back. Glynn (17) reports the case of a girl of 7. She had the appearance of a young man, with a black silky beard, a moustache and whiskers.

These cases therefore show uniformly hypertrichosis of the male type. All manifest a large clitoris, which shows the tendency towards male sexuality, and all showed an absence of menstruation, with the exception of one case reported by Bulloch and Sequeira (15), in which menstruation appeared at the age of a little more than ten years. The appearance of menstruation at this time can hardly be classed, however, as precocious.

A case of adrenal origin in a boy of 5½ is reported by Linser (15). The physical development was that of from 16 to 18. Sex characteristics were of the male type. The pineal, pituitary and thyroid glands were found to be normal.

As regards mentality and habits in these cases, the literature is far from satisfactory. It indicates, however, that while they show some aggressiveness, in the main, their psychic condition is below par. Pitman states that his case showed idiocy; Bulloch and Sequeira and Colcott Fox (15) state that their cases showed a dullness of intellect. Glynn's patient was dull and apathetic; she took no interest in her surroundings and would answer questions only if they were frequently repeated.

Hypergonadal Condition in the Male. Sarchi (18) published a case that showed a malignant tumor of the left testicle. At 5, the testicle was as large as that of an adult. The boy grew rapidly, his voice grew to a deep bass, and hairs appeared on his genitals. At 9 years, he was 143 cm. in height and weighed 44

kilograms. The left testicle was removed and an alveolar carcinoma was shown. Four months after the removal, his beard disappeared, his voice again became child-like and his genitals were getting smaller. His sexual impulses, emissions and erections ceased. His character in general reverted to the childhood stage.

A case of hypergenitalism was reported by Strauch (19) of the Cook County Hospital. In this instance no anatomico-pathologic changes were found. No cerebral symptoms were present. No tumor of the pineal was suspected. The boy was 11½ years old and had previously shown mental retardation. His genitals, including the prostate and seminal vesicles, were developed as in an adult, but no spermatozoa were found. His voice was strikingly deep. As to his psychic condition and habits: He was irritable and nervous, and cried whenever his mouth had to be examined. He was stubborn, disobedient, troublesome and showed a resentful disposition towards other children. At home he played with boys younger than himself. There was no evidence of sexual shame, nor was there any visible propensity for the other sex. He could not count to more than five, and even then he had to be helped. His handwriting was not legible, nor could he write his own name without having a copy placed in front of him. He attended school for three years, and he could not execute a simple example of addition, nor did he remember his songs or prayers.

Morse (20) reports a boy of 23 months with genito-somatic precocity and delayed mentality. An X-ray examination of the skeletal system revealed the bony development of a 6½-year-old boy. No spermatozoa were found in the emissions. Woods (21) and Lopez (22) report cases that are of undoubted hypergonadal origin. Both subjects showed remarkable strength. The former was 6¾ years old and was nearly 5 feet tall. He was so mischievous and full of animal spirits that he had to be placed in an industrial school. It took three policemen to get him there. The latter subject was a colored boy of 3 years and ten months; he showed genito-somatic precocity and lifted a man of 140 pounds from the ground with ease. The case of Gilbert Breschet (23) should also be included here.

The mentality and habits in these cases show no precocity. In fact, the subjects are retarded and, according to Moreau (24), Hofacker (25), Hudoverning and Popovitz (26), Ziehn (27) and Neurath (14), may even show idiocy and imbecility. Neurath, who reported 27 cases of this type, is quoted by Strauch (19), that "in most cases there existed the psychic function of their infantile age."

Pineal Tumors. Neoplasms of the pineal gland have drawn attention to the subject of pubertas precox, as no other condition has. The opinion once prevailed that pineal tumors exist only in the male. This, however, has since been disproven. Baily and Jellife (28) collected and reported in an excellent paper 59 cases of pineal tumors, together with an additional case of their own, making 60 in all. Seventeen cases showed involvement up to the age of 16. Fourteen of these occurred in the male and three in the female.

There is this to be said in reference to tumors producing precocious puberty, that while the pineal tumors occur predominantly in the male, tumors of the adrenals as hypernephromata, occur five times oftener in the female.

I must agree with Gordon (29) that the histories of the recorded cases are inadequate, not only as regards pineal tumors, but all the subject matter herein discussed. The clinical observations are too meagre, often, for correct endocrine interpretation, and it seems the further back one goes the more illuminating and keener are the clinical observations of the writers.

The following cases of pineal tumors bear on our subject.

Aesterich and Slawyks (30) report a boy who was a still birth baby, as a result of forceps delivery, but who developed normally during the first year of life. Convulsive attacks then set in. At 3, this child, who was formerly bright, became strikingly quiet and shy and sat in the corner and cried. Genitosomatic precocity then became apparent. Mentally he was somewhat precocious,—what the Germans call "altklug." This boy displayed no onanism.

Von Frankl-Hochwart (31) reported a boy who, at three, grew with excessive rapidity and showed mental precocity. At 7 years, his precocity was astonishing. He pondered and discussed at length the immortality of the soul and the life after death. This case made such an impression on Dana and Berkely (32), that it led to the well-known feeding experiments on the mentally backward children in the New York Public Schools and to the experimental work at Vineland by Goddard (33). At autopsy, in the case mentioned, a teratoma of the pineal was found. In fact most of the tumors of the pineal are teratomas.

Baily and Jellife (28), who went into the mental study of their case much more than any of the other writers, state that the boy who was formerly bright in school work began to show a failing memory. He also grew more reserved and apathetic. He showed a tendency towards depression and cried often. The Zeihn test "revealed a lack of retention, with a marked slowing of all responses."

Gauderer (28) reports a boy of 12 who had a fixed expression, was apathetic and who answered questions slowly but clearly.

Raymond and Claude (30) report the case of a boy of 10, who was mentally apathetic and answered questions well, even slightly better than most boys of his age. His memory was good, but he showed a slight depression.

Kidd (30) reports the following cases, by Pellizzi and Machell. The first case of Pellizzi showed genito-somatic, together with mental precocity; the other case did not. The first subject, although only 2 years old, had seminal emissions that contained spermatozoa. Onanism was not present.

Machell reports two cases, one of which was interesting. This boy at 17 months had erections and emissions. In addition to his genito-somatic precocity, he showed marked mental precocity. At 44 months of age, he showed a disdain for the toys of small children. His habits bespoke an older boy. His manner was independent; he was perfectly self-possessed with strangers, and his answers to questions were given in a loud, bass, stentorian voice.

Kidd (30), although he wrote a thorough review of the literature, historical, clinical, experimental, etc., of the pineal, mentioned nothing concerning the mentality in pineal involvement.

From a comprehensive study of the literature, by which the various types of puberatas precox were classified, together with their respective mentalities, it can be said that mental precocity is non-existent, aside from its manifestation in the pineal type. In fact, there is in the major number a hypo-mental state, which gradually shades off into absolute idiocy. The subjects are in the main childish, and their mentality bespeaks their true age. In those cases, in which, through tumor growth, intracranial pressure is produced, various degrees of mental disorder arise, but such are scarcely germane to our discussion.

A trait common to all cases of precocity is the reserve, thoughtfulness, or quiet they manifest. They like to sit in a corner by themselves. Stanley Hall (34), in speaking of the psychic traits attending normal puberty, states that, "Inner absorption and reverie is one marked characteristic of this age and transition." This observation can, I believe, be applied to our cases, and is not in itself indicative of abnormality. Some writers believe that early sexual desire is a sign of mental precocity. This I believe is incorrect. It is purely an instinct.

DIAGNOSIS

To reach a diagnosis as to the particular gland involved primarily, and especially if there is any tendency towards readjust-

ment, one must: (1) have the cases under close clinical observation; (2) study their metabolism, particularly, as Blair Bell has advised, the calcium output, and (3) make Roentgen ray examinations for skeletal development and for the disappearance of the epiphyseal lines, as shown by Krabbe (8), Lenz (10) and Timme (35).

The approach to a correct diagnosis is somewhat difficult at present, in view of the fact that glandular structures that are seemingly antagonistic, produce nevertheless the common syndrome, precocious puberty. However, upon analysis there are always found some points of difference in respect to the particular gland involved.

Gonadal Type. In the female type due to hyper-ovarianism we always get early menstruation. This leads to excess calcium elimination, and therefore we find the subjects (if of pure ovarian type) always short in stature. If the skeletal system is examined by Roentgen ray, we find the epiphyses of the long bones closed. This fact is borne out clinically, that girls who menstruate early are usually short and those who menstruate late are tall. This tends to hold for races as well as individuals. Again the distribution of the hair is of the female type, as are the secondary sex characteristics, facies and form.

In the masculine gonadal type there is also short stature, concomitant with closed epiphyses, marked male secondary characteristics, deep voice, enlarged prostate and seminal vesicles and often emissions, either sterile or containing spermatozoa. What seems characteristic of this type is the marked physical strength manifested.

Adrenal Type. In the female we find marked hypertrichosis and secondary characteristics of the male type,—large clitoris, male facies and absence of menstruation. The case of Irion is an exception.

While we were always taught that the cortex of the adrenal has for its function the production of sex characteristics only, the work of Cramer (36) indicates that the cortex also participates in the production of adrenalin. The question of blood pressure should therefore be taken into account in a differential diagnosis.

The male adrenal type is difficult to differentiate from the gonadal except, perhaps, by their stature. Both types manifest accentuated male characteristics.

Pineal Types. In these the Roentgen plates should portray a shadow due to the acervalus cerebri, as a result of early involution, as shown by Boas, Scholtz (37) and Timme (38). Whether pure hyperplasia of this gland should give precocious puberty, as indicated by the work of McCord (39), Dana and Berkeley

(32), etc., or hypoplasia or recession of the gland according to Marburg, it is at present impossible to say.

Finally one may say that there are undoubtedly individuals living today, who were cases of pubertas precox, and undetected as such, who will undoubtedly live to a ripe old age. What takes place here is a compensatory readjustment of the excessive secretions by their antagonists, just as we see in the ultimate adjustment in the syndrome of thymus, pituitary and adrenal of Timme (35).

CONCLUSIONS

The literature as a whole supports the following conclusions.

1. Pubertas precox arises in certain individuals, whose progenitors show a particular type of endocrine imbalance.
2. The condition may arise in utero, or as a result of functionating rests, i. e., tumors, later in childhood, previous to puberty.
3. The entire internal glandular system is involved, but primarily the gonads, pineal and adrenal cortex.
4. Gonadal types predominate, then follow the pineal, and last, the cortico-adrenal.
5. Pineal types occur mostly in the male; cortico-adrenal and gonadal in the female.
6. Mental precocity is very rare and is found only in those in whom the pineal is primarily involved, and then only in the male.
7. The mentality in the other types is either unaffected or retarded.
8. The manifest mental precocity is of the child-like, imaginative form, and has no real substantial basis.
9. With early diagnosis in the hyperplastic type, readjustment can be aided materially by proper endocrine therapy.

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THE ENDOCRINE SECRETION OF HEN-FEATHERED FOWLS

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In the older literature there are many references to changes that have been noticed in old hens and female pheasants that make these birds more like the males of their species. They become quarrelsome, they sometimes crow, the feathers change their color, etc. It has been recorded in several cases that these changes appear after the female has ceased to lay, and in a num-

Fig. 1, A. Sebright Bantam male; B. Sebright Bantam female.

ber of cases that the change was associated with a diseased condition of the ovary. Complete removal of the ovary of birds is a difficult operation owing to its irregular shape and to its close adherence to the body wall. Goodale has succeeded, nevertheless, in completely removing the ovary of young fowls. When the adult plumage develops in such birds it is like that of the cock of their breed. In the Leghorns, where the difference between the sexes is very great, the result is most striking. The comb and wattles, and the spurs also, grow larger than in the normal hen. Evidently something produced by the ovary—some internal secretion perhaps—inhibits the full development of the

plumage of the hen, of her comb, and sometimes also of her spurs.

Castration of cockerels is regularly practiced to make capons. The capon has all the characteristics of the male and its feathers may be even longer than those of the normal male. The comb, however, remains undeveloped, or, if already large, it dwindles to a fraction of its original size. Here removal of the "reproductive gland" does not change the characteristic plumage of the male, but does change the comb in the direction of the condition found in the hen.

There is one race of domestic fowls in which the cock is hen-feathered. The Sebright Bantam male, Fig. 1 A, differs from

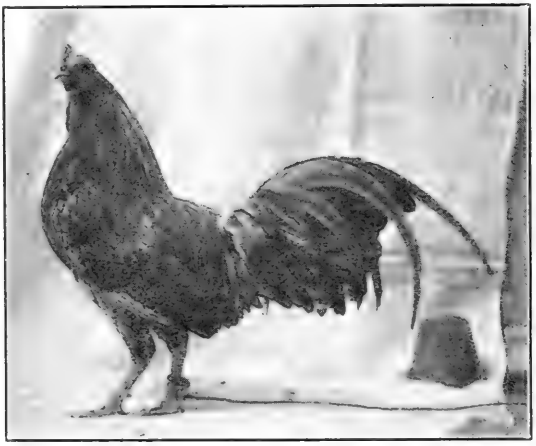

Fig. 2. Sebright Bantam male, after castration, showing cock-feathering.

the ordinary cock in that his feathers are like those of the hen, Fig. 1, B. Both sexes have golden feathers with a black margin. The most striking feature of the plumage of the Sebright male is that the feathers of the back and rump are rounded at the tip and lack the peculiar hackles of the ordinary cock. This resemblance of the male Sebright to the female suggested to me the possibility that if his testes were removed he might change as does the hen when her ovary is removed. In a word, he might become cock-feathered. I carried out some experiments of this kind in 1915, and the results have been fully described in one of the Carnegie Publications (No. 285, 1919). The result of the operation was most striking. As the new feathers came in, it was at once obvious that they were like those of the ordinary cock

bird. When the complete moult had taken place the birds appeared as shown in Fig. 2. The castrated male was now a rich orange color above; the black margin of the feathers over the whole dorsal surface had disappeared; the back and saddle feathers were long and pointed as were those of the neck also. All of these had the characteristic hackles at their outer margins. The tail was now covered with long yellow tail coverts, that are not present in this form in the hen-feathered male.

On the under surface of the castrated males the changes were much less, although the golden centers of the feathers had become darker. The comb and wattles diminished until they

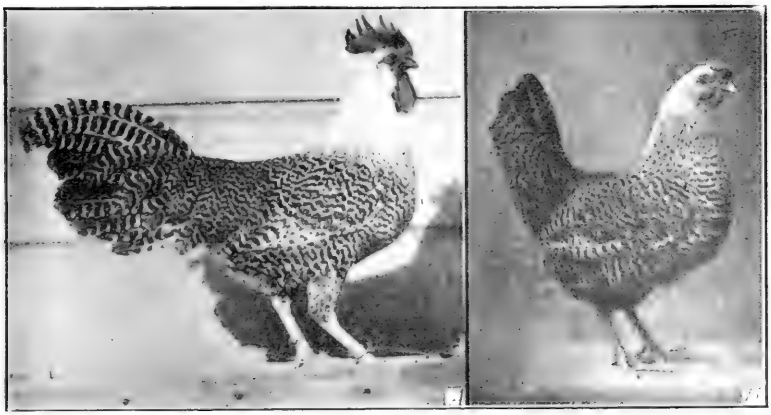

Fig. 3, A. Campine male, hen-feathered; B. Campine female.

were no larger than those of the hen. The effect is the same as in the true capon. Thus results confirmed expectation; the hen-feathered male changed after castration into a cock-feathered bird so far as the plumage was concerned.

There are a few races of poultry in which both hen-feathered and cock-feathered males exist. The Campines have two such kinds of males. In some countries one type is the standard; in other countries the other type. It is more difficult to make from a mixed race a type pure for hen-feathering than one pure for cock-feathering, since the former is a dominant Mendelian character and may carry, but not show, the recessive cock-feathered factor. For the purpose of my experiment it was necessary to obtain a race pure for hen-feathering, and this I succeeded in finding.

The feathers of the hen-feathered male, Fig. 3 A, are barred (except those of the neck) and are like those of the hen, Fig. 3 B. In the cock-feathered male on the contrary the feathers of the back and rump are white and pointed, while the tail coverts are black and long.

When a young cockerel of a hen-feathered breed is castrated he changes over, (Fig 4), as his new feathers come in, until finally he is exactly like the cock-feathered male. His neck feathers become very long and become completely white. The back and rump feathers lose their barring and become white, very long and pointed, and show well developed hackles at the margins. In

Fig. 4. Campine male, castrated, showing cock-feathering.

a word, the hen-feathered male comes to resemble the other type of male. The comb and the wattles, however, remain small as in ordinary capons. Concerning the source of the internal secretion that is probably involved in these changes, the following histological facts are of great interest. In the ovary of the hen there are groups of interstitial cells, called luteal cells (Fig. 5). They are large, clear cells in ordinary preparations, but are found to be filled with granules when methods of preparation are used that avoid the loss of this material. In the adult cock-feathered males these cells are entirely absent as a rule, or at best only sparsely found, and then with shrunken nuclei. In the Sebright cock and in the hen-feathered Campine large numbers of such cells, filled with materials, are present (Figs. 2, 3, 4). In the

hen these cells may be supposed to produce an internal secretion that affects the development of her plumage in such a way that it never shows its complete possibilities. When her ovary is removed this secretion is no longer produced, and she then develops her full plumage, which is the same as that of the male of her race. In the male Sebright and in the hen-feathered Campine the internal secretion produced by their luteal cells may be supposed to suppress in them also the full development of the plumage, but when they are castrated the cells are removed and cock-feathering develops.

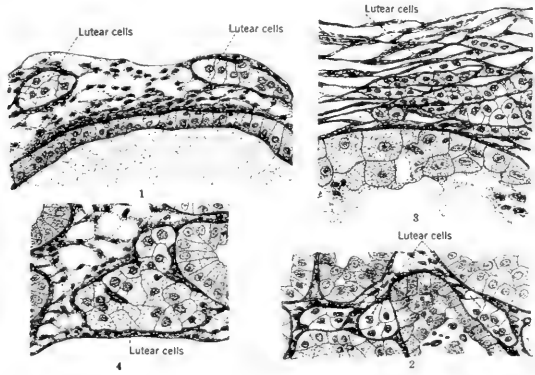

Fig. 5. Lutear cells: 1, in hen's ovary; 2, 3, 4, in testes of Sebright and hen-feathered Campine cocks.

In young chicks of ordinary breeds, the luteal cells are present, both in the males and in the females. This holds also for the young Sebrights as Dr. J. F. Nonidez has recently found. These cells disappear largely or entirely in ordinary breeds, as the birds reach maturity; but in the races with hen-feathering they continue to develop, and remain functional, producing in the males the same effects as they do in the hen of all breeds. The development of the comb and wattles of the male is dependent on the presence of the testes, but it appears that the luteal cells are not directly responsible for their development, because the comb of the hen is small. Some other part or tissue of the ovary and of the testes must be involved in the development of these organs.

ABSTRACT

SOME CONDITIONS AFFECTING THYROID ACTIVITY

W. B. Cannon and P. E. Smith

(1) Gentle massage of the thyroid gland in the cat for two or three minutes will cause an increased rate of the denervated heart amounting in some instances to 33 per cent. over the basal rate.

(2) Massage of another gland, e. g., the submaxillary, does not cause this effect.

(3) The augmentation of heart rate caused by thyroid massage occurs in the absence of the adrenal glands.

(4) Stimulation of the cervical sympathetic trunk as it leaves the stellate ganglia induces a similar augmentation of the rate of the denervated heart; this does not occur if the thyroid gland has previously been removed.

(5) If the cardiac fibres from the stellate ganglia are severed, as well as the vagus nerves, and an afferent nerve such as the sciatic or brachial is stimulated, under such a degree of anesthesia as will permit reflex retraction of the nictitating membrane and dilation of the pupil, there is a primary increase of rate, due to adrenal discharge, which is followed by the slowly developed increase characteristic of the thyroid effect.

(6) If the vagi and the cardiac fibres of the stellate are cut and the animal is asphyxiated under conditions which permit the eye changes described above, there is a similar primary rise due to adrenal secretion followed by the secondary thyroid effect.

(7) If the thyroid glands have been previously removed, sensory stimulation and asphyxia induce solely the increase of rate due to adrenal discharge. The development of the maximal increase of rate from thyroid activity, usually requires from 30 to 60 minutes and passes off in a similarly slow manner.

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PHARMACODYNAMIC SUBEPIDERMAL TESTS: II, INDIRECT TESTS; A, THYROIDIN

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A series of investigations is being undertaken in our Institute in an endeavor to ascertain to what extent the intracutaneous injections of endocrin substances and those especially related to the autonomic nervous system can be utilized in practical diagnosis. In a previous issue of this Journal, the results secured with pituitrin were briefly described (2).

The desirability of investigating thyroid material in this way was obvious although it seemed, a priori, less promising on account of our inability to utilize a definitely identified, pure active principle.

As compared with a control subepidermal injection of water, that of thyroid extract differs in giving rise to a larger papule and a greater degree and duration of erythema. The reaction was found to vary a great deal with the individual, however, being now more active and lasting, now so attenuated as to become indistinguishable from the control reaction. But the same variability in the reaction picture is seen following injections made in a given subject at the same time with other extracts, e. g., of ovary, thymus or testicle. The problem does not seem to lend itself, therefore, to a simple, direct attack. Can it be solved by *indirect* methods?

Among the different endocrin organs there are close relationships of interdependence, synergy or antagonism. In the case of adrenalin and pituitrin, characteristic reactions are directly attainable by means of subepidermal injections. In case of other endocrin organ extracts, as above mentioned, unequivocal reactions are not readily secured. The problem then presents itself: Can the adrenalin reaction be characteristically altered—attenuated or accentuated—by the use of extracts of different endocrin organs? The sensitivity of the organism to such materials might thus be disclosed. As a case in point, does the addition of thyroid extract in a quantity not in itself causing reaction lead to augmentation or attenuation of the adrenalin cutaneous re-

action as it has been reported by Falta to affect the metabolic reaction and by Oswald and others to affect the vasomotor reaction?

The test has given positive results in certain pathological but not in normal subjects (3). A given individual reacts distinctly to adrenalin in 1:200,000 dilution, but only feebly to 1:1,000,000. If to the adrenalin in these dilutions a small quantity of thyroid extract (0.01 to 0.005 cc.) be added (4)—a quantity which in itself gives no direct reaction distinguishable from that to distilled water,—*the adrenalin reaction is distinctly enhanced and more protracted,* as compared with the reaction to the adrenalin alone. The central red color in the reacting zone is also often deeper.

The same activation may be demonstrated in case of pituitrin instead of adrenalin and *this second indirect test may be found in cases in which the former is negative* (5).

Contrary to the results obtained with thyroid extract, other endocrin glands seem to attenuate the adrenalin reaction. We shall have occasion to report further upon these latter extracts as well as upon the clinical significance of the indirect *thyroidin test.*

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2. Ascoli, M. and Fagiuoli, A.: Pituitrin test. This Journal, 1920, **4,** 33-36.

3. It is presumed that the failure to obtain the phenomenon in the normal subject is due to the insufficient amount of active material in the thyroid extract employed. The result was the same, however, with Oswald's thyreoglobulin.

4. The extracts employed by us are of 25 per cent strength in physiological saline solution, obtained from bovine thyroids under a pressure of 350-400 atm. to the sq. cm. The extract is filtered through porcelain, preserved with ½ per cent chloretone and distributed in sterilized vials. For this preparation we are indebted to the "Instituo nazionale medico farmacologico" of Rome.

5. We have frequently alluded to the necessity of making the injections superficially and strictly subepidermically. This condition is all the more essential in the thyroidin test in whch are to be compared only differences in *intensity* of reactions of the same category such as could readily be produced merely by variations in the depth of the injections. In order to obviate error when differences are small, the test may be made in duplicate or triplicate and be regarded as positive only when the result is obvious and the difference easily appreciable to one not concerned in the result.

STUDIES ON DISORDERS OF THE THYROID GLAND

HYPERSENSITIVENESS TEST WITH ESPECIAL REFERENCE TO "DIFFUSE ADENOMATOSIS" OF THE THYROID GLAND.*

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Further experiences with my epinephrin hypersensitiveness test during the past year have led to a more intensive study of the so-called border-line cases. In these is found the familiar syndrome of asthenia, loss of weight and strength, nervousness of varying degrees, labile pulse, mild tachycardia, perspiration and tremor, sometimes depressions, and often slight elevation of temperature without, however, any special gross pathological findings in the thyroid gland on physical examination, and without positive eye changes such as are found in exophthalmic goitre. The diagnosis in these instances lies largely between mild chronic hyperthyroidism, incipient tuberculosis, neurocirculatory asthenia, effort syndrome, psychasthenia, psychoneurosis, neurasthenia and other allied nervous states or perhaps even certain chronic infections, for it seems possible that a syndrome of this character, if not actually caused by infection, may be made worse by it. In a series of these individuals most of whom had been suspected of having tuberculosis, while others were thought at first to have psychoneurosis or neurasthenia, and who had failed to improve after the ordinary medical and hygienic measures, there was finally obtained a positive epinephrin hypersensitiveness test which is so characteristic of hyperthyroidism, though, to be sure, not absolutely pathognomonic of it. Because of the failure of the ordinary medical and hygienic measures in the treatment of these individuals,—at Saranac Lake and other sanatoria; because, further, in those suspected of having tuberculosis, little or no tuberculosis was found upon expert examination; because in all there was a fairly uniform syndrome which resembled mild hyperthyroidism and, lastly,

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because of a positive epinephrin test, which is negative in pure tuberculosis, I felt justified in advising operation. This consisted usually in a bilateral partial resection of the thyroid gland. In view of the improvement following operation, and because of the characteristic change in the glandular histology, I felt that these cases formed a special and interesting group in thyroid disorders, exhibiting a new clinico-pathological syndrome which deserved reporting, in the hope that more interest and study be awakened in it.

Upon careful histological study of the thyroid gland removed in these cases I found a rather characteristic and striking pathological change which has heretofore escaped general notice, and to which I have applied the name, "Diffuse Adenomatosis." It is my purpose in this report to speak in somewhat greater detail with regard to the importance of this condition in the etiology of latent hyperthyroidism and with regard to its differentiation from incipient tuberculosis and other conditions with allied syndromy, by means of my epinephrin test. I shall speak also of the very definite improvement which follows thyroid resection and of the gross and microscopic pathological changes occurring in the thyroid gland.

It may be well to review briefly our knowledge of the histological changes which occur in the thyroid gland and which are associated with a definite, now well-recognized hyperthyroidism. Thus it is well to remember that the parenchymal, or in other words, the epithelial thyroid cells occur as two types: first, the acinar or aveolar cells surrounding the characteristic colloid and second, the so-called foetal or interstitial cells occurring in the interstices between the normal acini, but not taking part in the formation of the latter. Primary hypertrophy and hyperplasia of the aveolar epithelium, when mild, gives rise to a mild hyperthyroidism, such as is found associated with the hyperplastic thyroid gland at puberty or at other physiological periods, such as pregnancy and menstruation. More advanced aveolar parenchymal hypertrophy and hyperplasia is associated with the higher degrees of thyroid intoxication, and is found in the characteristic gland of exophthalmic goitre or Graves' disease.

The second well-recognized syndrome of hyperthyroidism depends upon the activity of the so-called "foetal-adenomata"

which occur as discreet circumscribed tumors or nodules which may be single or multiple and which are easily recognized, even in the very early stages. There is good reason for believing that these adenomata arise by hyperplasia and overgrowth of individual groups of the so-called foetal interstitial cells of Wölfler, and thus develop into the discreet, circumscribed and encapsulated foetal adenomata. I wish to emphasize here that there is not in the case of true adenoma a general overgrowth of this interstitial tissue in the thyroid gland, for upon this distinction rests the point of my paper. In both these instances of aveolar hyperplasia, namely, in the active gland at puberty and in exophthalmic goitre, I have found, upon cytological study, evidence of cellular activity in the occurrence of great numbers of mitochondria in the cytoplasm of the cells. I reported these findings in the Johns Hopkins Bulletin, May, 1916, and stated further that I felt I had proved from histological evidence that foetal adenomata of the thyroid were of themselves responsible for the hyperthyroidism which occurred associated with them. Furthermore, in both of these clinical states, I found that the epinephrin hypersensitiveness test was definitely positive, and the degree of reaction was remarkably parallel to the degree of toxicity clinically recognizable. The test gave thus confirmatory evidence of the presence of hyperthyroidism in these two conditions.

Before proceeding to a further discussion of the cases to be reported, it may be well to make a preliminary statement as to what the test really means, after my experience with it and after the experience of others. In the first place, it is an indicator of hypersensitiveness of the sympathetic nervous system. On the other hand, I am not prepared to say that all cases which show a positive reaction are, therefore, hyperthyroidism. However, we do know that the test is positive in all cases of hyperthyroidism, a fact which is founded upon abundant physiological research carried out particularly by Cannon and Levy. Furthermore, of all the diseases which may possibly be associated with a hypersensitive sympathetic system, hyperthyroidism is by all odds the most common, the exceptions being relatively uncommon. On the other hand, in the presence of a negative response to the test, one can state definitely, I believe, that hyperthyroidism is not present. To be able to differentiate to this extent is of great value in the diagnosis of obscure cases.

Again, I wish to point out that I am not advocating operation simply on the basis of a positive reaction; I am simply stating the facts as we know them with regard to the test, regardless for the present, of treatment advised.

The reaction is regarded as mildly positive when, after the injection of 0.5 cc. of 1 to 1000 epinephrin chloride (Adrenalin chloride, Parke, Davis & Co.) solution a rise of about 10 points in pulse or in systolic pressure or in both is obtained, and in which there are associated with this, certain clear-cut subjective and objective symptoms which have been described. It is stated by some that, exceptionally, positive reactions are obtained in cases of effort syndrome and even in so-called normal individuals and in neurasthenics. The response in such cases, however, is often atypical. A typical reaction is characteristically sustained and is apt to occur in two phases, a primary major reaction followed by a secondary minor reaction; it then disappears in one and one-half hours, leaving the patient practically normal. Again, the reaction is parallel to the degree of toxicity clinically recognizable just as is the metabolic reaction in the higher degrees of toxicity. After operation or after subsidence of the hyperthyroid symptoms, there is a fairly rapid subsidence of the characteristic hypersensitiveness.

Armed with these facts, I proceeded to a study of the less obvious cases which presented an obscure, though characteristic, syndrome, with negative eye signs and with few diagnostic findings in the gland. Many of the subjects were suspected of having tuberculosis, but upon expert examination were found to have little or none and showed no definite improvement after prolonged periods of rest. Finally, a positive epinephrin test was obtained and, after the failure of other measures, operation was advised. I wish to report now the results after operation and the pathological findings in the thyroid gland.

Space is not available in this brief report for a detailed presentation and discussion of the cases in this series. I shall, therefore, restrict my remarks to a summarized statement. There are in this group fifteen patients suffering with what I have called "Diffuse Adenomatosis" and presenting in general the syndrome of asthenia, mild tachycardia, nervousness, loss of weight and strength, tremor, perspiration and, in most of the cases, slight elevation of temperature. The majority of the

cases were observed during the past year at the Johns Hopkins Hospital and a few of the more recent cases at The Long Island College Hospital. Reports since operation have been obtained in all cases except two, and the time elapsed since operation varies from three to twelve months. The type of operation was the same in all instances, namely, a generous resection of both lobes together with the isthmus, leaving possibly one-fourth of the total gland substance. It seemed necessary to make this extensive reduction in order to obtain the desired benefit.

I may mention now, for convenience of consideration, the sub-groups of this series of patients, according to their previous suspected diagnosis and their previous treatment. The larger group, and perhaps the most interesting one, comprises ten patients in whom the diagnosis of tuberculosis was suspected, and all of whom had the benefit of sanatorium treatment and, incidentally, of expert pulmonary examination. The period of hygienic treatment varied from about three months of sanatorium treatment to irregular periods covering five years. In no case was there sufficient benefit from this treatment to warrant further rest or even to indicate that tuberculosis was the cause of the symptoms. The clinical syndrome in all of these cases is much the same and consists of the symptoms mentioned above. The individual cases did not vary sufficiently to warrant special discussion. The interesting feature about these patients is that upon expert pulmonary examination there was little or no tuberculosis found, and in all cases the epinephrin chloride test was positive, both at the sanatoria where the tests were carried out, and subsequently in the hospital under my own observation. In view of the fact that these patients failed to improve under medical and hygienic measures after long periods of time, that their syndromy seemed to be that of hyperthyroidism even more so than of other conditions which might give a more or less positive epinephrin response, such as diabetes, effort syndrome, neuro-circulatory asthenia, but which could be largely excluded by history and examination; and, finally, because of the positive epinephrin chloride test which has been found so constantly positive in the presence of hyperthyroidism, I did a partial thyroidectomy.

With regard to the clinical results following operation, I might say that I have reports from all but one of the cases, and

although the time elapsed since operation is hardly sufficient as yet to expect all the improvement that I think will come, nevertheless, after the comparatively short post-operative periods of three to twelve months, the results are so encouraging as to make me very hopeful about the ultimate outcome. In only one case was there failure of definite improvement, at least of the mental symptoms of which this patient suffered; physically she has definitely improved. The remaining patients showed a moderate to very remarkable improvement. The symptoms specifically reported as relieved are nervousness, weakness, palpitation, tremor, insomnia, perspiration, loss of weight and the mild febrile condition. These answers were in response to a definite questionnaire sent to these patients. Of the remaining cases of the previously suspected tuberculosis group there were five. One of these was a paraysmal tachycardia case referred to me by Dr. Barker; another, a young woman suffering with weakness, nervousness, and tremor, of unknown origin; the remainder complained primarily of nervousness and weakness.

In the gross and microscopic study of the thyroid glands from these patients I found some peculiarities which have lead me to think that we are dealing with a new clinico-pathological syndrome in thyroid disorders, which is a true hyperthyroidism based upon a peculiar and very interesting pathological change in the thyroid gland. This change is neither of the nature of that found in puberty hyperplasia nor in Graves' disease or exophthalmic goitre, nor is it of the type in which true discreet encapsulated nodules, the so-called "foetal-adenomata," are found. The glandular pathology in these latter types of thyroid disorder is readily recognized and is well known to be capable of producing hyperthyroidism. However, in this new and obscure group of which I am speaking, the following characteristics are fairly uniform. Upon physical examination the thyroid gland is often found moderately enlarged, but may be neither visibly or palpably so. It is fairly firm, and slightly granular or lobulated. No definite nodules are palpable, and signs of increased vascularity such as thrills or bruits in the gland or at the poles are not demonstrable. At operation one characteristically finds that a peculiar periglandular fibrosis has caused the gland to become loosely or sometimes quite firmly adherent by its thickened capsule to the prethyroid muscles and to the

large vessels and the sternomastoid, laterally. The appearance reminds one of a possible mild periglandular reaction, which sometimes makes difficult the delivery of the thyroid lobe. There is increased vascularity, particularly of a venous character, in the capsule of the gland. The thyroid arteries are only slightly if at all enlarged. The gland contains a moderate amount of colloid. It is of "rubbery" or spongy consistence, friable, more than normally vascular and has a marked tendency to ooze from the cut surface. There is not the familiar increased consistence of the gland as seen in exophthalmic goitre, nor is there the glistening character seen in colloid glands.

The microscopic findings are fairly uniform in these glands. The most characteristic feature is the readily recognizable increase in the interstitial cells the so-called foetal cells which are themselves characterized by being without any very definite arrangement. They are large and have a fairly clear protoplasm and a round vesicular nucleus. They can be distinguished from the lymphoid cell accumulations, which are also common, by the fact that the latter cells are much smaller, have very little protoplasm and a dense pycnotic nucleus. This interstitial tissue is distributed throughout the gland substance and is nowhere aggregated into encapsulated nodules as one sees in true adenoma. The glandular acini are mostly small and irregular in size. One sees often numbers of very small acini in the midst of, and apparently derived from, the interstitial tissue, and appearing in cross-section like a globule of colloid surrounded by 10 or 12 cells. The acinar cells themselves are usually low, thinned out and do not of themselves appear active nor are they active as indicated by the presence of mitochondria which are usually very few or practically absent. In other words, the hyperthyroidism which occurs with this change in the thyroid is not due to an increased activity of the acinar cells. In this respect the acinar cells differ from those seen either in the normal gland where they are cuboidal or in the puberty hyperplastic gland or in exophthalmic goitre, in which they are cuboidal to columnar and rich in protoplasm containing abundant mitochondria. Occasionally very small young adenomata are seen no larger than a wheat grain, but this is exceptional. These very small adenomata may possibly be regarded as an index of the fact that the foetal tissue in the thyroid is stimu-

lated to activity and overgrowth by some hidden force. There is some increase in the fibrous tissue which tends to divide the gland into small lobules easily recognized under the microscope. Because of the increased amount of diffuse interstitial tissue which is greater with the more toxic grades of hyperthyroidism found in these cases, and which we believe is derived from the so-called foetal cells of Wölfler; because of the numerous small apparently new formed acini, and the increase in lymphoid cell accumulations; because of the absence of true discreet adenomata and because, finally, of hypoplasia rather than hyperplasia of the alveolar cells, I have, for want of a better term called this condition "Diffuse Adenomatosis." This may not be a very fortunate term, but it has the value of being descriptive. I wish to emphasize again, that the appearance of these glands is decidedly different from that seen in puberty hypertrophy and hyperplasia and in exophthalmic goitre, in which there is a hyperplasia of the alveolar cells and in which the interstitial tissue is almost entirely absent. Furthermore, the picture is very different indeed from that seen in true adenoma, which occurs as an encapsulated tumor in an otherwise fairly normal looking gland.

I believe that the hyperthyroidism in these cases is dependent upon the activity of this so-called interstitial tissue, and not upon the primary alveolar cells, for when applying all the criteria we have in addition to the criterion of mitochondrial concentration, I find that the alveolar cells are more or less thinned out; there is no infolding and when investigated for the presence of mitochondria these latter structures are found very few in number. On the other hand, the interstitial tissue contains a moderate number of these structures, and at times they are quite numerous. In May, 1916, in the Johns Hopkins Bulletin, in an article entitled: "Functional Significance of Mitochondria in Toxic Thyroid Adenomata," I stated that, on the basis of histological evidence in addition to clinical reasons, foetal-adenomata of the thyroid were active and of themselves responsible for the hyperthyroidism associated with them. I believe this to be the case because of the very rich mitochondrial concentration in these adenomata, and because of the almost entire absence of them in the gland outside of the adenoma. Similarly, in puberty hyperplasia and in exophthalmic goitre, these mito-

chondria occur in moderate numbers in the former and are excessively numerous in the latter. This was a uniform finding. In colloid goitres they are very few or entirely absent. In other words, I believe that the hyperthyroidism in these cases is dependent upon the increase in amount and activity of the intersitial tissue derived from the so-called foetal cells and not upon activity of the alveolar or acinar cells themselves.

The question might be asked: Is this syndrome associated with "Diffuse Adenomatosis" a true hyperthyroidism? It might be contended that these persons were by nature endowed with a hypersensitive sympathetic nervous system, and that the operation merely reduces the more or less normal amount of thyroid secretion and thus renders the abnormally sensitive sympathetic less irritable, with a consequent improvement in the status of the patient. This objection might be valid, I think, if the thyroid presented a more normal appearance. But, because of the very definite pathological changes which are found and have hitherto been overlooked as a cause for hyperthyroidism; second, because of the fact that these patients failed to respond to medical and hygienic measures; third, because of the positive response to the epinephrin test, which is the rule in hyperthyroidism and, finally, because of the definite improvement after thyroid resection, I am of the opinion that we are dealing with a clinical state of mild chronic latent hyperthyroidism which has hitherto escaped notice.

If one were to rely upon the metabolic rate as an index of hyperthyroidism one would not suspect the cases belonging to this group, for as recently pointed out by Woodbury, the metabolic rate in these individuals is not particularly increased; in fact, it may be normal or only very slightly abnormal. A series of these cases were operated on by Webb and a definite improvement followed. I think Woodbury is correct in assuming that, regardless of the normal metabolic rate, these patients were suffering with hyperthyroidism. Consequently, the fact that the metabolic rate is not increased in these individuals does not to my mind indicate that they are not suffering with hyperthyroidism. I want to emphasize particularly that the epinephrin test, which is more sensitive than the metabolic rate determinations, is positive in these individuals, though mildly so, and hence is in this group of more diagnostic value than the met-

abolic test. This finding is somewhat similar to that in adenoma in which Woodbury also found that in the quiescent phase the metabolic rate may be found normal, and one would certainly not deny the presence of hyperthyroidism when the clinical syndrome is so clear, and when true circumscribed adenomata are felt in the thyroid gland and discovered at operation. In other words, the hypersensitiveness of the sympathetic is rather a persistent characteristic even in the quiescent phase of hyperthyroidism at which time the metabolic rate is normal. The basal metabolic level, therefore, is not so much an indicator of the disease as an expression of the degree of toxicity which is at any one moment present.

I think we are safe in saying on the basis of the physiological researches of Cannon and his associates, and of my results in the study of thyroid disease during the past six years, that epinephrin chloride is an indicator of hypersensitiveness of the sympathetic nervous system; that of all the diseases which are characterized by such a hypersensitive nervous system, hyperthyroidism is by far the most important and the one most frequently encountered. It would seem impossible for hypersecretion of the thyroid to be present in an organism without producing a hypersensitiveness of the nervous system and, therefore, a positive reaction to epinephrin. On the contrary, given a negative reaction, I feel that one can say definitely that hyperthyroidism is not present except in those late stages in which nervous and cardio-vascular degeneration have so far advanced as to render impossible a response to the drug. A negative reaction is thus of great diagnostic value. A typical positive reaction in a condition from which diabetes, neuro-circulatory asthenia and effort syndrome have been excluded—and this can often be done by other clinical methods—has a distinct diagnostic value, and at other times is confirmatory of a clinical diagnosis based upon ordinary observations and tests.

As compared with the increased metabolic rate as a criterion of thyroid intoxication, I think the test has, in the first place, the distinct advantage of being simpler and less liable to erroneous interpretation. With ordinary care it can be used by any one familiar with a blood pressure apparatus and the observation of cardio-vascular changes and with the general symptoms and signs of hyperthyroidism. It does not require the trained ex-

pert to obtain correct observations nor to make the proper interpretations. Again, in the milder states of hyperthyroidism in which the metabolic rate may be normal or only slightly increased, cases of which kind may thus be overlooked if reliance is placed upon increased metabolic rate alone, a positive epinephrin test often reveals the diagnosis. Again, observers have reported definite instances of clinical hyperthyroidism in which the metabolic rate is low. I have never seen a case of definite hyperthyroidism, clinically easily recognizable, which has failed to give a positive epinephrin test. This has been found true in a series of over 450 cases of thyroid disease. In my experience I think I have been able to differentiate the cases of neuro-circulatory asthenia so-called, which have given a more or less typical reaction, from hyperthyroidism by the fact that, in the former, there is very frequently a clear family history of nervous instability. There is an inherited constitutionally inferior nervous system. The symptoms in this condition are rather obscure and indefinite and upon closer examination it is found difficult for the patient to describe them clearly. They are found to date back to puberty or even into childhood, there being no definite recognizable starting point of the trouble. On the other hand there seems always, in my experience, to be a fairly definite starting point for hyperthyroidism. It is rare before puberty and frequently follows acute infections or severe psychic and nervous trauma. It may have its beginning at puberty, after pregnancy or after the menopause, the patient usually recognizing the time when the symptoms begin, whereas, previous to this time the general health may have been, and often has been, unusually good. Restricted to the epinephrin test alone one might have some doubt. Since it appears that a positive test may be found in the condition of so-called neuro-circulatory asthenia—which to my mind has not been demonstrated to be absolutely unassociated with thyroid overactivity—it may be helpful if this simple history test is applied, for in many cases a differentiation can thus be made from true hyperthyroidism. Again, I want to emphasize that I do not feel or say that in the presence of a positive reaction, particularly a mildly positive reaction, thyroid resection is indicated. I am speaking now simply of diagnostic facts, leaving the matter of operative therapy out of the problem.

SUMMARY

There is a group of so-called borderline cases which heretofore have been very difficult of diagnosis, and even more difficult with reference to a satisfactory treatment. The individuals belonging to this group are of no characteristic age but are mostly young adults. They present a syndrome characteristic of possibly hyperthyroidism, incipient tuberculosis, neuro-circulatory asthenia and allied conditions. They fail to show positive eye signs, or even positive clinical findings in the thyroid gland. They fail, furthermore, to respond to ordinary medical and hygienic measures. Upon further examination they are found to give a positive reaction to the epinephrin test, but on the other hand, as shown by Woodbury, in many instances they fail to show increased basal metabolism. In this type of case a rather extensive bilateral partial resection of the thyroid gland is followed by a very definite and often striking improvement. The thyroid gland upon microscopic examination shows a characteristic histological picture, heretofore unrecognized as responsible for a definite kind and type of hyperthyroidism. This change is not of the puberty hyperplastic type nor of the exophthalmic type, nor is the picture that presented by the well known discreet adenomata of the thyroid gland, all of which conditions are well known to be responsible for hyperthyroidism. In the group of patients reported here the change in the gland consists primarily in a definite and, at times, very marked increase in the interstitial so-called adenomatous tissue, together with increased amounts of lymphoid tissue and an associated hypoplasia of the primary alveolar or acinar epithelium. This interstitial tissue is not aggregated into nodules, but is scattered diffusely throughout the gland. This increase in interstitial tissue is not associated with aveolar hyperplasia, as seen in the puberty hyperplastic gland and exophthalmic goitre, but rather as stated with aveolar hypoplasia. It arises, doubtless, from the interstitial cells; produces a picture finally to which I have given the name of "Diffuse Adenomatosis," and which is capable of producing mild to moderate states of chronic hyperthyroidism. It is my opinion that this is a definite pathological-clinical entity, in fact a new type of hyperthyroid syndrome depending upon a new conception of pathological change in the thyroid.

The fact that this change is responsible for hyperthyroidism to my mind is shown by the fact, that in the first place there

is an associated syndrome produced which is more or less characteristic of the hyperthyroid state; second, there is a failure to improve under the ordinary medical and hygienic measures which are directed to the treatment of similar nervous conditions; third, there is a positive reaction to the epinephrin chloride test; fourth, after resection of the thyroid there is a diminution if not disappearance of this hypersensitiveness with a considerable improvement, in fact, almost a cure in some cases; and fifth, in the gland there are found changes which are characteristic and very different from the normal appearing gland, and very different also from the other well known pathological changes in the thyroid. Should one feel that these cases are not hyperthyroid there still remain to be explained the rather typical symptomatology, the positive epinephrin chloride test, the improvement after operation, and the very characteristic changes in the gland upon microscopic examination.

In conclusion, I wish to state that I do not hold that the epinephrin chloride test is pathognomonic of hyperthyroid states. I would say, however, that a negative test excludes hyperthyroidism, that in all except a few very severe cases of hyperthyroidism the test is positive and that there are some few conditions which give a more or less typical reaction and which are to be remembered as exceptions. The latter I think can be fairly well recognized after a careful history and physical examination. At any rate I feel that the test is practically always confirmatory, in many cases diagnostic, in others suggestive of the diagnosis, and leads to further and more careful search for causes in the small percentage of exceptions to the test. Again, there is a remarkable parallelism between the hypersensitiveness to epinephrin and the degree of hyperthyroidism present. The test is rather easily applied and one can follow the well known variations in the degree of hyperthyroidism present from time to time, and one can regulate the treatment accordingly. I am convinced that when intelligently applied it is of the greatest help in diagnosis, in treatment, and in prognosis, and furthermore, it has led directly to a clearer understanding of an obscure group of cases which, I believe, are dependent for their symptomatology upon a very definite pathological change in the thyroid gland, which has heretofore escaped notice. This change is capable of producing hyperthyroidism, and is different from the well

known pathological histology heretofore described. The condition might well be called "Diffuse Adenomatosis" of the thyroid gland.

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HYPOPITUITARISM

A Case Report

Henry H. Lissner, M. D.

The following case came under observation shortly before the War. Although its interest as bearing upon endocrine physiology and pathology was obvious, it was not possible on account of other imperative duties to devote the time to its study which it otherwise would have received. It is regretted, especially, that data for a detailed report on the cytological features of the pineal and other endocrine organs were not secured.

Family History. F. B. who was 23 months old, September, 1915, was the youngest of four children, one boy of 16 years and twin girls of seven. There is no family history of glandular trouble or diabetes.

Personal History. The patient's weight at birth was 8½ lbs.; labor was normal; he nursed up to the eleventh month, at which time he was placed on Mellin's food, barley water, and malted milk. He was apparently normal up to the ninth month, laughed, played, noticed what was going on about him and seemed to have a happy disposition. From this time on, it was noticed that he was gaining very rapidly and a photograph at this period shows an early tendency to deposition of fat and the early expression and phases of his condition.

At this time, also, he had his first convulsion and, for a time, at every urination he would close his eyes and fall forward in a convulsive seizure. These convulsions, occurring sometimes as often as seven a day, continued up to the age of fifteen months, when they became more severe in character but still remained of the flexor type. The number of convulsions for sixty-four days from the 15th to the 17th month of his life was 3.6+ spells a day.

Examination. The child has neither walked nor talked and because of his undeveloped condition, we cannot say whether or not certain symptoms which require some mentality for their determination, were present, such as headache, photophobia, and nystagmus. Because of the very thick layer of fat and small size of the blood vessels, the systolic pressure was difficult to

determine. It was found to be about 80. The diastolic pressure was not obtained.

Eyes. Examination of the eyes by Dr. F. K. Miller showed pupils normal and no apparent oculomotor paralysis. The eye-ground showed edema of the retina.

Photograph of subject at the age of 23 months.

Throat. Examination of the throat by Dr. C. H. Montgomery showed: "Tonsils and adenoid present; no bulging of the naso-pharynx; no epistaxis, no cerebro-spinal rhinorrhea."

General Condition. He has, fairly constantly, a pronounced facial cyanosis. Pressure in the anterior fontanelle causes a drawing up of the hands and thighs and an expression of pain and protest, rolling of the eyes, and it would seem that if continued it would bring on a convulsion. There have been

from the onset marked muscular weaknesses and inability to sit up. He makes no effort to help when picked up and falls limply to either side, due no doubt to a muscular dystrophy.

His appearance is very striking: his hair is coarse, light in color, and grows very rapidly; his fingers are puffed and tapering. His head is enormous, breasts are prominent, and there are rolls of fat which make decided creases about the neck, arms, legs and abdomen.

The external genital organs are diminutive. His weight at 15 months was 37¾ lbs.; at 2 yrs., 41¾ lbs.; at 3 yrs., 81 lbs.; practically doubling his weight in his third year. His measurements May 18, 1917 were as follows:

Circumference of head	55½	cm.
Fronto and submental	59	cm.
Chest under the breast	88½	cm.
Abdomen at the umbilicus	96	cm.
Thigh at the gluteal fold	53½	cm.
Calf of leg	30	cm.
Upper arm	27½	cm.
Height	100	cm.

The sugar tolerance test was done. He was given 60 gms. of levulose at 9:00 A. M. The urine secretion of the first hour was 5cc. and the test for levulose, negative. The second hour it was 13 cc. and the test was negative. The third hour secretion was 10cc. with a slight reaction indicating levulose in the urine but following this, there was total suppression up to 11:00 P. M. of the same day, when the kidney function gradually returned.

The convulsions continued very severe up to July, 1917, when he had two spells of explosive vomiting, following which the convulsions ceased. On the same day, he began to run fever between 99 and 101 degrees. His fever continued for one week, during which time it gradually increased up to 103 degrees. He was given small doses of aconite by his mother to reduce the fever and on the 19th, 20th, and 21st of July he was fever free. The fever started again, however, between 102 and 103 degrees, and on the 25th of July, he began groaning and gradually went into coma. The fever increased from 103 to 104 degrees until on the 30th day of July, when he died at 8:00 P. M. with an ante-mortem temperature of 107½ degrees.

Treatment: The treatment, as outlined, was two grains of pituitary extract three times a day. This was gradually increased until he was taking twenty two-grain tablets daily without any apparent benefit. There was no change in the mental development, muscular strength nor genitals. Because of the sudden increase in weight he was given 1/10 gr. thyroid extract three times daily. It seemed, however, to increase the number and severity of convulsions so that on the third day it was discontinued.

Autopsy and report on sections by Dr. Herman Zeiler follow.

Inspection: Body of child which has the appearance of being about seven years of age. Body in rigor mortis, and showed post-mortem discolorations, in the dependent portions. Genitals small; entire body appears puffed, but the pitting is not that of a true edema. Abdomen distended; neck very short; mammae well developed.

Palpation: Fontanelles closed.

Skull: Opening the skull the bones are hard and appear thickened. There is marked edema of the piaarachnoid; dura thickened.

The base shows a small sella with the anterior and posterior clinoid processes under-developed. No separation of sutures at the base. Middle ears are clear; ethmoidal and sphenoidal sinuses are clear.

Pituitary body present and under-developed. Incision of chest and abdomen shows fat of the chest about 2 inches thick, very pale; the layer of abdominal fat being somewhat thicker. No evidence of edema.

The pectoral muscles are thin and undeveloped; the abdominal recti very thin; sterno-cleido-mastoid muscles are thin and underdeveloped as are also the muscles of the legs.

Lungs show hypostatic congestion and a few epipleural hemorrhages.

Heart muscle pale; heart fatty and small; on the right side it shows thin musculation with fair musculature on left side. Valves competent. Thymus almost absent.

Abdomen: Shows pale, fatty omentum and very fat mesentary. The fat in the region of the round ligament, very abundant, being ¾ of an inch in diameter.

Spleen is soft and enlarged.

Liver normal in size and pale.

Intestinal tract normal except for retrocaecal appendix.

Pancreas appears enlarged almost to the size of an adult's.

Tissues Examined Histologically—Thyroid: Shows the usual glandular structure of the thyroid, lined by low columnar epithelium and no excess of fibrous tissue. The blood vessels are fairly numerous. There is no cyst formation of any of the glands and but few show colloid substance.

Testicles: The convoluted tubules are diminished in number and separated by abundant loose connective tissue. The cells lining the convoluted tubules are pale-staining and the nucleoli are well marked. No mitotic figures discovered.

Pancreas: Appears normal.

Spleen: Histologically is practically normal.

Kidneys: No increase in fibrous tissue. The cells lining a few of the convoluted tubules and collecting tubules show hyaline necrosis and an occasional tubule shows eipthelial casts.

Hypophysis: The line of demarcation between anterior and posterior lobes seems lost. Histologically, numerous thin walled blood vessels form a plexus surrounding strands of polyhedral cells arranged in three or four rows. These cells are of the usual two types found in this gland and intermingle without definite arrangement or regularity, the "chief" cells being far more numerous. Here and there are a few follicles lined by low columnar epithelium. There is an abundance of loose connective tissue.

SUMMARY

A child of 23 months was normal to the 9th month, when he began gaining rapidly in weight. The onset of symptoms was convulsions of the flexor type continuing up to within the month of his death. The family history showed no glandular trouble or diabetes. The eyes showed edema of the retina; the throat was negative. There was marked muscular dystrophy with profound facial cyanosis, diminutive external genitals, doubling of weight in the third year of life, low sugar tolerance and ante-mortem temperature of 107½ degrees. Treatment consisted of pituitary extract—whole gland—from 2 to 40 grains daily without any benefit. Thyroid extract seemed to irritate. X-ray plates of the skull showed a small sella turcica at the age of 23 months. An autopsy report and the histological report on various glands are included.

THE EFFECTS OF INANITION UPON THE ADRENAL BODIES—PRELIMINARY COMMUNICATION

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It must be admitted that it is still impossible to give a definite answer to the question, "What is the function, or what are the functions, of the adrenal bodies?"

Several important facts have been made out and some theories have been put forward. The facts are:

I. A definite chemical substance of known composition and possessing well marked pharmacodynamical activities can be extracted from the chromaphil tissues.

II. This substance, adrenin, can be obtained from adrenal medulla as well as from chromaphil tissues in other situations.

III. There is considerable evidence that adrenin is actually poured out into the circulation.

IV. The true adrenal body or cortex is related in some way to the development and growth of the sex organs.

The chief theories of modern times in regard to the functions of the glands apply only to the chromaphil tissue. It has been supposed that adrenin is continuously poured out and exercises a tonic influence upon the sympathetically innervated organs and tissues and so, for example, helps in maintaining the normal blood pressure. This theory has been generally abandoned. A more recent view is that the secretion of adrenin is of service only in certain physiological emergencies. The latter suggestion is certainly a more plausible one than the former, though it cannot be said to be firmly established.

The conception has been formulated that the thyroid and adrenal bodies form part of a mechanism for the chemical heat regulation of the body, and that the cortical adrenal and the chromaphil tissue both take part in this functional activity. This theory involves the conception of a widely reaching influence of the adrenal bodies, taken as a whole, upon the metabolism of the organism.

Recently McCarrison (1) has made the important discovery that in pigeons inanition gives rise to a remarkable enlargement of the adrenals. He remarks that, "This enlargement appears to be a true hypertrophy, since it is associated with a corresponding increase in the glands' content of the medullary secretion, adrenalin." It would appear from this quotation that McCarrison regards the cortex and medulla as constituting one gland whose whole function is the secretion of adrenin.

We have repeated McCarrison's experiments upon pigeons, and have also carried out similar experiments upon rats and dogs. We are able to confirm fully his observation that after a period of inanition there is always a distinct hypertrophy of the adrenal bodies. In pigeons the adrenal bodies are doubled in weight after inanition for 15 days. In dogs after a somewhat longer period of inanition the adrenal bodies are almost double the normal weight. In rats the hypertrophy is considerably greater than in pigeons and dogs, even when inanition is carried out for a shorter period.

We reach, then, the remarkable conclusion that, while the majority of organs and tissues in the body atrophy in starvation, the brain and heart remain unaltered and the adrenal bodies hypertrophy to a considerable degree. We have noted that the abdominal chromaphil body (2) in the dog is markedly increased in dimensions after 14 days' inanition, but the chrome reaction was less intense than in the normal dog. This indicates that, in future investigations, a differentiation will have to be made between hypertrophy of the chromaphil tissue and an increase of its adrenin content.

The question naturally arises, "Have we here to deal with a hypertrophy of the cortex, or of the medulla, or of both?" This point we do not pretend to have settled. McCarrison, as seen above, found the adrenin content increased in his starvation pigeons, though in a later communication (3) he notes a diminution of adrenin content in scorbutic guinea-pigs. It is not clear whether McCarrison regards these differing results as due to varying degrees of starvation, or whether he regards the scorbutic influence as something qualitatively different from the inanition influence. Our own results with inanition animals have not been quite consistent. In some cases the amount of chromaphil tissue and the amount of adrenin have been distinctly in-

creased as a result of inanition. In other cases (and these, contrary to expectation, were those of the longer periods of starvation), the opposite effect has been produced, namely, a reduction in the amount of chromaphil tissue, or in the intensity of its chrome reaction, and a reduction of the adrenin content as shown by the physiological test.

We consider these observations of McCarrison to be of the greatest importance since they demonstrate clearly a relation between the adrenal bodies and the general metabolism of the animal organism. Since other lines of work have so far taught us so little of the uses of the adrenal bodies, we are tempted to urge a vigorous pursuit of investigations bearing upon their metabolic functions.

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THE ROLE OF THE ENDOCRINE GLANDS IN CERTAIN MENSTRUAL DISORDERS

WITH SPECIAL REFERENCE TO PRIMARY DYSMENORRHOEA AND FUNCTIONAL UTERINE BLEEDING*

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Speaking generally, the importance of the hormone associations of an organ or of a body function varies with the degree of its automaticity. The highly volitional functions, such as the skeletal muscular movements, are under the control of the rapidly acting nerve mechanism, while the auxiliary influence of the endocrine apparatus is relatively slight. With the more primitive vegetative functions the reverse is true, for here the mechanism is usually essentially of the endocrine type, with a greater or less degree of contributory regulating influence on the part of the sympathetic nervous system.

Menstruation is a function which may certainly be classed as vegetative, and hence it is not surprising that the explanation of its mechanism is to be sought chiefly in a study of the functions of certain endocrine glands, and that the cause of menstrual disorders is not infrequently to be found in disorders of these structures. That there is, even in the case of menstruation, some association with the higher centers, is shown by the occasional occurrence of menstrual aberrations under the influence of profound psychic disturbances—the amenorrhea which is often seen in women who dread pregnancy, or in those with an intense longing for it; the occurrence of either amenorrhea or excessive menstruation as a result of sudden shock or fright, etc.

For nearly a hundred years, the ovary has been looked upon as essential to menstruation, but no attempt was made to explain the manner in which its influence is exerted, until the formulation of the well-known theory of Pflueger, in 1865. According to the latter, menstruation was explained as the result of a pelvic hyperemia induced reflexly by the pressure of a growing

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

Graafian follicle on the ovarian nerve terminations. This theory was quite universally accepted until it was disproved by the experimental work of Knauer, Marshall and others. These investigators showed that removal of the ovaries, thereby severing all their nerve connections, does not cause cessation of menstruation, provided that the ovaries be transplanted elsewhere into the body. In other words, the ovarian influence is exerted through the blood-stream and not through the nerves, i. e., it is of endocrine nature.

The next step was to determine which of the constituents of the ovary is responsible for the menstrual function. Is it the stroma, the follicles, or the corpus luteum? Without going into detail, suffice it to say that the weight of evidence is overwhelmingly in favor of the view that it is the corpus luteum which plays the most important role in this connection. It seems almost as certain, however, that the ovary produces more than one hormone. Marañón, for example, believes that the ovarian hormones may be divided into three groups: One, the genital, has to do with the menstrual cycle; a second, the sexual, with the morphological sex characteristics and a third, the general, assists in all the body functions.

The internal secretion of the ovary is closely interrelated with that of other endocrine glands, especially the thyroid, pituitary and suprarenal bodies. These relations are not easily defined in the present state of our knowledge, but their existence is demonstrated by the frequent influence exerted on menstruation by disease of any of them. Many interesting examples of these relationships suggest themselves for discussion—the role played by the ovaries in the development of the secondary sex characters; the effects of castration at various ages; the rare occurrence of female eunuchoidism; the relation between menstruation and ovulation, and between menstruation and lactation; the influence on menstruation of the thyroid, pituitary and suprarenal bodies, etc. For the purpose of this brief paper, however, it has seemed more profitable to limit myself to the discussion of two or three of the less obvious relations of the endocrine structures to disorders of menstruation.

First of all, I may pass with mere mention that form of amenorrhea now generally recognized as being due to hypopituitarism, and which, clinically, is commonly associated with obesity.

Fröhlich's report, in 1901, of the first case of adiposo-genital dystrophy, gave rise to much experimental work, which yielded results long since incorporated into clinical practice. Much has been written concerning the amenorrhea which is found in connection with hypopituitarism, and I shall not elaborate on the subject here.

The two menstrual disorders to which I wish to call especial attention, as regards their probable endocrine etiology, are (1) primary or spasmodic dysmenorrhea and (2) uterine hemorrhage of the type commonly spoken of as "idiopathic" or "functional."

Primary Dysmenorrhea. At first thought there would seem to be little connection between primary dysmenorrhea and the endocrine system, and yet I believe that an important relation of this sort does exist. By primary dysmenorrhea we mean that form of menstrual pain which occurs in the entire absence of discoverable disease in the pelvis. It is observed with great frequency in young nulliparous women, either single or married, and, in the aggregate, is the cause of a vast amount of suffering. The factors which have been considered instrumental in the causation of this form of dysmenorrhea may be summarized as follows.

1. *Mechanical obstructions of the uterine canal.* For many years after the publication of the work of Mackintosh in 1832, the view was held that spasmodic dysmenorrhea is always due to mechanical obstruction to the exit of menstrual blood from the uterus. Most commonly, it was assumed, the obstruction is due to anteflexion of the uterus. According to this view, the colicky pain so characteristic of the condition is due to spasmodic contractile efforts on the part of the uterine muscle. This conception is still quite prevalent among medical men, although the evidence is clearly against its correctness. For example, primary dysmenorrhea often occurs in the entire absence of anteflexion or of other obstructive lesions, and, on the other hand, it is not uncommon to find even very sharp anteflexions in women who suffer no dysmenorrhea whatsoever.

2. *Neurotic factor.* Aside from the actual hysterical cases, the importance of this factor lies in the fact that it increases the susceptibility to pain, and thus causes a magnification into actual

pain of the menstrual discomfort normally experienced by many women.

3. *Hypoplasia of the uterus.* There is little doubt that by far the most important factor in the etiology of spasmodic dysmenorrhea is defective development of the uterus. It is extremely common to find a greater or less degree of genital hypoplasia in women whose development otherwise is quite normal. These cases of uterine hypoplasia may be classified under three heads, according to the degree of hypoplasia. (a) In the *fetal type,* the arrested development occurs at a very early stage, so that the uterus resembles that of the fetus. The special characteristics are the small size of the uterus and the fact that it is made up almost entirely of cervix, the corpus uteri being exceedingly rudimentary. (b) In the *infantile type,* the uterus resembles that normally found in infants and young children. Here again the cervix predominates over the corpus, although the latter is not as rudimentary as in the fetal type. The uterus as a whole is larger and there is often an associated anteflexion, most commonly of the cervico-corporeal variety. (c) In the *subpubescent type,* the hypoplasia is relatively slight. Here, also, there is not infrequently an associated anteflexion. For a fuller discussion of these varieties of uterine hypoplasia and of their clinical significance, I would refer to a previous paper which I have published on the subject.

The pertinence of the question of uterine hypoplasia in connection with the present discussion rests on two factors: first, that an extremely frequent symptom of uterine hypoplasia, though not by any means a constant one, is primary or spasmodic dysmenorrhea; secondly, that the underlying cause of the various grades of uterine hypoplasia is undoubtedly of endocrine nature. In searching for a cause for the hypoplasia, we at once make contact with the endocrine apparatus in the body. Which of the endocrine glands is responsible for the defective development of the uterus noted in these cases? In the first place, does the ovary exert any important influence on the development of the uterus before the age of puberty, that is, during the fetal and infantile periods of life? Certainly no such influence can be assigned to the corpora lutea, for the latter do not appear before the age of puberty. The possibility suggests itself that some other element of the ovary may possess this function, but the evidence is not

convincing. Mayer believes that the growth of the uterus in very early life follows the general laws of body growth, and that it is not especially influenced by the ovaries. He believes, for example, that in the exceedingly rare congenital anomaly of absence of both ovaries, the uterus may still be present. With unilateral absence of the ovary, the uterus is usually quite normal, as I observed in a recent case. This observation is, however, of no particular significance when we consider that the ovarian influence is blood-borne, and would, of course, exert its effect equally upon the Müllerian ducts of both sides. Mayer attempted to attack this problem with greater directness by performing castration of the animal fetus in utero. The operation was performed transperitoneally, but, unfortunately, terminated fatally as the result of infection. While, therefore, the predominant influence of the ovary during menstrual life is universally admitted, there is no convincing evidence that it is equally important before this period.

There is much reason to believe that the earlier growth of the uterus is under the influence of other endocrine glands, especially, perhaps, the hypophysis. This seems all the more probable in view of the undeniable role played by the pituitary in the production of acquired sexual hypoplasia. For this there is abundant evidence, both experimental and clinical. It would be rash for those of us whose work is chiefly clinical to offer an explanation of the exact mechanism involved in these cases. The point which I wish to emphasize is merely that this type of menstrual disorder may, with reasonable certainty, be classified as an endocrinopathic manifestation.

Functional Uterine Bleeding. Another gynecological complaint the endocrine origin of which permits of very little doubt is the so-called functional uterine hemorrhage. This symptom is of very frequent occurrence, especially at the two extremes of menstrual life, puberty and the menopause. It may, however, occur at any age. In these cases the most careful examination may show perfectly normal pelvic organs, and yet bleeding may be persistent and perhaps very profuse. Most commonly it takes the form of menorrhagia rather than metrorrhagia. Cases of this type usually come to curettage sooner or later, and indeed, in the case of climacteric hemorrhage, the indication for this procedure is urgent, owing to the importance of excluding carci-

noma. In the non-malignant climacteric cases, and in those of puberty, the pathological report on the curettings has usually been some such designation as "normal endometrium," "hypertrophic glandular endometritis," "chronic endometritis," etc. It has seemed difficult to incriminate the endometrium as the cause of bleeding of this type. Equally unsatisfactory have been the efforts to explain this form of bleeding by such factors as artesiosclerosis of the uterus, the "insufficientia uteri" of Theilhaber, etc. The point which I should like to emphasize is that the endometrium in a very large proportion of these cases—I am not as yet prepared to put it in percentage figures—conforms to the type described by Cullen as hyperplasia of the endometrium.

The histological picture presented by this condition is extremely characteristic. As the term indicates, there is a genuine hyperplasia of the uterine mucosa, with an increase of both the epithelial and stromal elements. Owing to the epithelial proliferation, many of the glands become much enlarged and of cystic appearance. The disparity in the glands is perhaps the most conspicuous feature of this condition apparent on casual examination, so that as a rule the diagnosis may be made almost at a glance. That the cystic condition of the glands is not due to mere retention of the contents is suggested by the fact that the epithelium, instead of being flattened out, is commonly quite intact. Not infrequently the epithelial cells are seen to be several layers thick. The stroma is also markedly increased, and occasionally mitoses are noted. Grossly, the endometrium in these cases is almost always much thickened, sometimes enormously so. In the extreme cases curettage will often bring away large masses of fungoid tissue, which lead to a strong suspicion that a malignant condition exists. In other cases the thickening is relatively slight.

An endometrium of the type above described is never observed except in association with the symptom of uterine bleeding. The reverse is, of course, not true, for uterine hemorrhage may be due to many anatomic causes. With most of the ordinary pelvic lesions the endometrium is perfectly normal. It is of interest, however, to note that with certain pelvic conditions, especially myoma and adenomyoma, the endometrium may exhibit the condition of hyperplasia, as above described. There is some evidence to indicate that both myoma and adenomyoma are due to some as yet unknown aberration of ovarian function and, as we

shall see, there is little doubt that the same factor is responsible for hyperplasia of the endometrium.

The finding, in a case of uterine bleeding, of such a definite structural alteration as hyperplasia of the endometrium, would seem at once to take a case out of the category of functional hemorrhage. There is good reason to believe, however, that this characteristic change in the endometrium does not represent a primary lesion, but that it is secondary to a disturbed function of the ovary. Under normal conditions the endometrium is certainly subordinate to the influence of the ovary. The ever changing histological appearance of the uterine mucosa at different phases of the menstrual cycle is undoubtedly called forth by corresponding cyclical changes occurring in the ovary, and especially in the corpus luteum. So that there is nothing revolutionary in the idea that the characteristic picture of hyperplasia may be associated with some definite endocrine disturbance of the ovary.

Hyperplasia, generally speaking, is observed only during the reproductive life of the woman, that is, during the period of ovarian activity. This fact in itself would suggest some influence on the part of the ovary. Furthermore, curettage, in cases of hyperplasia, is most frequently unsuccessful in the relief of the accompanying hemorrhage, the latter symptom recurring in a large proportion of cases. Were the hyperplasia a local lesion in the endometrium, its removal should be followed by cure. That this is not the case would seem to indicate that the underlying cause, an endocrine disorder of some sort, still remains operative. Although repeated curettage frequently does not cure these cases, radium or the X-ray usually brings about a cessation of the abnormal menstruation, apparently by its destructive action on the follicles of the ovary.

As a matter of fact, there is no little evidence that almost all cases of uterine hemorrhage, with the exception of those due to such destructive lesions as cancer, are functional in the sense that the bleeding is due, in part at least, to disturbances of the ovarian secretion, as a result of the pelvic disease, whether this be myoma, pyosalpinx or some other condition. In other words, the simple congestion caused by these lesions is not in itself sufficient to explain the menstrual excess which is often present, and which is probably due to hyperfunction of the ovary. I shall not review the evidence along this line, but it is so impressive that no

intelligent gynecologist can afford to overlook the importance of the pathological physiology of the ovary in the consideration of possible causes of uterine bleeding.

Efforts have been made to ascertain whether the ovarian disorder is associated with any characteristic histological changes in the ovary. The most recent, and also the most valuable, work along this line is by Schroeder. According to this author, the secretory stage normally exhibited by the endometrium just before menstruation is absent altogether in cases of hyperplasia. In the latter, he concludes from his own studies, there is an absence of active corpora lutea in the ovaries. The hyperplastic endometrium, he believes, represents only a persistence of the proliferative stage which, in turn, is due to the persistence of the maturing Graafian follicles upon which this stage is normally dependent. The work of Schroeder is extremely suggestive but needs further confirmation before it can be accepted. Certainly the absence of the corpora lutea is not, as he says, a constant observation, for a well-marked corpus luteum, in the stage of late vascularization, was found in the ovary of one of my recent cases of hyperplasia.

As to the nature of the endocrinopathy present in these cases, we cannot as yet speak with much definiteness. In view of the excessive menstruation characterizing cases of this type, the natural assumption would seem to be that we are dealing with a hypersecretion of the ovary, or, at any rate, with that element of the ovary concerned with the production of normal menstruation. Since most of us are inclined to assign this role to the corpus luteum, it is not easy to explain the absence of corpora lutea which Schroeder believes to be the characteristic finding in the ovaries of these cases.

Hypersecretion of the ovaries (hyper-oöphorism, female hypergonadism) is a condition concerning which we know far less than we know about female hypogonadism. From what has been said, however, the evidence would seem reasonably complete that hyperplasia of the endometrium is the result of hypersecretion of the ovaries. I know of no other clinical condition concerning which this statement may be made with as much justification.

In this brief paper I have merely touched upon a few of the less obvious relationships which exist between the endocrine apparatus and the mechanism of menstruation. There is, perhaps,

no field in which the study of endocrinology is of such fundamental importance as in that of gynecology. The truth of this statement I trust will be apparent from the foregoing discussion of the etiology of three important menstrual disorders—one of the most common forms of amenorrhea, perhaps the most important type of dysmenorrhea encountered by the gynecologist, and a form of uterine hemorrhage the study of which had previously given rise to many theories, all inadequate.

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EFFECT OF SUBCUTANEOUS INJECTIONS OF THYMUS SUBSTANCE IN YOUNG RABBITS

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In a previous paper one of us (N. B. E.) reported the effect on full-grown rabbits of subcutaneous injections of desiccated thymus substance (Armour & Company). The doses administered were 10 mgm. and 20 mgm. per kilogram of body weight dissolved in a mixture of one part of glycerine to four parts of physiological saline solution. For control, other rabbits were injected with the glycerine-saline mixture. Each rabbit received forty injections during a period of eight weeks. At the conclusion of the experiment, half of the rabbits were autopsied. Both control and thymus rabbits gained in weight, the former 18.31 per cent, the latter 17.85 per cent. There was no apparent difference in the behavior of the two groups of animals. At autopsy the thyroid glands of the thymus rabbits averaged slightly heavier, 8.57 per cent, than those of the controls. There were no differences in the other organs.

Before this paper appeared, Olkon reported a series of experiments in which he had injected desiccated thymus gland (Armour & Company) suspended in physiological saline solution intraperitoneally into young guinea-pigs. He found that the injections produced marked loss of weight, muscular spasms and convulsions. As a control he injected into other guinea-pigs desiccated muscle protein. These injections caused similar results but in degree much less marked. He concluded, therefore, that the effect in the first case was a specific toxic action of the thymus substance. However, the doses of thymus substance which he employed were not based on body weight. He does not state the dose of desiccated muscle protein used.

Because of this difference in results, we have performed further experiments in which subcutaneous injections of desiccated thymus substance were administered to young rabbits. Twenty-four animals were used, comprising seven litters of three to five animals each. The rabbits of a litter were kept together and separate from all the others. One or two animals of a litter

served as controls; the others were given the thymus injections. The first four litters (14 rabbits) were six to seven weeks old at the beginning of the experiments; the others were nine to ten weeks old at the beginning. Details of the grouping of the rabbits by litters, their age, sex, etc., are given in Table 1. All were in good condition and apparently normal. The rabbits were fed and cared for under our personal supervision and the diet and environment were as uniform for all as it was possible to obtain.

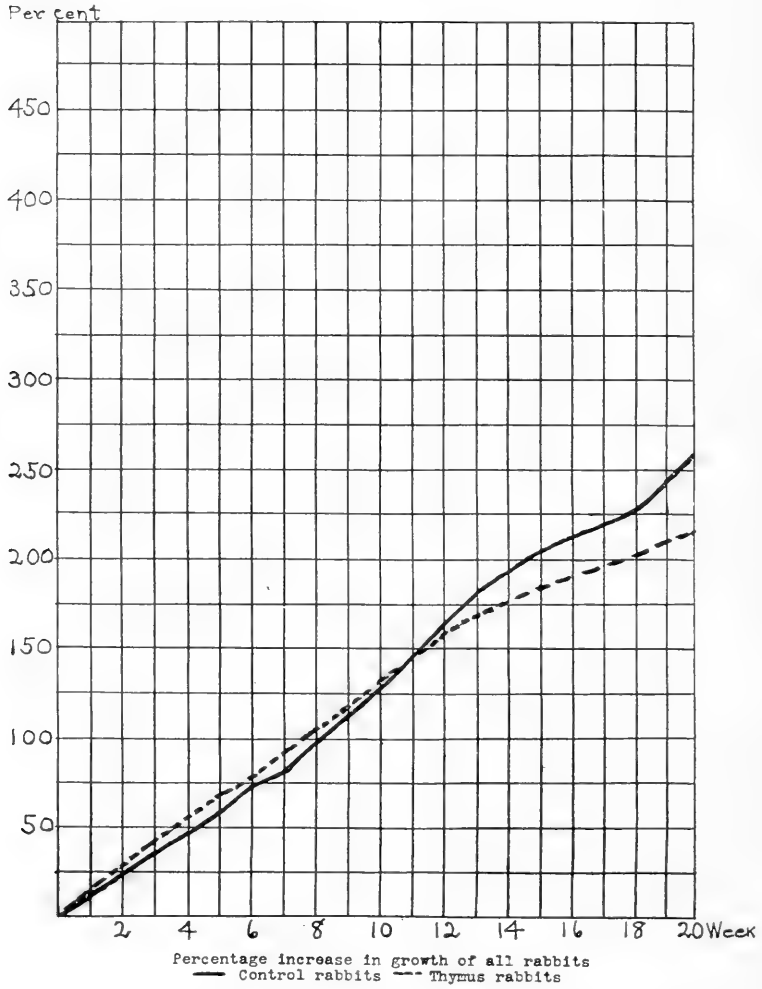
TABLE I

	Number	Litter	Age at beginning weeks	Sex		Genitalia
Group I		A	6	Female	Control	Normal
	2	A	6	Female	Thymus	Normal
		A	6	Female	Thymus	Normal
	4	B	6	Female	Control	Normal
	5	B	6	Male	Thymus	Normal
	6	B	6	Male	Thymus	Normal
	7	C	7	Female	Control	Litter during 20th week; pregnant at autopsy
	8	C	7	Female	Thymus	Pregnant at autopsy
	9	C	7	Male	Thymus	Normal
	10	D	7	Female	Control	Normal
	11	D	7	Male	Control	Normal
	12	D	7	Female	Thymus	Infantile
	13	D	7	Male	Thymus	Normal
	14	D	7	Female	Thymus	Litter during 20th week
	15	E	9	Male	Control	One testicle
	16	E	9	Male	Thymus	Normal (separate from others of litter from 10th week on)
		E	9			
	17	F	9	Female	Thymus	Pregnant at autopsy
Group II	18	F	9	Male	Control	Normal
	19			Male	Thymus	Normal
	20	F	9	Female	Thymus	Normal
	21	G	10	Male	Control	Normal
	22	G	10	Male	Control	Normal
	23	G	10	Male	Thymus	Normal
	24	G	10	Male	Thymus	Normal

As in our previous experiments we used for the injections powdered desiccated thymus gland (Armour & Company) one gram of which is said to represent approximately five grams of fresh thymus gland of the calf. This preparation is but indifferently soluble in water, so that we have found it better to mix the dry powder first with glycerine and then to dilute with physiological saline solution. By this means a satisfactory suspension for hypodermic administration can be obtained. We used one part of glycerine to four parts of saline solution and the final preparation contained twenty milligrams of thymus substance per cubic centimeter. A mixture of one part of glycerine to four parts of saline solution was made for the control injections. The materials were warmed to 37° C. and injected under aseptic precautions. No infection occurred in any of the rabbits, but with the larger doses considerable induration was

produced at the site of injection. The injections were given twice a week.

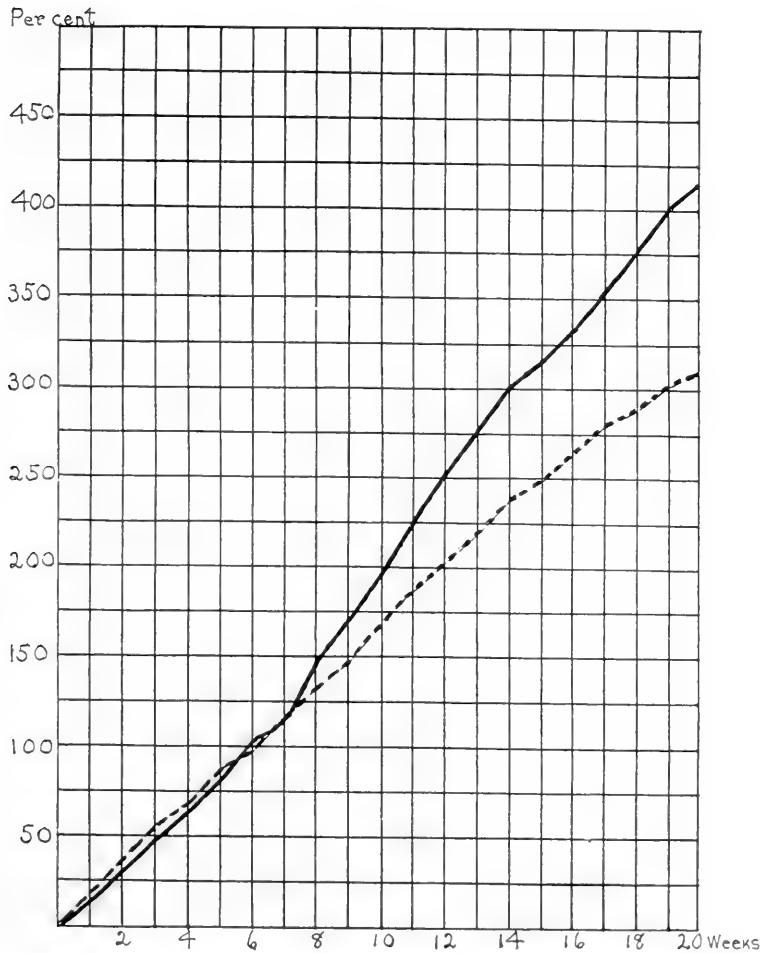
CHART 1



The initial dose for each thymus rabbit was two milligrams per one hundred grams of body weight. The dose was increased each week by one milligram per hundred grams to a maximum dose of ten milligrams per one hundred grams of body weight. This dose was continued to the end of the experiments. Each

control rabbit at the same time and under the same conditions received an injection of the glycerine-saline mixture proportion-

CHART 2

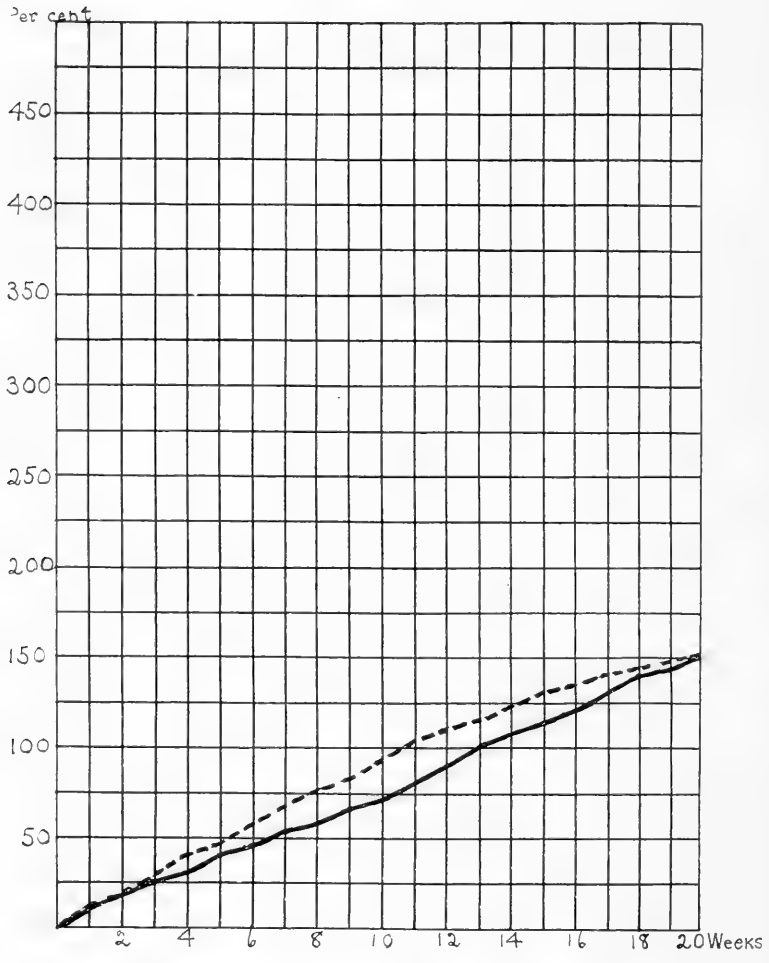


Percentage increase in growth of rabbits in group I
—— Control rabbits - - - - Thymus rabbits

ately equal in bulk. The injections were continued for twenty weeks, that is, until even the younger rabbits were apparently matured. One control and one thymus rabbit died during the course of the experiments. In both cases death occurred more than twenty-four hours after the last injection.

Each rabbit was weighed prior to injection. Growth and development progressed steadily in all. The average rate of

CHART 3



Percentage increase in growth of rabbits in group II
—— Control rabbits ----Thymus rabbits

growth is shown in Charts 1, 2 and 3. For the first ten weeks the average percentage increase of weight in the thymus rabbits is slightly greater than in the controls; but during the second ten weeks the gain in weight is considerably greater in the controls.

At the end, the controls have gained 262.41 per cent, while the thymus rabbits have gained 215.38 per cent. When the animals are grouped according to age, as indicated in Table 1, and the average gain for each age group computed, a more striking difference is observed. From the eighth week on the control rabbits of Group I, the younger group, gained much more rapidly than the thymus rabbits until, at the end of the experiment, the former have gained 414.57 per cent as compared with 308.66 per cent for the latter. On the other hand, the older thymus rabbits, Group II, maintained to the end the slightly greater percentage gain shown by all the thymus rabbits in the early weeks. The younger rabbits presumably had more active thymus glands. It is possible that the thymus injections added to this higher degree of activity of the rabbit's own thymus may have been just sufficient to affect the weight as described.

TABLE 2
Control Rabbits

Number	Weight when killed	Reduced body weight R. B. W.	Weight of thyroid in mgm. per kilo. of R. B. W.	Weight of thymus in mgm. per kilo. of R. B. W.	Weight of spleen in mgm. per kilo. of R. B. W.
1	3.105	2.950	9.1	2383.0	647.7
7	3.055	2.613	63.9	540.7	213.5
10	3.260	3.078	61.0	1330.4	501.4
11	3.355	3.208	78.8	1049.8	499.6
15	1.630	1.485	121.8	1587.8	1740.7
18	2.200	2.012	95.9	1427.4	240.0
21	2.140	2.049	95.1	562.7	315.7
22	2.210	2.132	110.6	1386.0	253.7
Averages	2.619	2.440	79.5	1283.4	551.5

None of our rabbits developed muscular spasms or convulsions. Their behavior was normal so far as we could detect.

At the end of the twenty weeks the rabbits were killed and autopsies performed. The method employed was practically that of Livingston and as described in our previous report. The weight of the animal minus urine and contents of the gastro-intestinal tract, i. e., reduced body weight, was determined. The thyroid and thymus glands and spleen were removed from each rabbit and weighed. The sexual apparatus was examined macroscopically. The reduced body weight and the weight of each of the glands removed, in milligrams per kilogram of reduced body weight, are given for the control rabbits in Table 2 and for the thymus rabbits in Table 3. A comparison of the figures shows that in the thymus rabbits the thyroid glands average 25.78 per cent heavier, the thymus glands 28.18 per cent lighter, and the

spleens 23.84 per cent heavier than in the control rabbits. A closer analysis reveals that the difference in the thyroids is confined to the younger group of rabbits. The average weight of the thyroids in the control rabbits of this group is 53.2 mgm. per kilogram of reduced body weight; the average weight of the thyroids in the thymus rabbits of the same group is 102.4 mgm. per kilogram of reduced body weight, a difference of 92.48 per cent. In the group of older rabbits, the thyroids in the controls averaged 105.8 mgm. and in the thymus rabbits, 96.8 mgm. per kilogram of reduced body weight, a slight difference in the opposite direction. We find the weight of the thymus reduced about equally in both groups. There is considerably more difference in the weight of the spleens of control and thymus rabbits in the

TABLE 3

Thymus Rabbits

Number	Weight when killed	Reduced body weight R. B. W.	Weight of thyroid in mgm. per kilo. of R. B. W.	Weight of thymus in mgm. per kilo. of R. B. W.	Weight of spleen in mgm. per kilo. of R. B. W.
3	2.575	2.397	99.2	1236.1	878.1
5	2.360	2.154	109.0	1295.2	295.2
6	2.535	2.391	148.4	1082.3	506.0
8	2.475	2.222	100.3	1137.7	546.8
9	2.640	2.429	109.5	916.0	518.3
12	1.815	1.678	85.2	101.9	758.6
13	2.340	2.184	90.2	904.3	787.5
14	2.515	2.241	77.6	1599.7	708.1
16	1.990	1.905	75.0	570.6	640.4
17	1.685	1.579	155.1	1067.1	1732.1
19	2.175	2.032	78.7	211.1	499.5
20	2.310	2.102	66.1	973.8	568.5
23	2.185	2.017	94.1	842.3	554.2
24	2.315	2.200	112.2	966.8	579.5
Averages	2.279	2.109	100.0	921.7	683.7

younger than in the older group. In the former, the spleens of the thymus rabbits were 34.22 per cent heavier than those of the controls and in the latter, 19.57 per cent.

The most striking feature of these results is the increased weight of the thyroid glands of the thymus rabbits of the younger group. Burget has shown that high protein diets produce thyroid hyperplasia. It is possible that protein would have the same effect when injected hypodermically. The thymus preparation employed in these experiments obviously contained a large amount of protein. Therefore, we cannot say positively that the increased size of the thyroids is not due to protein. However, if the causative factor were protein, the change should have been just as marked in one group as in the other, since both received proportionately the same amounts of the preparation and, there-

fore, of protein. As we have pointed out, the difference was limited entirely to the group of younger animals.

The increased weight of the thyroids occurring in the same group of rabbits which showed the relative loss of body weight may be indicative of direct action of some active principle of the thymus. As already mentioned, its greater influence in the younger animals might be because the thymus glands of these younger rabbits were normally at a more active stage when the injections started.

The total weight of the thyroid gland in rabbit number 1 A, a female control, was only 27 mgm., 9.1 mgm. per kilogram of reduced body weight. The thymus gland in the same rabbit was larger than in any of the other rabbits. It weighed 7.030 grams or 2383 mgm. per kilogram of reduced body weight. This finding does not support the idea that hyperplasia of the thymus causes increase in the thyroid. The large thymus might of course have been compensatory to a deficient thyroid.

With two exceptions, the sex glands of all the rabbits appeared normal. There was only one testicle visible in number 15 E, a control, and at autopsy no sign of another could be found. The internal sexual apparatus of number 12 D, a female of the thymus group, was infantile in type. The thymus gland of this rabbit was extremely small. It weighed 101.9 mgm. per kilogram of reduced body weight, only a twelfth of the average weight of the thymus glands of the control rabbits. This defect of the sexual apparatus was congenital since the organs were not even at the stage of development to be expected in a rabbit of seven weeks, the age of this animal at the beginning of the experiments. While our thymus injections cannot be said to have caused the retarded development neither do they appear to have caused any improvement.

Eleven female rabbits were used in these experiments, of which six could have become pregnant, and four did become pregnant. Of the other two, one was a thymus rabbit, the other a control. One thymus and one control rabbit each gave birth to a normal litter during the twentieth week of the experiment. The other pregnancies were noted at autopsy (see Table 1). There is no evidence that the thymus injections exerted any influence upon the sex glands of these rabbits.

CONCLUSIONS

1. Subcutaneous injections of large doses of desiccated thymus substance, while checking the putting on of weight in young rabbits, did not otherwise impair growth or development.

2. A considerable increase in the weight of the thyroid gland and spleen and a decrease in the weight of the thymus were produced in young rabbits by subcutaneous thymus injections.

The expenses of this research were defrayed in part by a grant from the James Cooper Fund for Medical Research.

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PRACTICAL ORGANOTHERAPY. The Internal Secretions in General Practice. By Dr. Henry R. Harrower, Glendale, Cal. The Harrower Laboratory, 1920, 268 p.

This is an ambitious little book written by an optimistic endocrinologist who attempts to crowd into 268 pages a resume of all the present knowledge on endocrinology and organotherapy. He succeeds in presenting his views on the subject in a readable and interesting manner, but with no great success as to scientific accuracy. The book contains statements which have not as yet been accepted, advancing claims which some experimenters and clinicians would be slow to accept.

All in all, this book must be considered in the light of a commercial publication and accepted in the same class as, for example, Merck's Index. Considering it from that viewpoint, the general practitioner will find many helpful hints on an interesting and timely subject.—M. B. G.

QUATRE LECONS SUR LES SÉCRÉTIONS INTERNES. By Prof. Eugene Gley, Paris. Paris, 1920, Baillière et fis, 154 p.

Professor Gley is competent, as few are, to indicate the course of development of endocrine science and to discuss the philosophic aspects of the subject. In a series of four lectures delivered before the "Sociedad de Biologia" of Barcelona in 1917, an engaging presentation of the matter was made, and the lectures are now fortunately available in book form. The topics covered were: the evolution and present status of the endocrine question; the physiological conditions necessary to internal secretion; new orientation of researches upon hormones and hormazones and, finally, the essential results of the study of the internal secretions—a revolution in biology.

The first chapter is a critique on the general doctrine of the internal secretions, centering about the work of Claude Bernard. As to the present status of endocrinology, Gley reminds us again that the doctrine has not acquired precision and stability *pari passu* with the rich accumulation of new facts. The field is encumbered with incomplete experiments, adventurous hypotheses, vain theories and even errors. Experimental observations are often applied without reflection and, indeed, without logic,—both of which, one may add, are eminently required.

In the second chapter are defined the precise conditions that must be met before an endocrine function can be postulated. Sundry new "Hormones" have been introduced which

we might have been mercifully spared had their sponsors comprehended these principles. To any who are sanguine of finding "hormone x" or y or z, this chapter is especially commended.

The third chapter comprises a critical discussion of methodology and the fourth, a formulation of a conception of the significance of endocrinology in the field of general biology.

In the present stage of development of our subject, all sorts of attempts at exposition of its underlying philosophy are perhaps to be expected. It is fortunate when, as in this case, the expositor is a master in the field, who has gone both deep and wide.—R. G. H.

ABSTRACTS

ACHONDROPLASIA, Effect of—on menstruation. Miller (J. L.), West Va. M. J. (Huntington), 1920, **14**, 366-367.

The article gives a brief resume of the leading characteristics of achondroplasia, and a report of two cases that have been under observation for twenty years, particularly in regard to their menstrual life.

The characteristics common to both patients were: both had mothers under the normal female stature, but normal in every other way; both were members of large families, their brothers and sisters being normal, except in one case they were slightly under normal adult stature. No history of other dwarfs in either family, and no evidence or history of thyroid trouble in either patient or any member of their respective families was elicited.

One patient, aged 26 years, height 4 feet 2 inches, weight 126 pounds, physical development typically achondroplastic, intellect excellent, began menstruating at the age of two weeks, the lochia having the gross appearance of an adult female, and has continued at twenty-eight day intervals until December, 1918, when she went into the menopause with the characteristic nervous and physical phenomena of this condition in the normal female. Pubic hair appeared at age of five or six years and breasts and facial appearance became that of the mature adult.

Case two: the subject was twenty-five years old, 3 feet 11 inches in height, and 125 pounds in weight; all features were very typical of achondroplasia, especially the marked bowing of the femurs and bones of both legs. The intellect was normal. Pubic hair and development of the breasts appeared about the 12th to 15th years, but no indication of the menstrual flow appeared until the twenty-first year, though for several months preceding the appearance of the flow there was a general malaise for a few days at four to six weeks' intervals. Corpus luteum and thyroid extract were tried at different times in the second case, but with no apparent result.

The conclusions are that the menstrual phenomena in these cases, and probably the physical development as well, were

due to some severe disorder of the endocrin system, and that probably in the first case certain hormones which normally stimulate growth and development of the sexual functions were present to an excessive degree, and in the second case insufficient or nearly suppressed.—Author's Abst.

ADIPOSIS DOLOROSA (Zur Kenntnis der Adipositas dolorosa). Grafe (E.), München. med. Wchnschr. 1920, **67,** 339-341.

The author describes a case in a woman of 21. The disease began at the same time as the beginning of menstruation, with psychical alterations, and gradually increasing adiposity. The blood sugar was normal. The thyroid could not be palpated. The symptoms are not those of Dercum's disease, for in Dercum's disease pain is not spontaneous, but the tumors are painful only upon pressure; such condition did not obtain in this case. There was a certain degree of periodicity in the symptoms. The patient showed an enormous retention of water. Oophorin, hypophysis and thyroidin had a good influence, as well on the retention of water as on metabolism, but were not able to cure the disease.—J. K.

ADIPOSITY, Cerebral versus lacteal—. Reuben (M. S.), Arch. Pediat. (N. Y.), 1919, **36,** 636.

To prove that every fat baby has not a tumor of the pituitary, the author reports a case of a girl, 10 months of age, who gave the following dimensions: circumference of head, 17½ inches; chest, 24¾ inches; length, 29½ inches; mid-thigh, 15¾ inches; mid-leg, 10½ inches. The anterior fontanel was closed. She did not show any symptoms of dyspituitarism; there was no hyperglycemia, no reaction to pituitary extract. The Wassermann was negative. The eye grounds were normal. An analysis of the mother's milk showed 6 to 7 percent fat, which the author felt accounts for the adiposity. He also reported another case of a child who weighed 7 pounds at 7 months and 35 pounds at one year of age. When last seen at the age of 6 years, she had not shown any signs of hypopituitarism.

—M. B. G.

(ADRENALS) Addisonian symptom complex. (Addisonscher Symptomenkomplex.) Wien. klin. Wchnschr. (Vienna), 1918, **31,** 799.

A classical case. No new data.—F. S. H.

(ADRENALS) The time relations of the blood pressure changes after excision of the adrenal glands, with some observations on blood volume changes. Bazett (H. C.), J. Physiol. (Lond.), 1920, **53**, 320-339.

The experiments described consist of some controls made at the commencement of an investigation of the relation of the adrenals to vascular tone. Animals may survive one to three days after excision of the adrenals, but low blood pressure is found some time previous to death. The time of development of these changes has not been carefully investigated.

Most of the work was done on cats; a few experiments were also made on rabbits. The rate of the fall of blood pressure was measured in animals in which the glands were removed under ether and which were then allowed to recover: in animals under continuous urethane anesthesia, and in animals previously decerebrated. It was found that excision of the adrenals in the cat is not followed immediately by a fall of blood pressure, but the changes develop more rapidly in decerebrate animals than in those under urethane anesthesia. They are least rapid in ether anesthesia followed by recovery from the ether. Urethane anesthesia may be used in cats for experiments lasting twenty-five hours or longer. The pressure falls 10 to 20 per cent lower than in ether or decerebration, and after eight hours of anesthesia may fall still further. Decerebrate preparations may be used for blood pressure experiments lasting several days, if care is used. Excision of the adrenals in a urethanized cat causes a fall in blood pressure in two or three hours, and death results in about ten and one-half hours. In the decerebrate cat excision of the adrenals is followed by a fall of pressure in one hour, and death in six hours. In ether anesthesia it is eighteen hours before the fall reaches 30 to 40 per cent. With excision of the adrenals there is an immediate slight dilution of the blood, but later as the pressure falls there is little further dilution. After adrenal excision under urethane, the various types of response to sciatic stimulation could not be obtained with any degree of constancy.—T. C. B.

ADRENAL insufficiency, Anatomical clinical study of two cases of—(Étude anatomo-clinique de deux cas d'insuffisance surrénale). Betchov (N.) and Demole (V.), Rev. méd. de la Suisse Rom. (Geneva), 1918, **38**, 379-386.

A detailed description of two cases of adrenal insufficiency presenting nothing new but substantiating the idea that "Ser-

gent's line'' is clinical evidence of a lessened adrenal efficiency. —F. S. H.

(ADRENALS) Addison's disease (Maladie bronzee d'Addison). Boinet, Marseilles med., 1918, **55**, 176-181.

A clinical report and autopsy findings of two cases of Addisonian coma following extreme fatigue. In three non-fatal cases adrenal opotherapy was successful in ameliorating the distress.—F. S. H.

(ADRENALS) A case of Addison's disease. Cabot (R. C.), Case Records Mass. Gen. Hosp. (Bost.), **6**, 920, No. 18, part 1.

The case of a carpenter aged sixty-four years is presented. The patient's family history is negative and his health had been unusually good. At twenty-four he had measles; at thirty-two typhoid fever without sequelae, except constipation. For ten years he had hemorrhoids with a little bleeding. He had occasional headaches. Before the typhoid fever he weighed 230 pounds, his best weight. His usual weight has been 190, and he thinks he has lost about fifty pounds in the past two years.

The patient's bowels have been irregular and constipated, especially for the past three or four years. Three years ago for a period of two weeks he was nauseated, and regurgitated all food in a few minutes after it had been taken. He was in bed on a diet. He recovered and again ate the same kind of food as the rest of the family, but less of it. He went back to his work. One year later he had a similar but much less severe attack lasting for a week. For five months he missed one or two days' work in a month, and then two months ago he gave up work entirely on account of general weakness. Since then, also, he has been unable to retain anything but a quart of milk a day, malted milk, spinach, and an occasional cracker. There has been no pain.

Examination revealed that there was no expansion of the left lung during respiration and the x-ray plate gave the appearance of an old tuberculous infection involving both lungs and the left pleura. Pulse, 92 to 129, was of poor volume and tension. Blood pressure: systolic 110, diastolic 80. Urine and stools negative. Blood: hemoglogin 70%, leucocytes 12,880 with 57% polynuclears, slight anisocytosis; Wassermann reaction negative.

The patient died on the third day after admission and autopsy revealed: tuberculosis of the adrenals by which they

were transformed into fibrocalcarous masses; arteriosclerosis and dilatation of the heart; chronic pleuritis; absolute tuberculosis of the bronchial lymph nodes, and cholelithiasis.—J. F.

(ADRENAL) The pathology of experimental rabies. I. The kidneys, adrenals, liver and spleen. Cornwall (J. W.), Indian J. Med. Research (Calcutta), 1919, **7**, 148-159; Abst., Chem. Abst., 1920, **14**, 2204.

Hyperglycemia is a late phenomenon in fixed-virus rabies. It is sometimes followed by glycosuria. There is little change in the glycogen content of the liver. The urine becomes acid (rabbits) and globulins are excreted with but little albumin. The specific gravity of the urine falls markedly on the 5th day and the percentage of chlorides at first increases and then decreases. The weight of the adrenal gland increases by one-third and autolytic changes occur, chiefly in the medullary cells. Kymographic studies show a diminution in the pressor effects of adrenal gland extracts during the 48 hours following sub-dural inoculation. This is followed by recovery and then toward the end of the disease there is a second diminution in the quantity of pressor substances. Chemical tests show a diminution of adrenaline in the adrenal glands of rabbits succumbing to fixed-virus rabies and also of guinea-pigs dying from intramuscular inoculation with street virus. It is concluded that growth of the rabies organism in the central nervous system causes irritative stimuli to pass along the splanchnic nerves to the adrenals and liver and gives rise to the discharge into the blood stream of an excess of sugar. Sometimes an excessive secretion of adrenaline occurs. Much damage is caused to the kidneys and adrenals by toxic agents in the blood derived from the growth of the rabies organism in the central nervous system.—R. G. H.

(ADRENAL) The pharmaco-dynamics of quinine. II. Some effects of quinine on the adrenals, kidneys, and spleen of healthy rabbits. Cornwall (J. W.), Indian J. Med. Research (Calcutta), 1919, **7**, 160-166.

Quinine administered intravenously and intramuscularly to rabbits over a period of 9 months causes damage to the cellular elements of the adrenals and kidneys and increases the rate of disintegration of the red blood corpuscles in the spleen.—Chem. Abst., **14**, 2218.

(ADRENALS) Direct transmission of Addison's disease (Transmission directe de la enfermedad de Addison). Es-

pina, Real Acad. Nac. de Medicina (Madrid), 1919, ——, —— (Mch. 15).

Espina gives a clinical description of two boys with Addison's disease whose father had died of the same disorder. The opinion is expressed that these cases arose through direct transmission from the father to the sons.—E. B.

(ADRENALS) Some observations on the functions of the suprarenal glands, in white rats. Exner (H. V.), Dublin J. Med. Sc., 1920, **4**, 79-89.

Investigation by means of asphyxiation experiments, performed on white rats, showed, that despite the presence of the adrenals, a fall of blood pressure was noted, similar to that in animals from which the adrenals were removed. This investigator concludes, therefore, that the adrenals normally play no part in the rise of blood pressure, despite the fact that an injection of adrenal extract produces this phenomenon. He also found that when the central end of the vagus was stimulated in those animals from which the adrenals were extirpated, sugar was found in the urine. He concludes that "the glycogenic function of the suprarenals is dependent on, or works in conjunction with, some nervous control, which functionates, at least in part, even in the absence of these organs."
—J. H. L.

(ADRENALS) Symptoms produced by the plexus solaris in tuberculosis of the lungs (La sindrome solare negli ammalati di tuberculosi polmonare). Gallotti (A.), Il Morgagni (Milano and Napoli), 1920, **62**, 81-96.

The author observed in two cases of tuberculosis of the lungs symptoms resembling tabetic crises or lead colic. No changes in the abdomen could be detected, even at autopsy. The "ligne blanche surrénale" of Sergent was present, and there was low blood pressure. Defective functioning of the plexus solaris is probably the cause of these symptoms. This point the author discusses in some detail. Cases have been described in which the plexus was compressed by tuberculous tissue; but even without these gross changes the affinity of the sympathicus for the toxins of the tubercle-bacillus is well known. The primary affection here is probably insufficiency of the sympathicus, the secondary, insufficiency of the adrenals.
—J. K.

(ADRENALS) The significance of the chromaffin system (Die Bedeutung des chromaffinen Systems). Hart (C.), Ztschr. f. ärztliche Fortbildung (Jena), 1920, **17**, 221-225.

An interesting general discussion without new facts. The author believes that Addison's disease is caused by a pathological process in the adrenals in patients with a hypoplastic constitution. As Graves' disease is also found in persons with this constitution the (very rare) combination of Graves' and Addison's diseases may perhaps be explained on the same basis. —J. K.

(ADRENAL) A case of uterine epithelioma presenting the typical characteristics of cortical suprarenaloma (Un cas d' epithéliome utérin presentant les caractères typiques du cortico-surrénalome). Hartmann (H.) & Peyron (A.), Gynec. et Obst. Rev. Mens. (Paris), 1920, **1**, 1-19.

The review of the literature reveals 11 reported cases of tumors of suprarenal type occurring in the internal genital organs of women. The paper is a report of a case operated upon by the authors. It was found that the broad ligaments were free and the tumor was intrauterine. Nine plates are shown of the histological findings compared with normal material.—F. S. H.

ADRENAL insufficiency in the infections (Insuficiencia suprerenal en las infecciones). Marañón (G.), Acad. med.-quir., 1919, ——, ——, (Mch. 18).

In all infectious diseases there are frequently accidents of the nature of collapses which have been heretofore attributed to alterations of the myocardium, the question of suprarenal insufficiency should be considered. Both types occur. These glands possess two functions, the one an antitoxic, protective function accomplished by the internal secretion of cholesterol of cortical origin, and the other the tonic effect of adrenalin of medullary origin. When this latter is diminished or lacking, collapse is produced. These accidents can be either chronic or acute; the first recall cases of Addison's syndrome; the second are rapid syncopes with hypothermia and asthenia resembling shock. They are very frequent in diphtheria and typhoid; sometimes they are observed in exanthematous typhus. Autopsy often shows small suprarenals with little adrenaline and cholesterol. During the life of the patient these constituents are seen to diminish in the blood. From these facts it follows that adrenaline should be administered in the form of extracts

of the whole gland in those infections in which collapse is feared.—E. B.

(ADRENAL) Nicotine apnea. Ozorio de Almeida (A.), J. de physiol. et path. gén. (Par.), 1920, **18**, 744-752.

When nicotine is injected intravenously into anesthetized dogs, a prolonged arrest of respiration is produced which can properly be called nicotine apnea. It is not due to the sharp rise in blood pressure following the injection since double vagus section does not inhibit the apneic effect. Neither stimulation of the central end of the cut vagus, nor ablation of the adrenals prevented the appearance of the characteristic re-response.—F. S. H., Chem. Abst., **14**, 2219.

ADRENALS, Chloroform narcosis and the— (Chloranarcozi e funzioni surrenale). Pitini (A.), Gazetta degli Ospedali (Milano), 1920, **41**, 415.

After narcosis with chloroform the content of adrenalin in the adrenal glands is diminished. Perhaps the high blood pressure in the beginning of narcosis and the low pressure during the rest of this period may be explained in this way, that first the chromaffine system is stimulated and produces more adrenalin. This would be followed by an exhaustion of the chromaffine system. [This idea was proposed by Elliott years ago.] The suggestion is again offered that injections of adrenalin are of use in narcosis.—J. K.

(ADRENAL) A case of hypernephroma in the renal hilus. Stenström (N.), Hygiea (Stockholm), 1919, **81**, 843-851.

The tumor, which occurred in a woman of 46 years, was the size of a Mandarin orange. It was histologically benign. —J. A. H.

(ADRENALS) Further observations on the relation of the adrenals to certain experimental hyperglycemias (ether and asphyxia). Stewart (G. N.) & Rogoff (J. M.), Am. J. Physiol. (Balt.), 1920, **51**, 366-377.

The paper is an answer to recent critics, especially Kellaway, with some new experiments to show that epinephrin output is not essentially concerned in the hyperglycemia induced by ether narcosis and by asphyxia.—T. C. B.

ADRENAL bleeding in the new-born (**Ueber Nebennierentblutungen bei Neugeborenen**). Toepffer (H.), Arch. f. Gynaek. (Berlin), 1920, **112**, 342-356.

A clinical and post-mortem description of an infant dying three days after birth with some evidence of adrenal involvement. The histological picture of the adrenals seems to justify the conclusion that the condition is the result of a primary, early occurring fatal thrombosis of the suprarenal vein, which in turn has caused chronic fibrous induration and local parenchymal necrosis. There had taken place extravasation of blood into the necrotic area. As a consequence of the act of birth arterial congestion apparently had occurred, resulting in a still further escape of blood into the tissues.—F. S. H.

(ADRENAL) The action of adrenin and of various extracts of glandular organs on veins. Tugane (S. H.), Sei-I-Kwai M. J. (Tokyo), 1919, **38**, 51.

Cow's method, with but slight alterations, was employed for registering the contractions of the veins which were obtained from freshly killed pigs, dogs and cats. The author observed that ring preparations of veins, when treated with adrenin, contract with reduction in volume just as do arteries, which indicates, in his opinion, that they are probably supplied with sympathetic venoconstrictor fibers. He found, on the other hand, that treatment with saline extracts of lymph gland, spleen, kidney, liver and muscles brings about a dilation of the ring preparations, indicating perhaps the existence of venodilator fibers. No histological evidence is presented.

—E. V. C.

ADRENAL syndrome, **Contribution to the study of— (Contribution al estudio de los sindromas suprarrenales).** Venegas (F.), La Clin. Castellana. 1919, ——, ——.

General review.—E. B.

ADRENIN, The intravenous injection of—in the treatment of hemorrhage (A propos des injections intraveineuses d'adrénaline dans le traitement des hémorragies). Bardier (E.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 91-94.

A continuation of studies already reported (see Endocrin. **4**, 105). Two experiments on exsanguinated dogs showed that in spite of the loss of blood and the serious symptoms resulting, the intravenous injection of adrenalin causes hyperten-

sion, acceleration and augmentation of the heart beat, and resumption of respiration. The action is of short duration—three to four minutes—but can be reproduced by successive injections.

Two observations on human subjects are also reported: one was a man of sixty with a severe crushing of the lower extremities and loss of blood, the other a woman, exsanguinated by rupture of a fallopian tube. Both cases responded to the adrenalin, but only the woman recovered. She lived eight days, and then died of pneumonia. The proceeding seems indicated as an extreme emergency measure, and may keep the heart going while preparations are made for transfusion.—T. C. B.

ADRENALIN, The effect of the subcutaneous injection of—on the heat production, blood pressure and pulse rate in man. Boothby (W. M.) & Sandiford (Irene), Abst., Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51,** 200-201; in full, Ibid, 407-421.

The results are reported of forty-six experiments on groups of patients showing variations in the activity of the thyroid, pituitary or adrenals, as well as a small group of normal controls. Adrenalin causes an increase in heat production, increase in the respiratory quotient, ventilation rate, respiration rate, heart beat per minute, volume of each beat, peripheral vascular dilatation and systolic and diastolic pressures. Not all come into play in any one case, but some combination. There is no relationship between the character of the adrenalin reaction and the degree of activity of the thyroid, and therefore the reaction is not indicative of the presence or absence of hyperthyroidism. The metabolic rate curve is similar to that of carbohydrate plethora and suggests the possibility that the increased heat production may be due to an excess of carbohydrate metabolites. There may also be direct chemical stimulation of cellular combustion.—T. C. B.

ADRENALIN treatment of rachitis (La adrenalina en la tratamiento del raquitismo). Corominas (F.), Arch. Españ. de Pediat. (Madrid), 1919, **3,** 215-224.

The author reviews the current theories with respect to the etiology of rachitis and insists that every case is accompanied by an endocrine dysfunction, which paves the way for the alimentary toxemias, etc. The parathyroids, thymus and suprarenals are the glands which play the major role in this

process by reason of their influence on the calcium metabolism. Corominas has used several extracts of endocrine glands as therapeutic agents and considers that adrenaline produces the best results, since it acts directly and at the same time whips up the endocrine system as a whole. It is preferably administered by the gastric route two to three drops daily of the one to a thousand solution.—E. B.

ADRENALIN, The excretion of—according to recent studies, particularly of G. N. Stewart and his students (De l'excrétion de l'adrénaline d'après les travaux récentes, particulierment cieux de G. N. Stewart et de ses élèves). Heitz (J.), Arch. de. mal du coeur (Paris), 1918, **11**, 215-218.

A review.—F. S. H.

Concerning ADRENIN. I. The alterations of the vasopressor action of adrenalin after its treatment with bacterial products (Zur Kenntniss des Adrenalins. I. Über die Änderung der blutdrucksteigeinden Wirkung des Adrenalins nach Behandlung desselben mit bakteriellen Produkten). v. Gröer (F.) & Hecht (A. F.); Biochem. Ztschr. (Berlin), 1920, **102**, 1-12.

When adrenalin is kept in contact with diphtheria toxin for a considerable period of time it loses its ability to cause an increased blood pressure in dogs. The bacterial nucleo-proteins have a still greater destructive action. This disturbing effect cannot be attributed to the presence of free OH-ions. When the toxin or the bouillon is boiled they are much less, if at all, active in destroying the effectiveness of adrenalin.—F. S. H.

Concerning ADRENIN. II. The alterations of the vasoconstrictor action of adrenalin under the influence of different hydrogenion concentrations and after its treatment with bacterial products and proteins (Zur Kenntniss des Adrenalins. II. Über die Änderung der gefässverengenden Wirkung des Adrenalins unter dem Einfluss verschiedener Wasserstaffionenkonzentationen und nach Behandlung desselben mit verschiedenen bakteriellen Produkten und Eiweisskörpern). v. Gröer (F.) & Matula (J.), Biochem. Ztschr. (Berlin), 1920, **102**, 12-38.

Under anerobic conditions alkali reacts on adrenalin to cause an initial increase followed by a decrease of its vasoconstrictor activity. This is accomplished through retarding the oxidation of adrenalin, the optimum effect being obtained

between PH=7.5 and PH=8.5. Contact with bacterial nucleoproteins has a similar effect even under anerobic conditions and regardless of the reaction of the medium. This property of the nucleoproteins is weakened by heating. Both nucleoproteins and other protein compounds retard the oxidation of adrenalin through which an air-current is passed: this reaction occurs regardless of the reaction of the medium and is lessened if the proteins be heated. Many true proteins, and also tuberculin, cause an increase in the adrenalin activity after long contact under anerobic and H atmospheric conditions; while they exert an inhibitory action on the disturbing effect of OH-ions. The adrenalin disturbing action of the diphtheria toxin is complex and bound up with the nucleoprotein as well as with the OH-ion activity.—F. S. H.

(ADRENIN) Bodily symptoms caused by emotion (Lichamelijke afroijkingen tengevolge van emotie). Kooy (F. H.), Neder. Maandschr. Geneesk. (Leiden), 1920, **1**, 29-44.

Cannon has reported that emotion (fear, rage) causes hyperactivity of the sympathicus and a hypersecretion of adrenalin. The author found in agitated patients with psychoses a higher amount of blood sugar and a higher blood pressure than normal. It is suggested that the changes in temperature (hysterical fever) and in the function of the intestines during emotion may perhaps be explained in the same way.—J. K.

ADRENIN, Action of Röntgen rays on—. Lüdin (M.), Strahlentherapie, 1918, **8**, 441; Zentralbl. f. Biochem., u. Biophys., **21**, 179.

Previous observations of Richter and Gerhartz have indicated that the action of adrenaline is impaired or inhibited by Röntgen rays. L. was unable to confirm these observations. By determining adrenaline according to the Magnus procedure in the surviving intestine, L. found that no change in the activity of adrenaline on account of the action of Röntgen rays could be detected.—Chem. Abst. **14**, 1125.

(ADRENIN) The substance in the blood-serum resembling adrenalin (Over de op adrenaline gelikjende stoffen in bloedserum). Rassers (J. R. F.), Nederl. Tijdschr. v Geneesk. (Haarlem), 1920, **64**, 785-791.

Of no immediate endocrine interest.—J. K.

(ADRENIN) The practical value of curved needle injection in the intercricothyroid region (La pratique usuelle de l' injection intercricothyroidienne par l'aiguille cousle). Rosenthal (G.), Bull. gén. therap. (Paris), 1920, **171**, 156-158.

Of technical interest, and mention of the use of adrenalin by this method.—F. S. H.

Effects of ADRENIN (Adrehalinwirkungen). Schlesinger (H.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 335.

A short note to the effect that injections of adrenalin in the aged may cause stenocardia and a fall of blood pressure. This may be explained by the fact that adrenin has an effect on the vasoconstrictor as well as on the vasodilator mechanism.—J. K.

(ADRENIN) Vascular reaction to epinephrin in perfusates of various H-ion concentrations. Snyder (C. D.) and Campbell (W. A., Jr.), Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51**, 199-200.

Confirmatory evidence is given to show that the reversal (dilator) effect of epinephrin may be due to H-ion concentration.—T. C. B.

(ADRENIN) Further observations on the relations of the central nervous system to epinephrin secretion. Stewart (G. N.) & Rogoff (J. M.), Abst. Proceedings Am. Physiol. Soc., Am. Jour. Physiol. (Balt.), 1920, **51**, 175-176; in full, Ibid, 484-524.

Former experiments on the epinephrin output after transection of the spinal cord at different levels in cats have been confirmed and extended by a new series of experiments. After section of the cervical cord the output of epinephrin was undiminished in several animals, while in others it was more or less diminished. When the brain and bulb were eliminated there was a full normal output. In survival experiments the output was one-half to one-third the normal average. In acute experiments with dorsal cord transections, the output was greatly diminished or abolished. Strychnine caused a marked increase in the output in both acute and survival cases. Further experiments on cats with denervated hearts confirm their previous conclusion that the reactions obtained do not constitute a demonstration of epinephrin output with asphyxia and nerve stimulation (as reported by Cannon and von Anrep), until it is

shown that redistribution of the blood with normal output cannot account for the reactions.—T. C. B.

(ADRENIN) Case of ptyalism during pregnancy treated with adrenalin (Un cas de ptyalism gravidique traité par l'adrénaline). Trillat (P.), Bull. Soc. Obst. et Gyn. (Paris), 1919, **4,** 85-87.

A primipara of 30 years complained of excessive salivation. On examination it was found that the patient was secreting from 900 to 1100 cc. of saliva daily. The daily oral administration of 10 drops of adrenalin 1:1000 for 3 weeks resulted in a gradual diminution of the output to normal.—F. S. H.

ADRENALINE, The use of—in obstetrics (Empleo de la adrenalina en la obstetricia). Udaeta, Soc. Ginecol. Española, 1918, ——, —— (Feb. 6).

This paper presents the clinical case histories of two cases of suprarenal insufficiency during pregnancy showing asthenia, hypotension, lumbar-abdominal pains, vomiting and Sergent's line. The administration of thirty drops of adrenaline a day generally resulted in relief of the symptoms and the satisfactory completion of the pregnancy at term.—E. B.

ADRENIN, Treatment of gestation osteomalacia with— (Behandlung des Gestationsosteomalazie mit Adrenalin). Wagner (G. A.), Wien. klin. Wchnschr. (Vienna), 1920, **33,** 324; Deutsche med. Wchnschr. (Berl.), 1920, **46,** 423.

Data reported elsewhere. See Endocrin., **4,** 247.—J. K.

ADRENIN, Treatment of influenza with— (Grippebehandlung mit Adrenalin). Wagner (G. A.), Wien. klin. Wchnschr. (Vienna), 1920, **33,** 324; Deutsche med. Wchnschr. (Berl.), 1920, **46,** 423.

Data reported elsewhere. See Endocrin., **4,** 247.—J. K.

ADRENIN, Abdominal complaints cured by— (Buikklachten onderdrukt door adrenaline). van Waveren (A. G. W.), Med. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** (i), 1716-1717.

From a patient with abdonimal pains the appendix was removed. During the operation pericolitis was observed. The operation had no influence on the pain, but it disappeared when 25 milligrams a day of dried adrenal gland was given.

The pain returned as soon as the administration of the adrenal was discontinued.—J. K.

(AUTONOMIC N. SYST.) Constitutional kinesthopathy (I cenestopatici constituzionali). Buscaino (V. M.), Riv. di Patol. nerv. e ment. (Firenze), 1918, **23,** 257-285.

The author during the war was struck by the unusual number of cases coming under his notice with such ominous diagnoses as epilepsy, dementia precox, etc., who after a time completely recovered. From the total number he was able to differentiate a group of two hundred with sufficient similarity as to permit their classification as "Constitutional cenestopathies." These are discussed in detail. Their general characteristics were neuropsychopathic heredity, cranial and facial asymmetry, abnormal kinesthesia, great irascibility and marked irritability throughout the vegetative mechanisms. They were predominantly sympathicotonic, as shown, for example, by tachycardia and vasomotor instability. For numerous other details those interested should consult the original. —G. V.

CORPUS LUTEUM, The physiology of the—. Hermann (E. T.), Minnesota Med. (St. Paul), 1918, **1,** 181-185.

A general discussion containing no new data.—F. S. H.

CORPUS LUTEUM extract, The use of—hypodermically in cases of repeated abortion without demonstrable cause. Hirst (J. C.), Am. J. Obst. (N. Y.), 1918, **77,** 662-664.

A report of three patients with histories of repeated abortion, two of whom were enabled to carry to term and deliver infants by the empirical use of 1 cc. of corpus luteum extract administered hypodermically once daily for periods of nine weeks. The cases were discussed and the results favorably commented upon.—F. S. H.

(CORPUS LUTEUM) The question of ectopic decidua (Zur Frage der ektopischen Deszidua). Lahm (W.), Arch. f. Gynaek. (Berlin), 1920, **112,** 427-435.

A description of the histological pictures of the decidua of a case of ectopic pregnancy, in which it is shown that no structural differences exist between this type and that found in the uterine decidua of two months or over. Since the case showed no histo-pathological structures L. is inclined to be-

lieve that the phenomenon is attributable to an abnormality in the locus of action of the corpus luteum secretion giving the decidual reaction.—F. S. H.

(CORPUS LUTEUM) The origin of the corpora lutea. Westman (Ax.), Hygiea (Stockholm), 1919, **81,** 865-879.

The author considers that the lutein cells originate from the cells of the vascular epithelium.—J. A. H.

DIABETES, Experimental studies on—. Series 1. Production and control of diabetes in the dog. Gross anatomic relations of the pancreas. 2. Effects of carbohydrate diets. Allen (F. M.), J. Exper. M. (Balt.), 1920, **31,** 363-380. Ibid, 381-402.

These studies were based upon a form of diabetes produced by the removal of the greater part of the pancreas of animals, leaving a remnant about the duct secreting normally into the duodenum.

Allen reports an extensive series of studies upon dogs in which, by removal of the greater part of the pancreatic tissue, a diabetes closely similar to the clinical human type is produced. It was found that the injurious effects of excessive carbohydrate diet are demonstrable in partially depancreatized dogs, in the same manner as in human patients. With severe diabetes there is rapid progress of emaciation and weakness and early death. With milder diabetes, there is frequently a transitional state following operation, when the fate depends on the diet. If the tolerance is spared for a time, recovery sometimes occurs to such extent that diabetes cannot be produced by any kind or quantity of feeding, but only by removal of a small additional fragment of pancreatic tissue. The proper degree of carbohydrate overfeeding is important in this early period for producing the most useful type of diabetic animals; namely, those having good digestion and general health combined with a permanent lowering of assimilative power, like the condition of human patients. In the early stage, glucose is more powerful than starch in producing diabetes, and animals which are progressing toward complete recovery on starch diet can be sent into hopeless diabetes by admixture of glucose. The difference seems to be merely of the rate of absorption, and indicates that a rapid flood of carbohydrate is more injurious to the pancreatic function than a slow absorption. Whenever permanent diabetes is present, so that complete recovery is impossible, starch brings on glycosuria more slowly than sugar, but just as surely. The difference in time in different cases amounts to days, weeks, or

months. The clinical lesson from such experiments is that even if a patient becomes free from glycosuria on withdrawal of sugar only, nevertheless other foods should also be limited. No significant differences were observed between the assimilation of different starches, or any extreme lowering of the carbohydrate tolerance by proteins, such as alleged by certain writers in connection with the "oatmeal cure." Repair of traumatic inflammation and hypertrophy of the pancreas remnant have been mentioned incidentally as the basis of the early tendency to recovery, and also hydropic degeneration of Langerhans islands as an accompaniment of the lowering of tolerance by excessive diet. These are believed to have their parallels in human cases, and are to be described more fully hereafter.—B. T. S.

DIABETES, Acidosis in relation to—. Anklesaria (B. N.), Indian M. Gaz. (Calcutta), 1919, **54,** 96-98.

A didactic exposition of the author's opinion that diabetes is caused by a low type of latent toxemia affecting the internal secretion of the pancreas.

DIABETES mellitus and war diet in Vienna (Diabetes mellitus and Kriegskost in Wien). Elias (H.) and Singer (R.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 561-562.

In Vienna, as well as in Berlin, the underfeeding incident to the war has had a good influence on diabetes. There are, however, differences. In Berlin the patients showed glycemia even when the urine was sugar-free; in Vienna, when there was no glycosuria the amount of blood sugar was lower than normal. In Vienna, elderly patients with diabetes during the war were in better condition than young patients. The good influences of underfeeding most probably are to be attributed to the small quantities of proteins ingested.—J. K.

DIABETES, The significance of extreme hyperglycemia in— (Zur Frage der Bedeutung extremer Hyperglykämie beim Diabetes mellitus). Friedländer (G.) Berlin. klin. Wchnschr., 1920, **57,** 207.

A man of 22 years showed diabetic symptoms for 3 weeks and died in coma. This coma was not the sort characteristic of diabetes, for there was no acidosis or air hunger. The urine contained 6 per cent of sugar and the blood, 1.03 per cent. The author considers this as a case of death by intoxication with "glycosis." No post-mortem changes were found.—J. K.

(DIABETES) Fats and lipoids in the blood in diabetes mellitus. [Ueber das Vorkommen und die Verteilung von Fetten und Lipoiden im Blute (Plasma) des Menschen bei Diabetes mellitus. Chemische Beiträge zur Kenntnis der Entwicklung und des Aufbaues spezifischer Lipamien. IV.] Fiegl (J.), Biochem. Ztschr. (Berl.), 1918, **90,** 173-214.

Analyses are reported of 100 cases of diabetic lipemia, with regard to technique and distribution of the blood fats and lipoids.—Physiol. Abst. **3,** 576.

(DIABETES) Zur Pathologie und Therapie des Coma diabeticum. Fischer, Deutsche med. Wchnschr. (Leipz. u. Berlin), 1918, **44,** 503.

No new data.—F. S. H.

DIABETES, Fat metabolism in—. Geelmuyden (H. C.), Norsk Mag. for Laegevid (Christiania), 1920, **81,** 479.

Geelmuyden's comparative study of the acute diabetes in pancreatectomized dogs and human diabetes has, he thinks, thrown light on the processes in the intermediate metabolism and their genetic connection, especially in regard to the production of sugar from fat. In research of this kind, he emphasizes, all the changes in the metabolism must be taken into account, not only the glycogen and blood sugar, the glycosuria and the ketonuria, but the migration of fat, the transformation of albumin, the total metabolism and the transformation of energy. Such studies hitherto have been restricted to only some of these elements and their interrelations have been overlooked. He shows that carbohydrates promote the formation of sugar from fat, and that the output of sugar is not increased by feeding fat unless a certain amount of carbohydrate is given with the fat. This he thinks is probably the reason why carbohydrates are so injurious in human diabetes. Diabetes in pancreatectomized dogs seems to be due to the very same anomaly in the metabolism as in human diabetes. The chief difference between them is that it occurs suddenly in the dogs, while in man it is of long, slow development.—J. Am. M. Assn., **74,** 1684.

DIABETES mellitus and complications, Treatment of—. Gilliam (H. A.), Kentucky M. J. (Bowling Green), 1918, **16,** 71-73.

General article containing no new data.—F. S. H.

(DIABETES) Dispensary treatment of diabetes. Granger (A. S.), Calif State M. J. (San Fran.), 1918, **16**, 524-526.

No new data.—F. S. H.

(DIABETES) The influence of menstruation on acidosis in diabetes mellitus. Report of a case. Harrop (G. A.) & Mosenthal (H. O.), Bull. Johns Hopkins Hosp. (Balt.), 1918, **29**, 161-163

An extensive case report, accompanied by urine analyses of a diabetic showing exacerbations during menstruation.
—F. S. H.

(DIABETES) Blood sugar concentration and blood sugar methods. Höst (H. F.), & Hatlehol (R.), J. Biol. Chem. (Baltimore), 1920, **42**, 347-358.

A comparative study has been made of the various methods for the determination of blood sugar; from the study the authors conclude that it is uncertain whether any of the blood sugar methods hitherto used give only the amount of glucose. Bang and Hatlehoel's method and Hagedorn and Jensen's method give in normal individuals and in diabetics values which approximately agree. Folin and Wu's method, as well as Meyers and Bailey's modification of Lewis and Benedict's method, may, at any rate in diabetes with hyperglycemia, give too high results. This is especially the case with the last mentioned method.—F. S. H.

DIABETES, The modern conception of the pathogenesis of—, with special reference to the pancreas (Der jetzige Stand der Pathogenese des Diabetes, mit besonderer Berücksichtigung des Pankreas). Herkimer (Gotthold), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 522-524.

The author believes that the endocrine function of the pancreas is due to the cells of the acini and the cells of the Langerhans islands. But when body cells, especially the islets, are changed by pathological processes diabetes occurs. The islets have no relation with the external secretion of the pancreas. Two cases are shortly described which prove that the liver plays an important part. In these cases the patients with diabetes got cirrhosis of the liver. They lost the diabetical symptoms. In both cases at autopsy, a cirrhosis of pancreas and liver were found.—J. K.

DIABETES; The results of past treatment and future problems. Joslin (E. P.), Bull. Johns Hopkins Hosp. (Balt.), 1918, **29,** 80-85.

A general view of the author's studies accompanied by charts and dietary tables.—F. S. H.

(DIABETES ADRENALS) Acetone in cerobrospinal fluid (Aceton in de ruggemergsvloeistof). Koopman (J.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** 1346-1350.

Acetone may be found in the cerebrospinal fluid in several pathological conditions. During diabetic coma acetone and diacetic acid are found and its pressure is high. When the pressure in diabetes tends to rise it is often significant of approaching coma. Acetone and diacetic acid may be found in the cerebrospinal fluid in diabetic acidosis, also. In a case of adrenal apoplexy it was likewise found.—J. K.

PANCREATIC DIABETES. The alteration of the diastatic activity of the liver and the lack of influence of the glycolytic capacity of muscle on the extirpation of the pancreas in the frog. [Über das Wesen des Pancreas diabetes. (Die Änderung der diastatischen Wirksamkeit der Leber und die Unbeeinflussbarkeit der glykolytischen Fähigkeit des Muskels durch Pankreas- exstirpation beim Frosch)]. Lesser (E. J.), Biochem. Ztschr. (Berlin), 1920, **103,** 1-18.

Induced pancreatic diabetes in the frog causes an increased glycolysis in the intact and isolated liver, while the glycolytic function of either intact or isolated muscles is no different than the normal. No valid conclusion can be drawn concerning the fate of the muscle glycogen from the results of intravenously injected grape sugar for the increase in CO_2 output does not occur if the glycogen content has previously been strongly reduced by hunger and work. The glycogen-poor liver synthesizes glycogen only slightly more rapidly than does the liver containing moderate amounts of glycogen. The fat-sparing action of sugar through the decomposition and rapid synthesis of glycogen in the liver are two coordinated processes, both of which occur only when the glycogen content of the liver passes a certain minimum which does not occur in pancreatic diabetes.—F. S. H.

(DIABETES) Influence of flying on glycemia (Influencia del vuelo sobre la glucemia). Marañón (G.), Siglo Méd. (Madrid), 1919, **65**, 573-574.

In a series of tests made on aviators it was found that an increased glycemia resulted from the flying, caused by the emotional state induced. In the majority of cases the blood sugar values were increased from the normal of 0.09 to 0.12 to values represented by 0.15 to 0.19. In the pilots the hyperglycemia was less, but nevertheless values above the normal were found. —E. B.

DIABETES and influenza. Motzfeldt (K.), Norsk Mag. f. laegevid (Christiania), 1920, **81**, 372-379.

During the influenza epidemic of 30 years ago diabetes was not infrequently noted in connection with this disease; few observations regarding this have, however, been published during the last epidemic.

Details are given of four cases of diabetes, in which the first symptoms set in during a regular attack of influenza, or shortly afterwards.

The diabetes was of a very mild form in spite of the youth of the patients (age: 35, 14, 15 and 20 years); in 3 of the patients the tolerance for carbohydrates increased considerably during the treatment. Particular interest attaches to case 1: During the course of influenza a man of 35 noticed a peculiar deep epigastric pain. Thirst and polyuria started, when the temperature had been normal for one week. On admission to the hospital one month later the urine gave a positive ferric chloride reaction; the sugar disappeared after 5 days treatment. The tolerance was tested one year and a half later; 500 grams of bread could then be taken without glycosuria. After 50 grams glucose, glycosuria appeared and lasted for 3 hours. The possibility of a pancreatic infection is suggested.—Author's abstract.

DIABETES, Dietetic treatment of serious cases of—(Zur diätetischen Behandlung schwerer Diabetesfälle). Petrén (K.), Deutsche med. Wchnschr. (Berl.), 1920, **46**, 589.

The chief principle in treatment of diabetes is restriction of proteins as well as carbohydrates. Only fat may be taken in unlimited quantities. The results are splendid. Meat is a poison in serious diabetes.—J. K.

(DIABETES) Coma diabeticum during pregnancy. (C. d. bei Schwangeren). Umber, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 589.

It is extremely rare that a pregnant woman dies in diabetic coma. The author saw three cases in which death thus occurred. Two of the patients were known to the author before pregnancy. Both had previously had acidosis, which had disappeared under a dieting regime. In all three cases the fatal influence of pregnancy on the diabetes was obvious.—J. K.

DIABETES innocens. Wynhausen (O. J.) and Elzas (M.). Arch f. Verdaungskrank. (Berlin), 1920, **26,** 33-53.

To decide whether a glucosuria may be considered as diabetes innocens the authors give to their patients on an empty stomach a test breakfast consisting of 150 gms. white bread with a little butter and a cup of tea without sugar or milk. Only these cases may be considered as "innocent" when before and after this test breakfast the blood sugar content is normal or when, after this breakfast, the blood sugar is between 0.15 and 0.17%. The amount of sugar in the urine does not permit a prognosis. Even high glucosuria may be perfectly harmless and accompanied with a normal blood sugar level.—J. K.

(DIABETES INSIPIDUS OSTEOMALACIA) Secretion of iodine in saliva in health and disease after subcutaneous injection of sodium iodide (Jodausscheidung im Speichel bei Gesünden und Kranken nach subkutaner Injektion von Jodnatrium). Zak (E.), Wien. klin. Wchnschr. (Vienna), 1920, **33,** 281.

When sodium iodide is injected subcutaneously it reappears in the saliva on the average in 9 minutes and 40 seconds, in men; in women after 7 minutes and 42 seconds; in men with osteomalacia 5 minutes and 14 seconds; in women with the same disease it appears in 4 minutes and 54 seconds. In osteomalacia the amount of iodine excreted in the saliva is larger than normal. In diabetes insipidus, without treatment, it appeared in about 4½ minutes. Treatment with strychnine lengthened the period to about 10 minutes.—J. K.

DUCTLESS GLAND SUBSTANCES, Influence of certain—on the growth of plant tissues. Budington (R. A.), Biol. Bull. (Woods Hole), 1919, **37,** 188-193.

In an attempt to learn what effects, if any, extracts of the endocrine organs of animals may exert on the growth of plant

tissues, onions were grown upon 120 cc. of Pfeffer's medium to which varying amounts of thyroid, pituitary and suprarenal substances were added. Addition of thyroid substance delayed the growth of the roots, apparently in direct proportion to the amount employed. There was no interference with the growth of the young leaves. Iodine, in the form of KI, did not show this effect. Pituitary and suprarenal substances exerted no appreciable influence.—W. J. A.

DYSTROPHIA MYOTONICA. Maase (O.) & Zondek (A.), Deutsche med. Wchnschr., (Berl.) 1920, **46**, 418.

In this typical case the endocrine symptoms consisted of large nose and lips, polyuria (hypophysis), low blood pressure and a small amount of blood sugar (thyroid), increased salt metabolism and a diminished protein metabolism (thyroid), and sexual impotency.—J. K.

A mass of ENDOCRINE EPITHELIUM in the roof of the mid-ventricle of the Algerian lizard (Amas épithéliaux endocrines dans le toit du ventricule moyen chez un lézard algérien). LeBlanc (E.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 162-163.

In the roof of the ventricle of Uromastix acanthinurus and in the basal region of the epiphysis, there exists, immediately under the ependymal epithelium, a mass of cells which suggests at once an endocrine gland, strikingly like the genital interstitial glands. Other saurians are to be investigated.

—T. C. B.

(ENDOCRINE ORGANS) A therapeutic suggestion concerning endocrines. Bandler (S. W.), Med. Rec. (N. Y.), 1919, **95**, 429-432.

Bandler believes that the future of medicine lies along the lines of endocrine therapy and states that in his own practice 90% of all prescriptions for internal use consist almost entirely if not wholly of endocrine extracts. "The varying forms of amenorrhoea, menorrhagias and metrorrhagias, threatened miscarriage, habitual miscarriage, sterility, the disorders and disturbances of the climacterium, and many other states met with in gynecological practice may be corrected in many instances specifically by a certain extract; in many other cases, by combination of extracts." The author believes that the influenza toxin exerts an almost selective action on the endometrium.

This conclusion is based on observations of the complications of the disease, especially in its sequelae affecting the uterus—which organ he considers lymphoid tissue, part of the thymicolymphatic system.

Normal secretion and interaction of the ductless glands preserves a proper state of growth, which leads Bandler to believe that the cause of benign and malignant growths will be found in abnormal gland function. He ascribes fibromata and myomata of the uterus to hyperpituitarism of the posterior lobe, with resultant hyperovarianism. He considers hyperactivity of the pituitary as responsible for many premenstrual disturbances. He further theorizes to the effect that in pregnancy, the placental secretion holds in check the menstrual activities of the pituitary, thyroid and ovaries and that failure to inhibit these glands results in habitual miscarriage. The nausea and vomiting of pregnancy are considered as due either to a toxic placental secretion or hyperactivity of the posterior lobe of the pituitary. The use of mammary extract, thymus, or placental extract to overcome hyperpituitarism is recommended, the statement being made that each one diminishes menstrual activity. Glycosuria of pituitary origin is emphasized and is controlled according to the author by mammary, thymus or placental extract. [The article contains many fascinating speculations which are advanced rather positively, but without much concrete scientific evidence to support them. Many of these brilliant theories may prove to be correct, but they cannot as yet be accepted].—H. L.

ENDOCRINE ORGANS, The influence of extracts of—on the secretion of the stomach (Über der Einflusz von Blutdrüsenextrakten auf die Magensekretion). Boeheim (T.), Archiv f. Verdauungskrankheiten (Berlin), 1920, **26,** 74-120.

The author examined the influence of injected extracts of endocrine organs on the function of the stomach after a Boas-Ewald test breakfast and after a so-called "plasmon breakfast" (15 grams plasmon dissolved in 300 cc. water). The following results were noted.

I. In cases with hyperacidity: After a plasmon test meal injections of extracts of all endocrine organs tend to diminish the quantity of content of the stomach. After injection of thymus or ovary this diminished quantity is only temporary and is followed by an increase. The acidity becomes still higher, though the influence of thymus and adrenalin is not so marked as that of the other extracts. Extract of thymus increases the quantity of peptones in the content of the stomach; the other

extracts, however, increase the quantity of albumoses. After a Boas-Ewald test breakfast all extracts excepting hypophysis increase the quantity of content of the stomach; hypophysis diminishes it. All extracts except thymus diminish the acidity; thymus increases it. Therefore, perhaps in some cases of hyperacidity organotherapy (thyroid or hypophysis) may advisedly be carefully tried.

II. In cases with normal acidity: After a plasmon breakfast thymus and hypophysis increase the quantity of content of the stomach; thyroid and ovary diminish it. Only hypophysis diminishes the acidity. After a Boas-Ewald breakfast all extracts diminish the acidity; thymus, hypophysis and ovary raise the quantity of content of the stomach, thyroid diminishes it. All extracts delay the digestion of proteins.

III. In cases with sub- and an-acidity: After a plasmon breakfast as well as after the Boas-Ewald breakfast injection of extract of pancreas produces a marked rise of acidity. The digestion of proteins goes further than without these extracts. Thymus and thyroid have the same influence. Therefore, these three organs may be tried in such cases. [For earlier observations along the same line see Rogers, Rahe and Ablahadian (Abst. Endocrin., **3**, 231-232).]—J. K.

(ENDOCRINE ORGANS) Experimental basis for organotherapy in infectious diseases (Experimentelle Grundlagen der Organtherapie bei infektious Krankheiten). Borchardt, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 533.

The author examined the influence of various glandular products on the formation of agglutinin for typhoid bacilli. Adrenalin, hypophysin and spermin subcutaneously gave an increase of the agglutinin-titer of the blood serum. Thyroid tablets administered by mouth had the same effect. [See also Koopman, Endocrin., **3**, 318-320.]—J. K.

(ENDOCRINE ORGANS) On the origin and significance of lipase in human blood (Herkunft und Bedeutung von fettspaltenden Fermenten des menschlichen Blutes). Caro (L.), Ztschr. f. klin. Med. (Berlin), 1920, **89**, 49-76.

This article is the report of a study of the influence of disease on the content of lipase in the blood. Adiposity, arteriosclerosis, many cases of Bright's disease and others give an increased lipase content. In the first stage of pulmontry tuberculosis an increase is observed; in the later stages, the lipase content diminishes rapidly. On the other hand, all diseases

with cachexia tend to diminish it. In lymphoid and myeloid leukemia no influence on the lipase was observed. Graves' disease, when accompanied by emaciation, presents a lowered lipase. In myxoedema no effect is observed. Now the question arises as to the origin of the lipase. Bergel has maintained that the lymphocytes produce this ferment. This cannot be true since there is no parallelism between the number of lymphocytes and the lipase content of the blood. This is also true with respect to the cerebrospinal fluid. Probably the lipase is a product of the endocrine system. The author believes that the pancreas plays an important part in its formation. The antagonists of this gland are the thyroid, the chromaffine system, the infundibulum, the ovary, and the thymus. These glands have an important influence on fat metabolism; increased function diminishes the fat in the body; diminished function increase it. Diminished function of these glands increases the internal secretion of the pancreas, which produces a large amount of lipase. When the opposite happens, the pancreatic function is diminished and its influence on the lipase content is demonstrated.—J. K.

ENDOCRINE ORGANS, Functions of—(Wesen und Wirken endokriner Drüsen). Hart (C.), Berlin. klin. Wchnschr., 1920, **57**, 101-104.

The author fed tadpoles with thymus and studied the resulting atrophy of the thyroid. The tissues of the animals showed a swollen aspect which may perhaps have some analogy with the tissue reactions in myxoedema. This is further proof that a monoglandular disturbance is followed by changes in the other organs of the endocrine system and that what appear to be monoglandular diseases are often polyglandular.—J. K.

(ENDOCRINE GLANDS) The use of x-rays and electricity in exopthalmic goitre and other disorders of the ductless glands. Hernaman-Johnson (F.), Arch. Rad. & Elec. (N. Y.), 1918, **23**, 91-99.

Brief case reports and general discussion from which it is concluded that x-rays are specific in the sense that the secretion of the thyroid may be diminished to any required degree, although cure cannot be effected in the face of persistent irritation from any source.

The carefully controlled use of x-rays in dysmenorrhea of ovarian origin is advocated.—F. S. H.

ENDOCRINE ORGANS, The significance of, in the toxemias of pregnancy (Die Bedeutung der innersekretorischen Drüsen für die Klinik der Graviditätstoxikosen). Hofbauer, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 589.

During pregnancy, metabolism is increased. This may be explained by the hyperplasia of thyroid, adrenals and hypophysis. These glands increase the irritability of the sympathicus and parasympathicus. This is perhaps the cause of the vomiting of pregnant women. It may be cured by extracts of ovary, which tend to diminish the irritability of the sympathicus. In eclampsia, the serum of the patients has vasoconstricting properties; the substances with these properties are probably produced by the increased function of the hypophysis-adrenal system. Therefore extract of ovary ought to be tried in these conditions. The edemas and the abnormalities of the kidneys in pregnancy may perhaps be explained by a dysfunction of the hypophysis-adrenal system.—J. K.

(ENDOCRINE ORGANS) The mechanism of vitamine action (Le mecanisme d'action des vitamines). Ganassini (D.) & Mancini (P.), Bull. gén. de Thérap. (Paris), 1920, **171,** 125-133.

A brief review of the physiological, pathogenic and therapeutic action of the vitamines in which the opinion is expressed that their physiological role is to regulate trophic exchanges in synergic connection with the trophic-regulatory function of the products of the glands of internal secretion.—F. S. H.

(ENDOCRINE ORGANS) On the decisive proof of the anatomical situation of the glands of internal secretion (Sur les raisons déterminantes du siège anatomique des glandes a sécrétion interne). Hallion (L.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 295-296.

The author claims priority by about ten years, for the hypothesis suggested by Ide, that the role of the endocrine glands can be explained by their embryologic origin (See Endocrin., **4,** 125).—T. C. B.

(ENDOCRINE ORGANS BLOOD SUGAR) Studies in the diastatic activity of the blood and blood sugar curves indicating a decreased carbohydrate tolerance in hyperthyroidism. Killian (John A.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17,** 91-93.

Patients received a breakfast of one egg, two slices of bread and a cup of black coffee or a glass of water. Two hours later the bladder was evacuated and 100 cc. of water drunk. One hour after this a specimen of urine and one of blood were taken as controls. Glucose was then administered in 50% solution, 1.75 gm. per kilo, body weight. At hourly intervals thereafter blood and urine samples were taken and the sugar content and diastatic activity were determined. Twenty-three cases were presented. Three hours after the standard meal the sugar in the blood varied, in normal cases, from 0.09 to 0.10 per cent. In Frölich's dyspituitarism, acromegaly and Addison's disease hypoglycemia was noted. In "hyperthyroidism" (type not specified) the blood sugar ranged from 0.11 to 0.13 per cent. In normal cases urinary sugar excretion ranged from 20 to 30 mg. for the control hour. In dyspituitarism, acromegaly and Addison's disease it was less. In hyperthyroidism, excretion varied from 248 to 95 mgs. In normal cases blood sugar reached its maximum, 0.13-0.15 per cent, in one hour and returned to normal in two hours. In endocrine hypofunction there was practically no increase in blood sugar. In "hyperthyroidism" there was hyperglycemia persisting 4-5 hours, accompanied by glycuresis. Blood diastase was decreased in the hypofunction cases and increased in the hyperfunction.—R. G. H.

(ENDOCRINE ORGANS) Observations on starvation bone-disease in Munich (Beobachtungen von Hungerknochenerkrankungen in München). Mayer, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 168.

The etiology of this disease is considered as a disturbed endocrine balance.—J. K.

(ENDOCRINE ORGANS) Therapeutic problems of the future. Middleton (G. W.), Northwest Med. (Seattle), 1919, **18,** 225-229.

In a general presidential address the author devotes a paragraph to the ductless glands. He refers to the more obvious diseases connected with perversion of the thyroid, adrenal and pituitary body; the neuroses of women associated with ovarian deficiency. The significant advance by Kendall in isolating the crystalline active principle of thyroid secretion is commended. He warns against bizarre commercial pluriglandular prescriptions, but prophesies an important destiny for scientific, dignified organotherapy.—H. L.

ENDOCRINOLOGY, Some phases of. Garretson (W. V. P.), Med. Press (London), 1918, N. S. **105,** 488-491; N. York M. J., 1918, **107,** 866-869.

A general discussion containing no new data save an admission of the conversion of a scoffer (the writer) to an adherence to the practices of endocrinology.—F. S. H.

ENDOCRINOLOGY, The present aspect of—. Lescohier (A. W.), Med. Rec. (N. Y.), 1919, **96,** 532-534.

The author wisely states that "the crying need of endocrinology at present is carefully controlled therapeutic investigation." He objects both to the class of practitioners who are wildly seizing upon organotherapy as a cure-all, and to the class of pessimistic skeptics who barely recognize any place at all for ductless gland therapy. He suggests that gland extracts will probably prove more valuable in the treatment of mild degrees of hypofunction than in outstanding clinical aberrations and accordingly urges that more attention be paid to the recognition of minor deficiencies.—H. L.

FRÖHLICH'S SYNDROME, Case of—(Un nuevo caso de sindrome de Frölich). Crespo Alvarez (A.), Siglo Mèd. (Madrid), 1919, **66,** 713-716.

A detailed history of an interesting case of Fröhlich's syndrome in a boy of 20 years.—E. B.

(GENERAL) The relation of the glands of internal secretion to surgery. Haeberlin (J. B.), Illinois M. J. (Chicago), 1918, **33,** 262-267.

A general discussion presenting no new data.—F. S. H.

(GENERAL) A method for manganese quantitation in biological material together with data on the manganese content of human blood and tissues. Reiman (C. K.) & Minot (A. S.), J. Biol. Chem. (Baltimore), 1920, **42,** 329-345.

While this paper is not primarily of endocrine interest, the data concerning the manganese content of various glands of internal secretion are given and thus made a matter of record.—F. S. H.

(GONADS HYPOPHYSIS) Eunuchoid gigantism (Ein Beitrag zum eunuchoiden Riesenwuchs). Jödicke (P.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berlin), 1918, **44,** Orig. 385-390.

Report of an acromegalic eunuch with high sugar tolerance, the condition being attributed primarily to the sex gland disturbance with resultant hyperfunctioning of the pituitary. —F. S. H.

(GONADS) Eunuchoidismus. Krisch, Deutsche med. Wchnschr. (Leipz. u. Berlin), 1918, **44**, 615.

Rather complete clinical report of two cases of eunuchoidism with no points of particular endocrine interest.—F. S. H.

(GONADS) Hypoplasia of the testicle in youth and its significance as regards the development of the gonads (Ueber die Hypoplasie der Hoden in Jugendalter und ihre Bedeutung für das weiter Schicksal der Keimdrüsen). Kyrle (J.), Wein. klin. Wchnschr. (Vienna), 1920, **33**, 185-188.

Hypoplasia of the testicle in youth is frequent. The hypoplastic organs are characterized by an increased development of the interstitial tissue. During puberty they may develop to a considerable extent but rarely become of normal size. Nevertheless an adequate function is usually present.—J. K.

(GONADS) The psychology and psychopathology of puberty with some remarks on the internal secretions of the sex glands (Zur Psychologie und Psychopathologie der Pubertät nebst einige Bemerkungen über die innersekretorischen Funktionen der Keimdrüsen). Münzer (A.), Berliner klin. Wchnschr., 1920, **57**, 346-349.

A general discussion in which no new data are presented. —J. K.

(GONADS) Hermaphroditism in man. Sheppard (H.), Anat. Rec. (Phila.), 1920, **18**, 259.

A dissecting room case is reported which is held to exhibit true hermaphroditism. Testes, located in the scrotum, and ovaries in the pelvic cavity, were present. The case is an unusual one if, as is stated, both ovaries and testes show a normal structure microscopically.—W. J. A.

(GONADS) Hermaphroditismus. Wagner (G. A.), Wein. klin. Wchnschr. (Vienna), 1920, **33**, 226; Deutsche med. Wchnschr. (Berl.), 1920, **46**, 423.

A description of two cases. The first subject was a "girl" of 16 years with a typical psycho-physical male status. The

penis was short and hypospadic. The scrotum was divided into two parts in one of which there was a testicle, and in the other a cryptorchidic testicle. The second subject was a girl of 21 years who had not menstruated. The characteristics were those of a female both as regards mind and the external genitalia, the clitoris and labia were normal. The vagina was 3 cm. in depth and there were no internal sexual organs. A bilateral herniotomy had been performed, but since a tumor was felt in the old scar a new incision was made and a testicle found therein attached to a normal funiculis. Histological examination of the removed organ showed it to be of normal tissue and containing no traces of ovarian cells.—J. K.

HYPOPHYSIS, The development of the human—. Atwell (W. J.), Anat. Rec. (Phila.), 1920, **18,** 220.

An account is given of the morphogenesis of the human hypophysis beginning with the stage of the 10 mm. embryo. The pars tuberalis, or "lobulus bifurcatus" of Bolk, can be recognized in the younger stages and is then traced continuously to the oldest. It is shown that Herring's "tongue-like process of the pars intermedia" is developed quite independently of the pars intermedia. Thus the name applied by Herring is misleading.—W. J. A.

(HYPHOPHYSIS) Presentation of a case of diabetes insipidus. Clausen (J.), J. Missouri State M. Assn. (St. Louis), 1918, **15,** 189; Proc. Wash. Univ. M. Soc. (St. Louis), 1918, **48,** 8.

C. reports that the injection of pituitary extract invariably caused a marked reduction in the urinary output and thirst, the daily output falling from 7 liters to 2, per diem. The dose given was 0.25 to 1 cc. once a day, and was ineffective when given by mouth.—F. S. H.

(HYPOPHYSIS) The history of a case of acromegaly with gigantism in the family. Craft (M. T.), Neurol. Bull. (N. Y.), 1918, **1,** 32-34.

A very interesting personal report by the patient of the development of the acromegalic condition accompanied by blindness and the statement that a paternal uncle was a famous Kentucky giant.—F. S. H.

(HYPOPHYSIS) The acromegalic tendency and the theory of the internal secretions (Ueber Akromegaliodismus und zur Theorie der inneren Sekretion). Ehrmann (R.), Ztschr. f. phys. u. diätet. Therap. (Leipzig), 1918, **22,** 343-345.

Several observations were made of individuals demonstrating by x-ray examination the classical acromegalic picture, who failed to give marked evidence of hypophyseal disturbance at autopsy. The author theorizes on the absence of the effective secretion from the glandular parts of the adrenals but presents no experimental data.—F. S. H.

(HYPOPHYSIS) A study on the separation of the physiologically active portion of the posterior lobe of the pituitary body. Fenger (F.) & Hull (Mary), J. Biol. Chem. (Balt.), 1920, **42,** 153-158.

This paper reports an attempt on the part of the authors to separate in pure form the oxytocic principle of the posterior lobe of the pituitary. It is concluded on hardly sufficient evidence that the uterus-contracting principle does not occur in the fresh gland in free or crystalline form, but is linked to or part of some protein complex. "In its original protein association the uterine stimulus is insoluble in ether, petroleum ether, chloroform and practically insoluble in absolute alcohol. It is sparingly soluble in 95 per cent alcohol, but yields a highly active split product when treated with hot 95 per cent alcohol. The split product is amorphous in nature, very hygroscopic and much more sensitive to desiccation than the original basic material from which it was derived." Alkaloidal reagents are not sufficiently good precipitants for general use in the isolation of the active principle.—F. S. H.

(HYPOPHYSIS) Case of hypophyseal tumor showing improvement under x-ray treatment (Einen durch Röntgenbestrahlung gebesserten Fall von Hypophysentumor). Fleischer & Jüngling. München. med. Wchnschr., 1918, **65,** 1362.

A report of a case of hypophyseal tumor in a 55 year old woman with acromegalic symptoms and visual disturbances. She was distinctly benefited by 2 x-ray applications at intervals of four weeks. The technique of the applications is given in brief and is not applicable to American made apparatus.

—F. S. H.

(HYPOPHYSIS) Cases of hypophyseal tumor (Fälle von Hypophysentumor). Gerhardt, München. med. Wchnschr., 1918, **65,** 950.

Report of two cases of hypophyseal tumors, one in a 24 year old soldier and the other in a 51 year old laborer. Evidence of acromegaly was present in each case.—F. S. H.

(HYPOPHYSIS) Headache and dyspituitarism in the light of therapeusis. Glassburg (J. H.), Med. Rec. (N. Y.), 1919, **96,** 461-463.

Glassburg emphasizes the desirability of limiting of the term dyspituitarism to exclude acromegaly on the "hyper" side and infantilism on the "hypo" side, but to include all other disorders of pituitary secretions. In this way a definite class of cases can be recognized which may be benefitted by organotherapy, whereas gland extracts are useless in acromegaly and infantilism. Cases of dyspituitarism will show signs and symptoms of both hyper- and hypo-activity depending on the stage of the disease. Dyspituitarism is not necessarily accompanied by an abnormal sella turcica. The author presents a typical case in which the bitemporal headaches, muscular fatigue, etc., were promptly relieved by pituitary extract, 4-8 grains a day by mouth. It was noticed that administration of the extract at the menstrual period resulted in increased flow; the author therefore cautions against using it at that time.—H. L.

(HYPOPHYSIS) A case of acromegalic gigantism (Un caso de gigantismo acromegalico). Gouce (F.) & Poyales (F.), Pediatria espan. (Madrid), 1919, **8,** 271-283.

A report of a girl of eight years afflicted with acromegalic gigantism. The case is very well presented. No glycosuria was present but a slight hyperglycemia was found.—G. M.

(HYPOPHYSIS) A physiological response to the administration of pituitary. Hammett (F. S.), Patten (C. A.) & Suitsu (N.), Am. J. Physiol. (Balt.), 1920, **51,** 588-592.

A study of the changes induced by administration of pituitary substance, in the total nitrogen, non-protein nitrogenous constituents, sugar and alkaline reserve of human blood. The experiments were carried out on six human males who were not endocrinopathic. The period of observation covered nine weeks; the first three weeks no pituitary was fed; during the second three weeks a 2-grain tablet of desiccated pituitary substance was given three times a day; during the last three weeks the pituitary was discontinued. The only valid and consistent change noted was in the blood uric acid. In four out of the six cases the ingestion of pituitary substance caused an increased concentration of uric acid in the blood. This is interpreted as being due, probably, to a decreased permeability of the kidney.—T. C. B.

(HYPOPHYSIS) A case of suspected tumor of the pituitary body. Hansell (H. F.), Trans. Coll. Phys. (Phila.), 1918, 3.s., **39**, 365.

Brief case report presenting no new data.—F. S. H.

(GENERAL) Gastric changes of endocrine origin (Algunas alteraciones intestinales de origen endocrino). Hernando (T.), Med. Ibera (Madrid), 1919, **8**, 239; **9**, 523, also Acad. med.-quir. espan., 1919.

The glands of internal secretion act on the digestive tract through the mediation of the vegetative nervous system indirectly and directly by their secretions. The author studied the endocrine supervision in many cases of diarrhoea and constipation. In all the Basedowians studied diarrhoea frequently occurred and many cases of the latter disorder presented symptoms of hyperthyroidism (18 cases of hyperthyroidism out of 149 chronic diarrhoeas). The intestinal disturbance is explained on the basis of a vagotonia which in turn determines the hyperthyroidism. The same reasoning applies to the occurrence of diarrhoea in many cases of suprarenal insufficiency. As to treatment it should correspond in general with the observed syndrome, belladonna and atropine as moderators of the vagus, and adrenaline (principally as enemas according to de Woorden) which bring about the the least moderating action in an indirect manner exciting the sympathetic. Constipation is also influenced by the endocrine glands. Here hypopituitarism comes into play (the constipation of Fröhlich's syndrome) and in some cases of senile constipation also (atrophy of the hypophysis in the old). Hypersuprarenalism by its sympathicotonic action is a factor. It is possible to understand the constipation of the arterio-sclerotics and the climateric in which ovarian insufficiency plays a role since this also has its effect on vagotonia. Finally there exists a certain group of cases of hyperthyroidism exhibiting constipation in which vagotonia is determined by a condition of the intestinal musculature which is much more frequently found in the cases of hypothyroidism. This intervenes by virtue of a lack of vagal tone and diminution of calcium metabolism, which in turn diminishes the neuromuscular excitation of the intestine.—E. B.

(HYPOPHYSIS) Gigantism (Riesenwuchs). Hoffmann. Deutsche med. Wchnschr. (Berlin), 1920, **46**, 311.

A demonstration of a woman of 21 years with gigantism, multiple exostoses and myxoedematous symptoms of the fatty tissues of the legs. These symptoms developed after a fall 8

years previously, when the hypophysis was injured. No symptoms of a tumor were noted. Sexual functions were normal. The author considers this disorder as due to dysfunction of the pituitary.—J. K.

(HYPOPHYSIS) Akromegalie. Högler, Wien. klin. Wchnschr. 1918, **31**, 769.

A case report presenting no new features.—F. S. H.

(HYPOPHYSIS) Roentgen observation of the pituitary region in intracranial lesions. Johnson (G. C.), Am. J. Roentgenol. (N. Y.), 1918, **n. s. 4**, 555-563.

An extended study with 15 plates of the pituitary region by means of the x-ray. J. concludes that the first requisite for study of intracranial lesions, particularly of the sella, is a wide familiarity with roentgenograms of the normal conditions. There is a wide variation in size and character of the sella which must be considered within the limits of normal. Pituitary struma manifests itself by deformation and destruction of the sella and rarely by visualization of the tumor itself.
—F. S. H.

(HYPOPHYSIS) Hypophysentumor. Killian, Berl. klin. Wchnschr., 1918, **55**, 891.

Of technical interest.—F. S. H.

HYPOPHYSIS, Secretion antecedents in the pars intermedia of the—of the pig. Lewis (D. D.) & Maurer (S.), Anat. Rec. (Phila.), 1920, **18**, 238.

Two kinds of epithelial cells are described for the juxtaneural portion of the pars intermedia. These are: "(1) cells related to the colloid-containing vesicles, and evidently the secretory source of this colloid; (2) the secretory cells which are the characteristic element of the pars intermedia, hitherto vaguely described as finely granular, basophile, neutrophile, etc."—W. J. A.

HYPOPHYSIS, Diabetes insipidus with destruction of the posterior lobe of the— (Diabetes insipidus bei Zerstörung des Hypophysenhinterlappens). Neubürger (K.), Berlin. klin. Wchnschr., 1920, **57**, 10.

A description of a case of diabetes insipidus with a metastatic cancer in the pars nervosa. The anterior lobe showed no changes.—J. K.

(HYPOPHYSIS) Hypophyseal adiposity in children (Ueber Kinder mit hypophysärer Adiposität.) Peritz, Berlin. klin. Wchnschr., 1920, **57**, 379.

The most ordinary cause of hypophyseal adiposity in children is a syphilitic hydrocephalus. Blood sugar is often increased. The author demonstrated some of these cases and also a case of hypophyseal dwarfism, caused by syphilis.
—J. K.

(HYPOPHYSIS) Akromegalie. Pribram, Deutsche med. Wchnschr, 1920, **46**, 424.

This classical case was remarkable because of its beginning during puberty.—J. K.

HYPOPHYSIS and Raynaud's disease (Hypophyse and Raynaudscher Krankheit). Pribram, Berlin. klin. Wchnschr., 1920, **57**, 67.

Data reported elsewhere. See Endocrin., 1920, **4**, 279.
—J. K.

The HYPOPHYSIS cerebri of the American marmot (Marmota monax) with special reference to changes during hibernation. Rasmussen (A. T.), Anat. Rec. (Phila), 1920, **18**, 255.

The author has not found the marked changes in the hypophysis which other writers have reported as taking place during hibernation. The most constant and striking alteration occurs after waking up when the basophilic cells become very prominent and show large vacuoles and a conspicuous "macula."
—W. J. A.

(HYPOPHYSIS) Pituitary feeding and egg production in the domestic fowl. Simpson (Sutherland), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17**, 87-88.

Clark in 1915 reported that feeding desiccated hypophysis resulted in marked increase in egg laying by hens. Simpson repeated Clark's experiments, using hypophysis from both adult and young cattle. The experiments were made in three stages: when egg laying was low and declining, when it was

at its height and again when it was low. White Leghorn hens were used as experimental animals. The results were completely negative, not only with the dosage used by Clark (the equivalent of 20 mg. fresh gland) but also with double and treble this dosage.—R. G. H.

HYPOPHYSIS, The action of extract of—on the distribution of the blood (Die Wirkung der Hypophysesextrakte auf die Blutverteilung). Rosenow, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 559.

Intravenous injection of extract of hypophysis produces in normal individuals a momentary increase of the volume of the arm, as may be proved by use of the plethysmograph. This may be explained by the constricting effect of hypophysis extract on the blood vessels innervated by the splanchnic nerves. The author recommends this method for the functional study of the splanchnics.—J. K.

HYPOPHYSIS, A biological study of the—. Saito (T.), Sei-I-Kwai M. J. (Tokyo), 1919, **38,** 328 (Japanese).

The chief points indicated in this paper are that the weight of the hypophysis of the horse varies with the month of the year; that it is relatively much larger in the horse than in either the cow or man, and that its weight decreases during the fourth month of pregnancy in the horse and during the third month in man.—E. V. C.

(HYPOPHYSIS) Cure of a case of meningitis after endonasal operation for hypophyseal tumor by trypaflavine infusions (Heilung einer Falles von Meningitis nach endonasaler Operation eines Hypophysentumors durch Trypaflavininfusionen). Spiesz (G.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 207-209.

Of no immediate endocrine interest.—J. K.

(HYPOPHYSIS) Contribution to the pathogenesis of dystrophia adiposo-genitalis (Bydrage tot de pathogenese der dystrophia adiposo-genitalis). Stenvers (H. W.), Nederl. Maandschr. Geneesk. (Leiden), 1920, **1,** 45-60.

Stenvers describes three cases of dystrophia adiposo-genitalis. The first case was a girl of 17, without menstruation, with adiposity. The diagnosis was tumor of the hypophysis. Death followed some hours after operation. At autopsy the

hypophysis proved to be normal, both grossly and microscopically, but the infundibulum of the third ventricle was very atrophic. The second case was a girl of 21; the menses had become irregular and finally ceased. There were symptoms of brain pressure. The skiagram showed an enlarged sella. The post-mortem examination disclosed a normal hypophysis and a large tumor in the right temporal lobe of the brain with dilatation of the third ventricle. In this case there was no adiposity, but the changes in the third ventricle were not so great as in the first one. The third case, a boy of 14, had headache, giddiness and vomiting. There were eye symptoms. During two years the boy became fatter and fatter and acquired a female form. The skiagram showed changes which may be explained only by dilatation of the third ventricle. These changes developed pari passu with the adiposity. The author concludes that dystrophia adiposo-genitalis is caused by a disease of the third ventricle; this may be caused by a tumor of the hypophysis, but also by any process causing increased intracranial pressure. [An obvious comment is that cerebral pressure may result in functional inadequacy of the hypophysis as well as hypophyseal tumor cause cerebral pressure.]—J. K.

(HYPOPHYSIS) Paroxysmal nasal hydrorrhea based on dyspituitarism. Strauss (S. G.), Med. Rec. (N. Y.), 1919, **96,** 463-464.

Strauss records case of periodic discharge of copious colorless mucous from nose, 2 months after striking forehead against a door. Discharge would last about 6 weeks, then suddenly cease, to reappear in 3 months. Physical characteristics of patient suggested dyspituitarism and whole pituitary gland was administered with prompt and so far (6 months) permanent relief.—H. L.

(HYPOPHYSIS) Atrophia adiposo-genitalis. van Valkenburg (C. T.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** (i), 997-998.

A description of a case of a boy 14 years old with symptoms of meningitis, dullness, epilepsy, Argyll-Robertson pupil, negative Wassermann reaction, optic neuritis, no changes in urine or blood, loss of memory and confabulations. The testicles were small. The patient gradually became more fat. Post-mortem examination showed tubercles in the cerebellum, tuberculosis of the pia-mater, infundibulum, optic nerves and tract, also a large thymus, small pancreas, atrophic testicles.

atrophic adrenal medulla and a normal thyroid, parathyroid and hypophysis were noted. The blood vessels in the latter were increased in number and were congested.—J. K.

(HYPOPHYSIS) The relations between experimental polyuria after "piqure" and diabetes insipidus (Die Beziehungen der experimentellen Piqure—polyurie zum Diabetes insipidus). Veil, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 558-559.

The author describes two classes of diabetes insipidus, one in which the blood contains an increased amount of Na Cl and one with a normal amount of NaCl in the serum. In the first cases the urine is poor in NaCl, in the latter there is generally hyperchloruria. "Piqure" in the fourth ventricle produces polyuria with an increase of NaCl in the urine; "piqure" in the midbrain produces polyuria with hypochloruria.—J. K.

(HYPOPHYSIS) Dystrophia adiposo-genitalis, with report of a case. Whyte (G. Duncan), China M. J. (Shanghai), 1920, **34,** 139.

A typical case is reported in a man of 46 years which showed only temporary improvement on feeding hypophysis. —E. V. C.

(HYPOPHYSIS ADRENALS) Prophylaxis of paralysis of the intestines (Zur Verhütung der Darmlähmung). Zondek (B.), Zentralbl. f. Chir. (Leipzig), 1920, **46,** 270-272.

Unger has advised the administration of asthymolysin after operations as a prophylaxis against paralysis of the intestine. Asthymolysin is a combination of 40 milligrams hypophysis and 0.8 milligrams adrenal. Zondek calls this a bad combination as hypophysis will increase the tonus of the intestine, but adrenaline will inhibit the peristalsis by stimulation of the sympathic apparatus.—J. K.

(INTERNAL SECRETIONS) The importance of a knowledge of the internal secretions and its availability for practical gynecology (Die Bedeutung der Lehre von der inneren Sekretion und ihre Nutzanwendung für die praktische Gynäkologie). Aschner (B.), Monatsch. f. Geb. u. Gynäk. (Berlin), 1920, **51,** 130-136.

A polemical reply to H. Fehling's article of the same title (idem. **50,** 143) and defending the author's book, "Die Blut-

drüsenerkrankungen des weibes und ihre Beziehung zur Gynäkologie und Geburtshilfe." (Wiesbaden, Bergmann, 1918).
—F. S. H.

INTERNAL SECRETIONS, Influence of—on the formation of bile. Downs (A. W.), Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt), 1920, **51**, 193-194.

See Endocrin., 1919, **3**, 214.

INTERNAL SECRETIONS, Vitamines and—(Vitaminen en inwendige afscheiding). van Driel (B. M.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64**, (i), 1350-1361.

A general review without new data. The author concludes that the avitaminoses are closely related to endocrine disturbances because in all such conditions the endocrine organs (with the exception of the hypophysis and the adrenals) are atrophied, and because in certain forms of the disorder the amount of adrenalin in the adrenals is increased.—J. K.

INTERNAL SECRETIONS, The. Friedman (E. D.), Med. Rec. (N. Y.), 1919, **96**, 916-935.

The author's intention apparently was not to present anything new, but to compress into ten pages a resume of our knowledge of the internal secretions. He has packed an extraordinary amount of information into this article, including a historical survey. He then crowds an immense amount of information under the headings: thyroid, hypophysis, adrenals, pineal, thymus, sex glands, internal secretions, uterus, parathyroids, pancreas, internal secretion of the alimentary tract, placenta and spleen. It is obviously impossible to abstract this paper, for it is a veritable abstract in itself. It might be recommended to those unfamiliar with endocrinology, who might desire a rapid introduction to its essential features.
—H. L.

INTERNAL SECRETION, Feeding rats on glands of—. Gudernatsch (J. F.), Anat. Record (Phila.), 1918, **14**, 35. (Proc. Am. Assn. Anat., 1917.)

Gudernatsch reports the results up to the time of going to press of feeding seven sets of albino rats on a mixed diet plus desiccated thyroid, thymus, hypophysis, testicle, ovary, and mammary gland respectively, one set being used for control. Thyroid fed rats when pregnant deliver many dead, or the young die early. The remaining rats are classed in three

groups: 1. Hypophysis; thymus. 2. Normal. 3. Testicle; ovary. The animals in group 1 grow faster and the animals in 3 slower than normally. Testicle- and ovary-fed homologous animals do not live as long as the others and a decline in weight often begins as early as seven months. Heterologous testicular and ovarian feeding causes an improvement in growth over the homologous fed animals. The members of group 1 are fine breeders and the young are viable. Females of group 3 are poor breeders in respect to the vitality of the young. Pituitary fed animals seem to be precocious in adolescence.—F. S. H.

INTERNAL SECRETIONS, Pernicious anemia and the—. Schauman (O.), Finska. Läk. Sällsk. Handl., 1919, **61**, 796-827.

The author calls attention to certain critical constitutional impulses which may precede anemia. They are primarily achylia, dental caries, and glossitis. He further points out that there are certain points of similarity between Addison's disease and pernicious anemia, such as bronzing of the skin; in certain cases extraordinary good condition of nourishment, stomach and intestinal symptoms of like nature, etc. Among other symptoms present in pernicious anemia significant of an endocrine possibility are polyuria, cardiac enlargement, temperature increases of a peculiar kind, etc. It is also emphasized that the blood changes in themselves may be considered as of an internal secretory nature. The disturbances of the internal secretory balance combined with constitutional anomalies of the hemopoietic apparatus are the fundamental causes, the exogenous influences are but the adventitious motivations of the disease.—J. A. H.

LIPODYSTROPHIA PROGRESSIVA, Sequel of the case of— shown on January the 24th, 1919. Weber (F. P.) and Gunewardene (T. H.), Brit. J. Child. Dis. (Lond.), 1920, **16**, 200-204.

The authors present the findings in what they claim to be the first published autopsy in lipodystrophia progressiva. Their patient was a girl of 13 who died from chronic pyemia. The body was wasted, but by naked eye examination the fat was practically completely absent from the subcutaneous tissue of the upper part of the body above the pelvis. A moderate amount of fat was present in the gluteal regions, orbits, omentum, about the kidneys, heart and pericardium and under the serous membranes. Microscopic sections of the scalp and abdominal wall show that fatty tissue is almost completely, if

not completely, absent. One of the sections of the suprarenal glands included a little of the surrounding retroperitoneal tissue. Definite fatty tissue was present in this. In no section were there lobules of embryonic fatty tissue such as are found in the fetus and in infants. No abnormality was found in either the ovary or pituitary body. In the suprarenal bodies there appeared to be less lipoid tissue than usual, but the effect of the infection which caused death cannot be excluded. In the thyroid there was an excess of colloid of a degree, however, that is often found at autopsy. It fell far below that which frequently occurs at puberty. Little significance could be attached to this excess of colloid if it were the only unusual feature, but it appeared to be associated with fibrosis and an actual diminution in the size of the gland. The thymus gland was represented by a scanty remnant. Original report of this case abstracted in Endocrin., 1920, **4**, 138.—M. B. G.

MENSTRUATION AND PREGNANCY, Disorders of—after accidents [Menstruations und Schwangerschaftsstörung nach Unfall (Verbrennung)]. Beckey (K.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttgart), 1920, **82**, 257-283.

Of no endocrine interest.—F. S. H.

Vicarious MENSTRUATION (Über vikariierende Menstruation). Roth (A.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1920, **51**, 41-57.

A statistical presentation, of no specific endocrine interest. —F. S. H.

MYOTONIA, Variations of—(Varietäten der Myotonie). Kastan, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 311.

Of no endocrine interest.—J. K.

MONGOLISM, The symptoms of— (Zur symptomatik des mongolismus). Moro, München. med. Wchnschr., 1920, **67**, 360.

Data reported elsewhere.—J. K.

(ORGANOTHERAPY) Ductless gland therapy. Masterman-Wood (J. L.) and Torquay (L. M.), Practitioner (Lond.), 1919, **102**, 259-270.

The author believes firmly in careful clinical experimentation in opotherapy, in addition to laboratory investigations,

and believes that the practicing physician may thus help to shed light on what is yet to be discovered in the domain of endocrinology.

Taking up hypothyroidism he emphasizes the inability of the thyroid in this condition to react to iodides or to metabolize iodides brought to it. This condition frequently follows acute infections. In the secondary constitutional stage of syphilis, the thyroid is profoundly depressed and iodides medication is consequently ineffective until the thyroid has recovered. Reference is made to the interesting experience of Rendle Short, who states that he has found thyroid extract quite as effective as iodide of potassium in healing tertiary syphilis. He therefore recommends thyroid extract where iodides fail. Some toxemias do not inhibit the thyroid, but stimulate it to increased activity, as in early tuberculosis. Some of the symptoms of tuberculosis are sympatheticotonic and resemble those of Graves' disease. The authors suggest that in children, adenoids, nocturnal enuresis, slight want of mental alertness, sluggish bodily movements, slightly sleepy appearance of the eyes, sluggish bowels and foetid stools, and a tendency to develop flat foot are sometimes indicative of hypothyroidism and are markedly relieved by small doses of thyroid extract. A case of asthma is cited which was relieved by thyroid extract. An ingeneous hypothesis is constructed to explain this phenomenon. They believe that the vagus is exerting a preponderant influence, inducing bronchial spasm and that thyroid extract stimulates the suprarenals, which in turn stimulate the sympathetic system and overcome the vagus spasm. The wonderful efficiency of adrenalin in attacks of asthma corroborates this viewpoint. Other cases of sub-thyroidism are cited, in which administration of thyroid extract was efficacious. They stress the importance of recognizing mild degrees of thyroid deficiency. The article is suggestive, but not entirely convincing.

—H. L.

ORGAN EXTRACTS. Note on the use of—in place of virulent blood in immunization and hyper-immunization against rinder-pest. Boynton (W. H.), Philippine J. Sc. (Manila), 1918, **13**, Sect. B, 151-158.

Of no endocrine interest.—F. S. H.

ORGANOTHERAPY in certain diseases of childhood. McCready (E. B.), Med. Rec. (N. Y.), 1919, **96**, 529-532.

A large part of the article is a tribute to Sajous' doctrines in the domain of the ductless glands. The rest of the paper

contains much of general matter not readily abstacted. The author concludes that the endocrine glands control metabolism and preside over growth and development in infancy and childhood; they are essential to mental, physical and reproductive efficiency in adult life, and they maintain metabolic balance in the period of decline. Many diseases and conditions of childhood are manifestations of organic inferiority in the etiology of which dysfunction of the endocrine glands is a more or less prominent and contributing factor. Treatment directed toward the stimulation, modification or correlation of the action of the endocrine glands is a promising field of therapeutic endeavor, but treatment by organotherapeutic preparations should be preceded by a careful analysis and evaluation of the symptoms of endocrinous dysfunction. The usually employed doses of organic preparations, particularly of thyroid, are too large, are administered without due care, often in unsuitable cases, and tend to discredit a valuable therapeutic measure.—H. L.

(OSTEOMALACIA) Statistical observations on the increases in rickets and osteomalacia in Berlin (Statistische Bemerkungen zur Frage der Rachitiszunahme und des Auftratens der Kriegsosteomalazie in Bereiche von Gross-Berlin). Engel (H.), Berlin. klin. Wchnschr., 1920, **57,** 35.

Of no immediate endocrine interest. [In the German literature at the present time are appearing various articles on osteomalacia, postulating endocrine factors. To forestall lost effort on the part of those interested, the endocrine bearing of each will be indicated.—Ed.]

OVARY, Observations on the follicular atresia in the rabbit. Asami (G.), Anat. Rec. (Phila.), 1920, **18,** 323-343.

In the rabbit atresia has been observed to occur in the small as well as in medium and large size follicles. In the case of the medium and large follicles the primary factor is the degeneration of the granulosa, while in the early stages of atresia of small follicles changes occur in the egg as well as in the granulosa, and of these the changes in the egg are the more pronounced. These atretic processes do not show any definite relation to the sexual cycle such as occurs in the guinea pig. The article is not primarily of endocrine interest, but attention is drawn to Loeb's suggestion that the normal proliferation of the granulosa is probably dependent upon an internal secretion of the ovum which acts as a growth stimulus.

What the primary cause of the observed atretic changes may be constitutes an interesting question possibly of endocrine portent.—W. J. A.

(OVARY) Ovarian insufficiency as a probable cause of epilepsy. Ashe (J. S.), Dublin J. Med. Sc., 1920, 4, 142.

Ashe cites three cases of patients that have been benefited by ovarian administration. In one following a bilateral tubal pregnancy, menstruation ceased entirely. Concomitant with this the subject had what the author designates "hystero-epileptic attacks." Injections of the fresh fluid extract of ovarian tissue stopped these attacks. Epileptic attacks in another case followed an attack of mumps. Feeding of ovarian tissue stopped them. In a third case a polyglandular mixture, including ovarian substance, decreased the attacks. It is suggested that the toxin which serves as a predisposing factor in certain cases of epilepsy is produced by absence, diminution or change in the ovarian ferments leading to some polyglandular deficiency. The imbalance thus set up leads to the production of toxins which act on the cerebral cortex, causing the epileptic seizures.—J. H. L.

OVARY, Precocious puberty due to tumor of the—(Genitalismo precoz por tumor ovarico). Cortiguera (J.) & Lopez Albo (W.), Rev. de pediat, 1919, —, —.

A report of a girl of 10 years who had menstruated since 6 years of age. She was born with much hair on her head and an early development of somatic and mental characteristics was noted out of proportion to her years. At eight months she cut her first teeth. Her physical appearance was that of a person of 20 years (pubic hair, developed mammae with colostrum, etc.). Her abdomen was enlarged as if she were in the sixth month of pregnancy. Palpation gave evidence of a smooth, spherical and movable tumor underneath the skin. A laparotomy was performed and an ovarian tumor found.—E. B.

OVARY, On an anomaly of development of the—in Ascaris megalocephala (Sur une anomalie du développement de l'ovarie chez l'Ascaris mégalocephala). Dragoiu (J.) & Faure-Fremiet (E.), Compt. rend. Soc. de biol. (Paris), 1920, 83, 123-124.

A histological description of the ovaries and genital tract of a sterile female.—T. C. B.

OVARY, Pathological pregnancy and tumors of the—(Pathologische Schwangerschaft und Eierstocksgeschwülste). Fraenkel (L.), Berlin. klin. Wchnschr., 1920, **57**, 1-3.

Of no immediate endocrine interest.—J. K.

(OVARY) The time of ovluation (Het tijdstip der ovulatie). van der Hoeven (P. C. T.), Nederl. Maandschr. v. Geneesk. (Leiden), 1920, **1**, 16-22.

Of no endocrine interest.—J. K.

(OVARY) Rythmical recurrence of the typical oestrus cycle after ovarian transplantation. Long (J. A.) & Evans (H. M.), Anat. Rec. (Phila.), 1920, **18**, 245.

Successful transplantation of the ovaries in the rat has been accomplished by the authors in 14 instances. In most successful cases the first interval after the operation was only slightly longer than the dioestrous interval of normal cycles. Sections show that such transplanted ovaries are essentially normal in containing healthy and atretic follicles, corpora lutea of several ages, and interstitial tissue.—W. J. A.

(PANCREAS) Hemorrhagic pancreatic necrosis and diabetes with acidosis (Ausgedehnte hämorrhagische Pankreasnekrose und Diabetes mit Acidose). Caro & Winkler, Deutsch. Arch. f. klin. med. (Leipzig), 1918, **125**, 147-159.

A detailed clinical, post-mortem and histological description with plate of one case of hemorrhagic necrosis of the pancreas accompanied by diabetes with acidosis.—F. S. H.

(PANCREAS) A consideration of the surgical hazards in diabetic patients. Foster (Nelles B.), Ann. Surg. (Phila.), 1920, **71**, 382.

This paper is based upon a review of the clinical records of two good hospitals. Glycosuria is not a reliable guide in the estimation of the severity of diabetes. The disease, however, can be diagnosed and its severity estimated by a determination of the degree of hyperglycemia. Infections tend to increase the severity of the disturbance of carbohydrate metabolism and, in that way, to bring about a variable degree of acidosis. Anesthetics, and especially ether, intensify the disordered processes. Based upon his experience, it is the author's opinion that a case with a CO_2 combining power of its plasma of less than 40 does not present a reasonable margin of safety for

surgical procedures. The author outlines his preoperative treatment and dietetic management of cases of diabetes mellitus. The object of this treatment is the restoration of normal metabolism and its success is measured by the blood sugar and CO_2 combining power of the plasma.—J. F.

(PANCREAS) Reply to Albu concerning the diagnosis of pancreatic cysts (Bermerkung zu Albu: Zur Diagnostik der Pankreaszysten). Holzknecht (G.) & Jonas (S.), Berl. klin. Wchnschr., 1918, **55**, 582.

Of technical interest.—F. S. H.

PANCREATIC DIABETES, The pathology of—(Das Wesen des Pankreasdiabetes). Lesser, Berl. klin. Wchnschr., 1920, **57**, 310.

Data reported elsewhere. See Endocrin., **4**, 296.—J. K.

(PANCREAS) Some remarks on the blood sugar in diabetes mellitus. Lindblom (S.), Hygiea (Stockholm), 1919, **81**, 753-759.

In diabetes the ability to regulate the relation between production and consumption of sugar, so that equilibrium obtains without glucosuria, is arrested or destroyed. In this case there must of necessity be a higher blood-sugar content than is compatible with the kidney permeability, so that the organs or eventually their centers react with a decreased production or an increased destruction. The hyperglycemia present in diabetics acts then in opposition to the metabolic disturbance. Hyperglycemia is then in a certain degree an advantageous symptom. According to this conception the urine of many diabetics does not become sugar-free in spite of the residual hyperglycemia but because of it. The favorable action of the oat-cure is explained on the basis of the suddenly increased hyperglycemia.—J. A. H.

PANCREAS and diabetes mellitus, The relation between the—(Die Besiehungen des Pankreas zum D. m.). Seyfarth, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 589.

The author does not believe that the islands of Langerhans are special organs related to carbohydrate metabolism. It is not true that in diabetes only the islets have undergone pathological changes; at least it has never been proved. For the development of diabetes it is necessary that large parts of the

gland be destroyed and that this pathological process proceeds so rapidly that regeneration is impossible.—J. K.

(PARATHYROID) Parathyroid studies. I. The normal anatomy of the parathyroid glands. Bergstrand (H.), Acta. Med. Scand. (Stockholm), 1919, **52**, 791-856.

These studies were made on human material. A follicular arrangement of the gland cells was found, at times the follicles being grouped in actual glandular nests with lumena. With Bielchowski's stain a hitherto unknown lattice net work was brought out, the fibrils of which surround the capillaries and extend out through the follicle, binding together the individual parenchyma cells. There is only one type of cell present, the so-called chief cells. The "achromatic protoplasm" of these cells is an empty space produced by shrinkage. The granules of the cells are artefacts which have arisen through the precipitation of the protoplasmic net by fixation. The cells of Welsh are degenerated chief cells, their eosinophilia is not concerned with granules. However, there are present in these cells granules of another type, which have been established as fat granules and unrelated to the colloid formation. The parathyroid cells are quite rich in fat granules: the fat is stable, gives the reactions for neutral fat, and is neutral. The colloid arises partly through degeneration of the Welsh cells and partly by secretion from these cells as from the chief cells. The so-called "eosin red components" are formed of the normal intercellular secretion. The interstitial tissues contain large deeply granulated cells with long processes and large vacuoles. The granules show the same metachromatic properties as the histogenic mastcells, but give, however, a positive test with Schulze's oxidase reaction in differentiation from the latter. Perhaps they are identical with Erdheim's pigment cells.—J. A. H.

PARATHYROIDS, Therapy of postoperative tetany (Zur Therapie des postoperativer Tetanie). Borchers (E.), Zentralbl. f. Chir. (Leipzig), 1920, **46**, 293-297.

The only treatment of postoperative tetany is transplantation. Of course, one may see failures, but other treatment has never succeeded. Especially administration of parathyroids by mouth has no effect. The best organs for transplantation are fresh parathyroids from children dying during accouchement.

—J. K.

(PARATHYROIDS) On the origin of the muscular tremors, clonic and tonic spasms in parathyroid tetany. Luckhardt (A. B.), Sherman (M.) & Serbin (W. B.), Proceedings Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51**, 187.

Parathyroidectomy was performed in dogs after they had recovered from transections of the cord at various levels. Without transection the neuromuscular phenomena are less severe in the hind limbs than in the fore limbs. With transection the fibrillary contractions occur posterior to the transection; may be present in the hind limbs independently of the fore limbs; may persist in the hind limb when its musculature is isolated. Clonic spasms persist. Tonic spasms are less pronounced. There is a great increase in reflex irritability just prior to and during an attack of tetany, followed by a corresponding nervous depression after the attack. Graded doses of strychnine can produce a condition not to be distinguished from tetany. Experiments on dogs seem to show that the cerebellar arc reinforces, but does not initiate the tonic spasms.

—T. C. B.

PINEAL tumor, A case of— (Een geval van gezwel van epiphyse). Hekman (J.), Med. Tijdschr. v. Geneesk. (Haarlem), 1920, **64** (i), 1891-1893.

A girl of 14 years had, when she was 3, fallen from a chair striking her head on the floor. Of recent years her sight has become worse and worse, and she has become very fat. From time to time she has epileptiform attacks. Menstruation began at 11. The child is very erotic. There are neurological symptoms of an old encephalitis in the neighborhood of the capsula interna (paresis of left arm and leg with high jerks; Babinski's symptom, etc.). Both eyes show an optic neuritis. The fatness, the increased sexuality and the eye symptoms may be considered as evidence of localization of the etiologic process in the pineal gland.—J. K.

(PITUITARY) Demonstration of an apparent one-sided acromegaly (Demonstration einer schienbar halbseitige Akromegalie). Biedl (A.), Wien. klin. Wchnschr., 1918, **31**, 487-488; Med. Klin. (Berlin.), 1918, **14**, 577-579.

A description of a case of one-sided acromegaly presented before the scientific association of German physicians in Bohemia. The acromegalic phenomena were exhibited on the left side in all their usual distinctiveness. No enlarged sella turcica was observed under x-ray examination. The anamnesis

records a gradual enlargement of the left arm beginning in the fourth year. The existing complaint was sudden loss of vision, pain in legs, fever, and anuria, which were regarded as due to acute meningeal or cerebral disturbance. No satisfactory explanation of the unilateral growth is given.—F. S. H.

(PITUITRIN) Labor with special reference to pituitrin, morphine and instruments. Harrison (A. G.), J. Arkansas M. Soc. (Little Rock), 1918, **14,** 211-212.

Cautions against the indiscriminate use of pituitrin in labor.—F. S. H.

(PLACENTA OVARY) Substances that increase the growth of the sexual organs (Ueber Substanzen die das Wachstum des Genitale wirksam anregen). Schroeder, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 417-418.

The opinion is expressed that infantilism in women is caused by hypofunction of the ovaries. The author tried the influence of extracts of various organs on the genitalia. From an ether-acetone-alcohol extract of the placenta he obtained a cholesterin-like substance which when injected daily into young rabbits in doses of from 0.3 to 0.5 grams caused hypertrophy of the muscles and mucous membrane of the vagina and uterus. The influence of the ovaries and fallopian tubes was slight. When the same procedure was carried out with males the utriculus masculinus responded by hypertrophy, while the effect upon the epidydimus and penis was negligible. The extracts seem to be effective even when diluted to one-fiftieth. Extracts from other organs were tried but, with the exception of the liver, gave uniformly negative results. Commercial preparations of the ovary were without effect.—J. K.

POLYGLANDULAR DISORDER (Pluriglanduläre Erkrankung). Pribram, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 424.

A demonstration of a 26-year-old girl who had complained for three years of headache, goitre, and cessation of menstruation. Two years previously strabismus set in with diplopia. The fingers became thicker. A strumectomy was performed. At present there is hemianopsia, insufficient power of renal concentration, an enlarged sella turcica, claw-like hands and hypoplasia of the genitals. After the removal of an adenoma of the hypophysis the eye symptoms improved, but diabetes developed. This case is characterized as a diseased condition of the thyroid, hypophysis, pancreas, and ovaries.—J. K.

(PROSTATE) The action of prostatic extracts on isolated genito-urinary organs. Macht (David I.) & Matsumoto (S.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17,** 102-103.

The action of prostatic extracts on the contractions and tonicity of uterus, fallopian tube, bladder, vas deferens and seminal vesicle was studied in vitro. Extracts were made from ram's, dog's, bull's, steer's and human prostates. All the tissues mentioned were stimulated, the uterus and fallopian tube with least quantities, bladder and uterus, next, and vas deferens and seminal vesicles requiring the largest amounts. It was concluded that prostatic extracts have no specific or marked influence on the tonus and contractions of the bladder,—at least, under the conditions of the experiments reported. A more extensive report is to appear in the Journal of Urology.—R. G. H.

PROSTATE, The action of extracts of the—on the isolated genito-urinary organs. Macht (D. I.) & Matsumoto (M.), Proc. Am. Physiol. Soc., Am. J. Physiol. (Balt.), 1920, **51,** 203.

The uterus, fallopian tube, bladder, ureter, vas deferens and seminal vesicle are all stimulated in vitro by aqueous extracts of mammalian prostate, including the human. Different organs require different doses. The conclusion is that prostatic extracts can not be regarded as having any specific influence in vitro on the tonus and contractions of the bladder.
—T. C. B.

PUBERTY (La pubertad). Blanc Fortacin (J.), Soc. Españ. de Obst. y Ginec., 1919, ——, ——.

Puberty is considered in its physiology and its pathology as an endocrine event in which the secretions of the genital glands, the hypophysis, the thyroid and the suprarenals take part as excitants of the sexual development while the thymus and the pineal act as inhibitors. The harmonious action, reaction and interaction of the endocrine system determines the successful pubertal development; a disturbance in the balance results in the evolution of a pathological condition.—E. B.

(SPASMOPHILIA) Case of spasmophilic diathesis, with some remarks on the types of convulsions occurring during the suckling period. Wirseen (J.), Hygiea (Stockholm), 1919, **81,** 992-997.—J. A. H.

(TESTIS) Spondylitis rhyzomelica (of Marie-Strümpell). Hertzberger (L.), Inaug. Dessertation, Amsterdam, 1920.

The author considers "spondylitis rhizomélique" as due to gonadal dysfunction. It is much more frequent in men than in women. The subjects are nearly always sterile. In some respects the disease resembles osteomalacia but differs among other ways in that it is characterized by high calcium content of the bones. Osteomalacia is often seen in localities where Graves' disease is common, whereas, in Holland the spondylitis is rather frequently seen in the Friesland district, where myxedema is the common thyroid disorder. In spondylitis rhyzomélique, the administration of ovarian preparations leads to marked augmentation of excreted phosphates and urates. The thesis is further supported by the arguments that the sex-glands are known to have an important relationship to osteogenesis and that in the subjects of this malady a history of gonorrhea is often obtainable.—J. K.

(TESTIS) Induced testicular degeneration and accompanying hypertrophy of the interstitial tissue. Kuntz (A.), Anat. Rec. (Phila.), 1920, **18**, 137.

Experimental evidence is presented to show that hypertrophy of the interstitial tissue in the testis occurs more promptly as an accompaniment of degeneration of the seminal epithelium than as a compensation process. In the series of operated dogs reported bilateral degeneration of the testis followed unilateral vasectomy with occlusion of the duct. In unilateral castration the testis on the unoperated side showed no evidence of degeneration.—W. J. A.

(TESTICLE) Myotonische Dystrophie. Minkowski, Berl. klin. Wchnschr., 1920, **57**, 234.

Dystrophic myotonica is a polyglandular disease. The author demonstrated a case with cataract and atrophy of the testicles.—J. K.

TESTICLE, Tissues of the—and avitaminosis (Tessuto testiculare ed avitaminosi). Novaro (P.), Gazetta degli Ospedali (Milano), 1920, **41**, 424.

The author observed that pigeons fed on a diet without vitamine B show degeneration of the epithelium of the tubuli testiculari and a hypertrophy and hyperplasia of the interstitial cells.—J. K.

THYMUS hyperplasia in children, Clinical study and treatment of—(Beiträge zur Klinik und Behändlung der Thymushyperplasie bei Kindern). Birh (W.), Monatschr. f. Kinderheilk., 1918, **14**, 363.

Birh reiterates the clear distinction between the symptom-complex of status lymphaticus and simple thymus hypertrophy. In the latter condition there is an isolated enlargement of the thymus dating back to fetal life, and here death comes from suffocation from pressure of the thymus on the trachea in a congenitally predisposed child; in such cases radiotherapy gives the best therapeutic results. In five cases reported by the writer there was rapid cure, from a clinical standpoint, with a gradual diminution of the gland itself as shown by radiographic examination. One of these cases showed a recurrence, but the others were followed to the fifth year of life, and showed a definite cure. The diagnosis of thymic hyperplasia is based upon a cardinal triad of symptoms; stridor, increased thymic dullness and radiographic evidence of enlargement. Other signs are attacks of asphyxia, dysphagia and, especially, lymphocytosis.—W. H. D.

Enlarged THYMUS gland in childhood. Brayton (H. W.), Proc. Connecticut M. Soc. (New Haven), 1918, **126**, 117-127.

This paper presents in a brief manner seven case reports in which enlarged thymus was diagnosed by x-ray examination. Three of the children died before radium therapy could be initiated; the remaining four responded satisfactorily to the treatment, and later x-ray pictures demonstrated reduction of the enlarged gland.—F. S. H.

(THYMUS) Thymic asthma in infants (L'asthme thymique chez les enfants). Exchaquet (L.), Rev. méd. de la Suisse Rom. (Geneva), 1918, **38**, 403-404.

E. considers that Paltauf's theory of the status thymo-lymphaticus is not supported by the facts and that from his own observations the mechanical action of a hyperplastic thymus is sufficient to explain the syndrome. He divides the cases into two categories: the one consists of individuals from 6 days to 14 months old, who are continually bothered with respiratory difficulties; the other group comprises those children in whom crises of suffocation occur while they apparently are in good health. Diagnosis is sometimes uncertain but can ordinarily be arrived at by exclusion. Radio-therapy lasting from two weeks to six months proved uniformly successful. The

report is followed by a brief discussion of thymus size and treatment.—F. S. H.

(THYMUS) Studies on acute leucemia. Lindblom (O.), Svenska. Läkaresällsk. Handl., 1919, **45,** 83-338.

It is of particular endocrine interest that the author found thymus alterations not only in the cases of lymphatic leucemia but also in several of the myeloid types. In 5 cases of the latter type myeloid inclusions, mainly of a perivascular type, were encountered.—J. A. H.

THYMUS, Changes in the—of children following different infectious diseases (Veränderungen der Thymusdrüse der Kinder bei verschiedenen Infektions-Krankheiten). Takeuchi (K.), Fukuoka-Ikwadaigaku-Zasshi, 1919, **12,** 25.

The author has made a study of the changes in the thymus gland in different infectious diseases, including "Ekiri," dysentery, simple enteritis, diphtheria, septicaemia, pneumonia and tuberculosis. Altogether he has collected 252 cases of which 162 were examined microscopically as well as macroscopically. He concludes that the chief changes are degenerative and destructive. He noted marked destruction of the so-called small thymus cells of the cortex and medulla, enlargement and phagocytosis of the reticulum cells of the cortex, and degenerative enlargement of the Hassall's corpuscles. In consequence of these regressive processes it is possible to recognize a primary increase and secondary atrophy of the parenchyma, an initial increase and subsequent decrease in the eosinophile cells, followed by an increase in the interstitial tissue. The regressive processes increase in proportion to the duration of the illness, reach a maximum between the 2nd and 4th days, and then gradually slacken. In the most acute infections, such as "Ekiri," dysentery and diphtheria, destruction is most apparent, while in the more chronic conditions there is more atrophy.
—E. V. C.

((THYROID) The causative factors of hematocele of the thyroid gland. Anon., Med. Rec. (N. Y.), 1919, **95,** 198-199.

The editor discusses the mechanism in formation of thyroid hematocele, and considers it comparable to a pelvic hematocele only that purulent transformation is much more frequent in the former. —H. L.

(THYROID) The physiological action of the proteinogenous amines. III. The influence of the proteinogenous amines, phenyl-and p-oxyphenylethyl amine on the carbohydrate metabolism of the liver (Beiträge zur Kenntniss der physiologischen Wirkung der proteinogenen Amine. III. Über den Einfluss der proteinogenen Amine, Phenyl-und p-Oxyphenylethylamine auf den Kohlenhydratstoffwechsel der Leber). Abelin (J.), and Jaffee (I), Biochem. Ztschr. (Berlin), 1920, **102,** 39-57.

The subcutaneous injection and feeding of phenylethylamine and tyramine raise the catabolic processes of white rats and cause a lowering of the glycogen content of the liver. In view of the results on the gas exchange under similar conditions, it is concluded that this increased carbohydrate oxidation is related to a glycogen destruction in the liver. Since the injection of these amines and the feeding of the active substances of the thyroid lower the glycogen content of the liver and the animals remain alive, these compounds can be used to get this organ of the rat glycogen free.—F. S. H.

(THYROID) The physiological action of the proteinogenous amines. IV. Influence of di-iodo tyramine and tyramine on the development of frog larvae (Beiträge zur Kenntniss der physiologischen Wirkung der proteinogenen Amine. IV. Einfluss von Dijodtryamin und Tyramin auf die Entwicklung von Froschlarven). Abelin (J.), Biochem. Ztschr. (Berlin), 1920, **102,** 58-88.

Tyramine usually acts as accelerating agent for frog larva metamorphosis. This action is greatly increased if iodine is attached to the tyramine molecule, and is similar to that obtained when thyroid feeding is tried. The thyroid acts to increase disassimilation in that growth is retarded and metomorphosis accelerated. Di-iodotyramine gives this effect only on larva of a certain age, since young tadpoles are mainly inhibited in growth. Feeding with KI or iodo-lipoids had no accelerating effect on the metamorphosis of either young or older larva. Phenylethylamine in weak concentrations acts as a narcotic and shows itself to be a strong local anesthetic. [Cf. Swingle, Endocrin. **3,** 114-115.].—F. S. H.

(THYROID PARATHYROID) Strumipriva tetanie. Arnstein (A.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 224.

A demonstration of a woman of 54 years with sclerotic symptoms in muscles and connective tissues, who had a goiter

for 25 years. Four days after the removal of the goiter tetany developed in its classical form.—J. K.

(THYROID) Murillo's method for the evalution of antithyroid serum (Acerca del mitodo de Murillo para la valoracion del suero antitiroideo). Banus (J. S.), Siglo Méd. (Madrid), 1919, **66**, 668-671.

Murillo's method is based on the effects by which the antithyroid serum raises the resistance of guinea-pigs to the amount of diphtheria toxins necessary to produce death within twenty-four hours. Autopsy has shown the inhibition of the adrenal defensive mechanism. The author describes a series of experiments which showed the role played by the thyroid in the antitoxic defense against cocaine, which is taken as further proof in the confirmation of the defensive function of the gland. —E. B.

Vital THYROID-PARATHYROID activities. Ball (C. F.), Vermont Med. (Rutland), 1918, **3**, 17-20; 33-37.

A review—F. S. H.

(THYROID) Creatine and creatinine metabolism in myxoedema and the effect of the administration of thyroidin upon it (Kreatin-kreatininstoffwechsel bei Myxoedem und unter Einwirkung von Thyroidin). Beumer (Hans), & Tseke (C.), Berlin klin. Wchnschr., 1920, **57**, 178-179.

A patient of 13 years with myxoedema was treated with thyroidin and the creatinine metabolism studied. Large amounts of creatine were excreted but no changes were observed in the creatinine output. In normal individuals the same reaction is obtained after the administration of thyroidin, although it is less intense. The reaction in myxoedema may be explained on the basis of an increased destruction of proteins under the influence of the thyroidin.—J. K.

THYROID intoxication, Observations on—. Blackford (J. M.), Northwest Med. (Seattle), 1919, **18**, 199-201.

The author studied 74 exopthalmic goitre autopsies. All subjects under 40 years were found to have persistent thymuses of varying size. One-half of those over 40 had a large thymus and one-half no thymus at all. From these facts Blackford formulates the following deductions: 1, the thymus plays no causative role in exopthalmic goitre because half of the

older people died of that disease but had no thymus; 2, the thymus may exert a protective influence in exopthalmic goitre. These conclusions would be difficult to reconcile with the observations in cases of exopthalmic goitre which have been improved or cured by thymectomy. From a clinical standpoint, study of histories and autopsies suggest that if a patient with exopthalmic goitre lives one year after the inception of symptoms, he probably will not die from the disease before ten years have passed, and if then, usually from cardiac degeneration. No case of exopthalmic goitre showed active tuberculosis. No case of thyroid carcinoma was observed developing from exopthalmic goitre. About nine months after inception of symptoms most patients become suddenly very much worse. Operation at this time is accompanied by a very high mortality—25 per cent—and hence is contraindicated. Sometimes the patient without surgical treatment dies, but usually medical measures serve to tide them over this acute period. The author believes that x-ray, bromide, ergot, quinine, cold, etc., are of no benefit; that basal metabolism has been decreased only by rest and by operative reduction of the amount of functionating thyroid tissue. "In other words, exopthalmic goitre is a medical disease only until the patient is known to be in condition for operation; then operation should always be undertaken." [Many internists will disagree with the last pronouncement.] Many thymuses were found at autopsy in cases in which excellent stereoscopic x-ray pictures failed to reveal the gland,—even on review of plates after the autopsies. Thyrotoxic adenomata have been proven toxic by basal metabolism studies aside from clinical observation, and by striking improvement following operation, but they have no characteristic pathology. The author refers to the extraordinary power of Kendall's thyroxin in accelerating metabolism. He has shown that in heart block thyroxin will increase the ventricular rate, proving that it has a direct effect on cardiac tissue, and further emphasizing the relation of thyroid intoxication to cardiac degeneration.—H. L.

(THYROID) Blood picture in hyperthyreosis and goiter (Blutbefunde bei Hyperthyreose und Struma). Blank (G.), Deutsch. Arch. f. klin. Med. (Leipzig), 1920, **132**, 16-34.

The diagnosis of Graves' disease may be very simple, but in cases where certain characteristic symptoms are absent it may be extremely difficult. Kocher has reported that in Graves' disease the white corpuscles are diminished; that there is a neutrophil leucopenia with a relative or absolute lympho-

cytosis. Many authors have been unable to confirm these findings as typical of the disorder. Blank has carefully examined the blood in many cases of hyperthyreosis and goiter. He concludes that many contradictions in the literature may be explained as due to faulty diagnosis or bad technic in examining the blood. In Graves' disease the blood picture changes incessantly. In 30 per cent of the cases poikilocytosis was observed; in 50 per cent of such cases, and also of goiter, polychromatophilia was found. Basophilic stippling of the red corpuscles proved extremely common in both conditions seen in approximately 75 per cent. The number of blood platelets was diminished in 43 per cent of the classical cases of Graves' disease; in the formes frustes and in simple goiter this was never observed. In only 23 per cent of the classical cases of Graves' disease was the quantity of hemoglobin normal. In the others it was sometimes diminished, but is also often increased. In hyperthyreosis and in goiter the number of red corpuscles was normal. The color index in Graves' disease was sometimes high. It was found that neutrophilic leucopenia may be observed just as often in Graves' disease as in simple goiter. The number of eosinophilic leucocytes in both conditions was normal. Increase of the number of large mononuclear leucocytes was more frequently seen in the classical Graves' disease than in other diseases of the thyroid. In half the number of all diseases of the thyroid the number of lymphocytes was normal. In the remainder it was either increased or diminished. From these facts it may be concluded that the blood picture of Kocher has no diagnostic value in diseases of the thyroid.

—J. K.

(THYROID) Loss of flesh in women during the war (L'amaigressement des femmes au cours de la guerre). Blum (P.), Prog. Mèd. (Paris), 1918, **33**, 15.

Having eliminated from consideration those women whose loss of weight during the war was attributable to abnormal diet or tuberculosis, B. noticed that the greater number of those losing weight had the symptoms of thyroidism more or less complete. Four cases are reported as examples. The phenomenon is considered the effect and not the cause of the troubles, the causative factor in B.'s opinion lying in the sympathetic system.—F. S. H.

(THYROID) Basdowian psychosis (Psicosis basedowiana). Brabo (K.), Gac. med. Castellana, 1919, ——, ——.

A well studied case of hyperthyroidism accompanied by

mental confusion. The patient was much improved by antithyroid treatment.—E. B.

(THYROID) Cardio-thyroid syndromes (Sindromes cardio-tiroideos). Cañizo (A.), Siglo Médico (Madrid), 1919, **66,** 81, 130.

The author reports two cases of hyperthyroidism with the ordinary symptomatology of that disorder but with, in addition, predominating circulatory disturbances. The first patient had had a very light attack of "grippe." The second was a typical case of "Kropfherz." The patient had a persistent goiter which enlarged with each successive pregnancy, but diminished in the interim. She had had ten children. During the last pregnancy, following a great grief, the goiter, which had previously continued as the simple type, became hyperplastic, giving rise to the typical Graves' tetrad of symptoms. Only the cardiac conditions need be mentioned. By percussion and radiography, the cardiac area was found to extend to the sixth intercostal space, and laterally, to the mammillary line. Upon auscultation the tones in the mitral area were weak but in the aortic area somewhat resonant. The pulse,—100 beats per minute,—was small and compressible. There were irregularity and perpetual arrhythmia. In view of the fact that there was no history of antecedent infection or toxicosis, the author reasonably concludes that the cardiopathy is to be ascribed to the goiter.

In goiter two classes of cardiac disturbances are encountered, those due to the mechanical effects of the thyroid tumor and those due to thyrogenic toxins. Both Cañizo's cases were undoubtedly of the latter class. Various theories as to the mechanism whereby the cardiopathy is produced in such cases have been offered. Cañizo leans toward the idea that the continuous tachycardia with which the patients have to contend,—a condition which, in the hyperirritable state of the patients is readily evoked and continued by such causes as emotions, pregnancy, etc., keeps the muscle fibres over-active and without the normal rest period of ordinary diastole. This ultimately leads to nutritive failure and degeneration of the fibres, with consequent dilatation of the heart.—E. B.

THYROID activity, Some conditions affecting—. Cannon (W. B.) & Smith (P. E.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1920, **17,** 88-89.

See Endocrin, **4,** 386.

(THYROID) Two cases of interest in relation to the function of the thyroid. .Carmichael (F. A.), J. Kansas M. Soc. (Topeka), 1918, **18,** 83-85.

A report of two patients, each of whom showed a different degenerative process affecting the thyroid. The first was a case of calcareous degeneration of the thyroid in a cretin. On palpation the gland appeared slightly enlarged, somewhat indurated and irregular in outline. On removal the gland was found to weigh 105 grams and to contain numerous calcareous deposits varying in size from very small to that of a large bean. A rather complete histo-pathological report is given.

The second case was one of benign or slow-growing malignancy. No detailed description is given.—F. S. H.

THYROID, Surgical treatment of Exopthalmic Goitre. Crile (G. W.). Surg. Gynec. & Obst. (Chicago), 1920, **30,** 27.

Previously published in abstract. See Endocrin, **4,** 163.

(THYROID) Treatment of myxoedema by transplanting portions of a hyperplastic gland. Dowd (C. N.), Ann. Surg. (Phila.), 1920, **71,** 518.

The transplants were placed in the cancellous tissue of the head of the left tibia, in the preperitoneal tissue beneath the rectus abdominis, and in front of the rectus. Fifteen small punctures were made in other parts of the abdominal wall and little fragments of the gland were inserted. Marked improvement in the patient's condition is reported. After five months, dessicated thyroid was prescribed, however, as a precaution, for the patient's improvement was really remarkable.—J. F.

(THYROID-PARATHYROID) The influence of thyro-parathyroidectomy in the dog on the formation of natural antibodies and amount of heterohemolytic power of serum [Sur l'influence de la thyro-parathyroïdectomie (chez le chien); sur la formation d'anticorps naturels; dosage du pouvoir hétérohémolytique du serum]. Garibaldi (A.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 251-252.

In a former communication (See Endocrin **4,** 330), Garibaldi has shown that thyroidectomy favors the formation of immune antibodies in the rabbit. This raises the question of the regulatory role of the endocrine glands on the activity of the "antigenic organs." If this function exists, it is difficult to understand the results of Mlle. Fassin and Marbe, who found a diminution of natural heterohemolytic power after thy-

ro-parathyroidectomy, while Frouin obtained a contrary result. The present note records the author's observations upon the effect of thyro-parathyroidectomy on the natural heterohemolytic properties of dog serum. Protocols are given and the conclusion drawn that in the dog, thyro-parathyroidectomy increases the natural heterohemolytic power of the serum. The suggestion is made that the thyroids and parathyroids may play some role in blood regeneration. [See also Koopman, Endocrin. **3**, 318-320].—T. C. B.

(THYROID) Endemic goiter and cretinism in the high valleys of Alberche and Tormes (Sobre un foco de bocio y cretinismo endemico en los valles altos del Alberche y el Tormes). Goyanes, Siglo Méd. (Madrid), 1918, **65**, (2) 43; 85; 162; 182.

This is the first study of importance of the geographic distribution of endemic goiter and cretinism in Spain. Bircher supposed that these conditions arise only on lands that are marine sediments, and particularly on the marine deposits of the lands corresponding to the primary palaeozoic, triassic and tertiary periods. The observations of Goyanes in the valleys of Tormes and Alberche make possible the affirmation that formations of the archaiac group, granite, gneiss and crystalline deposits, are also sources of endemic struma. It is evident that water is one of the most important agents in the transmission of the supposed living cause of goiter. The theory that there are in the drinking water certain dissolved chemical substances such as calcium, magnesium, iron, etc., that determine the origin of endemic goiter is discredited. The studies of Marine and Lenhard and of Gaylor explain the appearance of endemic goiter on the basis of a living organism since they have observed in the affected regions the presence of hypertrophied thyroids in certain fish, as the trout. Goyanes could not find such conditions in the trout he studied. The experiments of McCarrison are cited, on the production of experimental goiter in man, and of its intestinal origin. A study of the dates in connection with the production of goiter seems to show that the water is not the only medium of contagion. The author's conclusions are as follows: Endemic goiter and cretinism appear to be diseases of infectious origin the source of which, however, is not known; cretinism is the result of a congenital hypofunctioning thyroid; it cannot be denied but must be affirmed that the transmission of the infectious agent from mother to child determines the congenital goiter and cretinism; sporadic goiter is also an infectious disease. Some infections produce thyroiditis similar to goiter (Chagas disease); the in-

fectious agent may invade the body through the bite of an insect; it is possible that the germ resides in the soil, by preference in those in which the organic material in decomposition is more abundant, but no statement can be definitely made that it is determined by any particular geological formation. It cannot be denied that water may be a medium of transmission and it is very probable that the endemic spreads by immediate contagion and mediation in the living; the strumous infection if not congenital at least appears very early in life; the intestinal localization of the organism is probable but not demonstrated.—E. B.

(THYROID) Some observations on goiter. Hawks (J. K. P.). Illinois M. J. (Chicago), 1918, **33,** 221-224.

An expression of the theory that the cause of the prevalence of goiter in the middle West is due to the drinking of the subterranean water of the glacial drift, which is analagous in its composition to the glacial waters of Switzerland, where goiter is so prevalent. Hawks considers that practically all goiters are surgical, and should receive early operative treatment.—F. S. H.

Reinforcing THYROID extract. Harrower (H. R.). South Calif. Pract. (Los Angeles), 1918, **33,** 39-40.

On the basis of the hypothesis that hypothyroidism means sub-oxidation: sub-oxidation means toxemia: toxemia means hypoalkalinity, and hypoalkalinity means demineralization, H. reinforces thyroid extract with a combination of salts closely following the salt composition of the blood. Treatment consists in giving ⅛ gr. to ½ gr. U. S. P. thyroid t. i. d. and 5 grs. of the salt mixture at the same time.—F. S. H.

THYROID function, Clinical results with a method of testing—. Harrower (H. R.), Med. Rec. (N. Y.), 1919, **96,** 722-725.

Reference again to the author's thyroid function test originally published in the Medical Record, August 3, 1918. This consists in the administration by mouth of four doses each ½, 1 and 2 grains of thyroid on three successive days, recording the pulse rate at regular intervals during this time, and noting symptoms such as irritability, twitching, breathlessness, etc. It is recommended by the author as a simple method of differentiating between hypo- and hyper-thyroidism. [The accuracy of such a test is open to question. A careful history and thor-

ough clinical examination would probably reveal more information, and if more precise studies were indicated, a Goetsch test or basal metabolism estimation would be preferred].—H. L.

THYROID hyperplasia and the relation of iodine to the hairless pig malady. I. Hart (E. B.) & Steenbock (H.), J. Biol. Chem. (Balt.), 1918, **33**, 313-323.

In an extended study of the hairless pig malady which occasions so much economic loss among the hog-raisers of Wisconsin, Hart and Steenbock have obtained evidence supporting the view that the disease is caused by a low iodine assimilation by either intestine or thyroid, resulting in a goitrous condition of both mother and young. This condition apparently interferes to a greater extent with the fetal development than with the normal maintenance of the mother.

When young sows are fed high-protein-level rations which have low laxative effects, and have accompanying conditions of lack of exercise and unclean surroundings, they are prone to develop thyroid enlargements. This is not so prevalent among the older sows. It is considered possible that some rations are so low in iodine as to make the scarcity of this element the direct cause. However, the authors state that the stage has not yet been reached when it is wise to advocate the general use of iodine in the feed of all brood-sows. But they do consider that in regions and on farms where hairless pig production is endemic or persistent in character the direct use of iodides should be made. [See also Smith, Endocrin. **3**, 262-272].—F. S. H.

Surgery of the THYROID. Haskins (J. B.), J. Tenn. State M. Ass. (Nashville), 1918, **11**, 91-96.

Of surgical interest, mainly.—F. S. H.

(THYROID) The question of iodine combination in the thyroid (Zur Frage der Jodbindung in der Schildrüse). Herzfeld (E.) & Klinger (R.), Biochem. Ztschr. (Berl.), 1919, **96**, 260-268.

When the tissue liquid is squeezed from pig thyroids and various iodine solutions are added thereto a certain amount of the element combines with substances in the extract. The results of these studies seem to indicate that the iodine in the thyroid is not only combined with the decomposition products of the protein surface, but is also in large part "built into" the cell protein. The authors conclude that these observations

speak against the conception that the iodine is an actual part of the thyroid secretion.—F. S. H.

(THYROID) Chemical studies of the physiology and pathology of the thyroid gland (Chemische Studien zur Physiologie und Pathologie der Schildrüse). Herzfeld (E.) & Klinger (R.), Münch. med. Wchnschr. (Munich), 1918-19, **65,** 647-651.

From the results of their studies on the effects of thyroidectomy the authors come to the conclusion that the thyroid secretion is not a protein complex, but is a dialysable split product. They consider that iodine is not an actual constituent of the secretion, but are of the opinion that its role is that of stimulating the formation of the secretion.—F. S. H.

(THYROID) Case of tertiary luetic thyroiditis accompanied by a high-grade laryngeal stenosis. Hœggström (A.) & Bergstrand (H.), Acta oto-laryngolog. (Stockholm), 1920, **2,** 207-237.

Hoarseness, air hunger, difficulty in swallowing, and cyanosis were present in a patient 41 years old. A tumor arising from the thyroid surrounded the larynx and trachea. Tracheotomy was performed on account of oedema of the glottis and suffocation. The Wassermann reaction was positive. Mercury treatment resulted in improvement, but this failed to last, and death ensued from suffocation about six months after the first appearance of the symptoms. Histological examination of the thyroid showed both interstitial and parenchymatous alterations. Each was a combination of gumma formation and interstitial chronic fibroplastic inflammation. A high grade of sympathetic involvement was also evident in the surrounding tissues. The parenchymatous alterations consisted in a proliferation of the thyroid follicles, which were entirely similar to those present in Basedow's disease. The parenchyma still present in traces in the gummatous necrosis was, however, of normal structure. This circumstance, taken with regard to the rest of the normal colloid, speaks for the idea that the proliferation of the follicles was of recent date, and a consequence of the action of the infectious agent.—J. A. H.

(THYROID) Goiter: Its early diagnosis and treatment. Holland (J. W.), Bull. Univ. Maryland School Med. (Balt.), 1918-19, **3,** 183-194.

A general presentation of the classification, causes, symptoms and treatment of goiter with clinical records of four cases, presenting no new data.—F. S. H.

(THYROID) Esophageal obstruction due to accessory thyroid. Hopkins (F. E.), Ann. Otol. Rhinol. & Laryngol. (St. Louis), 1918, **27,** 1258-1260.

Report of a case.—F. S. H.

THYROID response to overstrain. Hoxie (G. H.), Med. Herald (St. Joseph), 1920, **39,** 19-20.

The author cites the literature to show the tendency to consider thyroid hypertrophy as a reaction to adreninemia, to toxemia or to fatigue. He cites the experience of the troops in France as proof that the symptoms of hyperthyroidism may be simply such an attempt on the part of the body to maintain its chemical equilibrium. In brief, his experience was that soldiers came back to the base hospital after exhausting battles, with exposure to gas and infectious disease, showing a low blood pressure, dilated heart, and similar signs of exhaustion. The blood pressure would gradually rise until it reached 160 mm. With this increase in pressure was urinary urgency, tremor, heightened reflexes, and an increase in the size of the thyroid. In other words, in this stage the men presented the picture of Graves' disease.—Author's Abst.

(THYROID) Clinical data on goiter. Jones (E. G.), South. M. J. (Birmingham, Ala.), 1918, **11,** 682-685.

No new data.—F. S. H.

(THYROID) An unusual case of cretinism. Kerley (C. G.), Arch. Pediat. (N. Y.), 1919, **36,** 465-468.

This is the report of a case of a girl eight and a half years old, who displayed typical symptoms of cretinism when first seen by the author. Continual treatment for one year with thyroid extract 0.5-1.0 grain twice daily gave an increase of 6⅝ inches in height and of 8¾ pounds in weight, and also produced an appearance of normality. The case was reported because of the unusually good results obtained in one year's time, and despite its beginning at a relatively late age.

—M. B. G.

THYROID in uterine hemorrhage. Klass (O. C.), J. Oklahoma M. Ass. (Muskogee), 1918, **11,** 125-128.

A partial review of the literature and brief description of the favorable results obtained with personal cases of uterine hemorrhage by the use of thyroid extract. No details are given.—F. S. H.

(THYROID) Thyreohypoplasia congenita. Kasten, Med. Klin. (Berlin), 1918, **14**, 503; Deutsche med. Wchnschr., 1918, **44**, 559.

A demonstration of a 7-year-old girl presenting the classical symptoms of a hypoplastic thyroid.—F. S. H.

(THYROID) Acute strumitis (Akuten Entzündungen des Kropfes). Klose (Heinrich), Berlin. klin Wchnschr., 1920, **57**, 202.

A general review.—J. K.

(THYROID) Further course of the earlier described cases of retarded muscle contraction [Weiterer Verlauf der früher vorgestellten Fälle von verlangsamter Muskelkontraktion (Myxödem)]. Kramer, Berl. klin. Wchnschr., 1918, **55**, 989.

Three cases of retarded muscle activity were diagnosed as of hypothyroid etiology and thyroidin therapy initiated. The results in all three patients were good. There was increase in weight, decrease in lassitude, and a psychic rehabilitation. The muscular retardation has entirely disappeared and the reflexes have become normal.—F. S. H.

(THYROID) Myxoedema adultorum. Krisch (H.), Deutsche med. Wchnschr. (Leipz. & Berlin), 1918, **44**, 871.

Brief description and clinical findings of a case of myxoedema benefited by thyroid treatment.—F. S. H.

(THYROID) Local anaesthesia and technic of operations in goiter (Zur örtlicher Betäubung und Technik der Kropfoperationen). Kulenkampff (D.), Zentralb. f. Chir. (Leipzig), 1920, **46**, 246-249.

Of technical surgical interest.—J. K.

(THYROID ADRENALS) The influence of thyroid feeding upon carbohydrate metabolism. II. The epinephrine content of the adrenals of thyroid-fed rats. Kuriyama (S.), J. Biol. Chem. (Balt.), 1918, **33**, 207-213.

The epinephrine content of the adrenals of normal, medium sized rats is 2.2 mg. per gm. of the gland. In comparing this finding with the results of other investigators, the author decides that the epinephrine content of rat adrenal is the nearest to that of the dog, larger than that of the cat, and smaller than

that of sheep and calf. Thyroid feeding of either short duration with large doses or long duration with small doses does not materially change the epinephrine content, nor the weight of the adrenals of medium sized albino rats.

Kuriyama considers that if hypersecretion of the adrenals really exists in experimental hyperthyroidism, these results indicate that the excess of epinephrine is promptly transported into the circulation, the adrenaline content of the adrenals being kept fairly constant.—F. S. H.

THYROID, Cold abscess of the— (Abcès froid du corps thyroïde). Labey (M. G.), Bull. et mem. Soc. de chir. de Paris, 1918, **44**, 697-698.

Presentation of a specimen of abscessed thyroid removed from a goitrous woman. The diagnosis of tuberculous thyroid is given.—F. S. H.

THYROID in immunity, On the role of the—(A propos du rôle de la thyroïde dans l'immunitè). Launoy (L.) & Lévy-Bruhl, Compt. rend. Soc. de biol. (Paris), 1920, **83**, 90-91.

An answer to Garibaldi. (See Endocrin. 1920, **4**, 330.) In the author's experience thyroidectomy does not enhance the production of antibodies.—T. C. B.

(THYROID) A case of cretinism. Lennox (W. G.) & Read (B. E.), China M. J. (Shanghai), 1920, **34**, 140.

The case is that of a boy, 18 years old by Chinese count, who was admitted to the Peking Union Medical College Hospital, and who showed marked improvement on feeding six grains per day of dried thyroid gland.

The authors remark upon the fact that this is the only instance of cretinism which they have found in 35,000 cases treated at the dispensary, and that "perusal of a number of hospital reports from various parts of China fails to show record of cases of cretinism." This is the more remarkable since goiter is quite common in the vicinity of Peking and in other districts. They note, in addition, that the remarkable prevalence of goiter in some parts of China, and the fact that the Chinese are said to drink only hot tea, are inconsistent with the view that goiter is due to an infection caused by drinking unboiled water. The paper is accompanied by careful urine and water analyses.—E. V. C.

(THYROID) Graves' disease (Ueber die Basedowsche Erkrankung). Liek. Deutsche med. Wchnschr. (Berlin), 1920, **46**, 445-446.

The author observed 160 cases, including 100 of which the subjects were operated upon. There exists an intimate relation between the thyroid and brain. The "circulus vitiosus" in Graves' disease is: Increased secretion of the thyroid—increased irritability of the brain—increased secretion of the thyroid. Treatment may try to diminish the irritability of the brain or the hypersecretion of the thyroid. The first treatment, the internal one, is suitable for light cases only. The prime essential of this treatment is absolute psychical rest. The author is not convinced that x-ray treatment or milk of thyroidectomized goats has any therapeutic value. The best treatment attacks the thyroid surgically. The most important element is not the operative technique but the preparation of the patient. Before the operation he should be isolated and kept in bed for many days. The author advises ether anesthesia. The narcosis must begin and finish in bed, and not on the operation table. Of his 100 operated patients 3 died immediately after the operation; 2 died some time later of other diseases; 15 cannot be traced; 52 are cured; 20 are much better, and 8 are just the same as before the operation. Of these 8 cases, two underwent removal of the thymus; only in one case was any influence seen. In 3 other cases, after failure to benefit from thyroid extirpation, x-ray treatment of the ovaries was efficacious in curing the disorder.—J. K.

THYROID insufficiency after influenza (Dos casos hipotiroidismo post-grippal). López Albo (W.), Progresos de la Clinica (Madrid), 1919, **7**, 217-220.

The author gives the clinical histories of two children of 10 and 11 years, respectively, who, following an attack of influenza, developed extreme somnolency and headache. The fact that the cases improved under thyroid therapy is taken to indicate that they were due to hypothyroidism. They might, perhaps, be regarded as walking forms of encephalitis lethargica.
—E. B.

THYROID, A case of post-influenzal—hypo-function (Un nuevo caso de hipofuncion tiroidea post-grippal). Lopez Albo (W.), Prog. de la Clin. (Madrid), 1919, ——, ——.

Clinical history of a patient who presented the following conditions after having had a slight attack of the grippe:

paresthesia, general malaise, cephalagia, chills, cold extremities, lack of appetite, and edema of the eyelids. He was cured by thyroid therapy. The author is of the opinion that this case can be included among the thyroid disturbances of Lévi and Rothschild.—E. B.

(THYROID) Simple goiter—A public health problem. McCord (C. P.) & Walker (R. C.), Mod. Med. (Chicago), 1920, **2**, 124-132.

McCord and Walker have compiled all recent data with reference to the prevalence of simple goiter throughout the world, together with measures for the prevention of the occurrence of this disease. From the evidence available in these data they draw the following conclusions. The prevalence of simple goiter is common to many portions of this entire country. Inexpensive and readily applied measures have been devised for the eradication of this condition. These measures, although not yet fully standardized and simplified, have been demonstrated to be harmless and practicable. The school age coincides with the age of the highest incidence of goiter. The public and high school systems afford a splendid mechanism for carrying out these measures. It is believed that faithful application of these measures by public health workers, school and industrial physicians will go far in stamping out this widespread and distressing malady.—Author's Abst.

(THYROID) The surgical treatment of exophthalmic and thyrotoxic goiter with special reference to bilateral resection. MacLean (Neil J.), Surg. Gynec. & Obst. (Chicago), 1919, **29**, 475-480; Trans. West. Surg. Ass. (Minneapolis), 1919, **28**, 89-104.

The author points out the diversity of opinion between internist and surgeon in the treatment of exophthalmic goiter and the lack of unanimity as to operative indication and operative technique among surgeons themselves. It is stated that medical treatment in Graves' disease has not been satisfactory and the mortality and morbidity statistics of Sattler, Hector McKenzie, Kuttner and Hale White are quoted. While McCarrison says "there is no definite proof that the cures effected by surgical means are more lasting than those effected by medical means," Osler and Forchheimer are quoted as advocates of surgical treatment as both logical and scientific. The various surgical procedures are discussed, and the method of bilateral resection of the thyroid as advocated by Halstead was

the method adopted in the cases recorded, and had been the method used before the author heard Dr. Halstead's paper in Washington in 1913.

Emphasis is laid on the preparatory treatment for operation, especially having patience to wait until the wave of thyroid intoxication has well passed. By adopting this method the annoyance of preliminary ligation of vessels could in many cases be dispensed with and the complete operation of bilateral resection done in one stage. Emphasis is laid on the fact that exophthalmic goiter should never be considered a surgical emergency. The anaesthetic used in all cases was a combination of local anaesthetic (¼ of one per cent anocaine with adrenalin) and nitrous oxide with oxygen to induce unconsciousness. The operation consists in the low collar incision of Kocher and a flap of skin, superficial fascia and platysma dissected upwards. The infrahyoid muscles are separated in the mid-line and retraced laterally or, if necessary, divided transversely. Each lobe is then freed and dislocated from its bed. The superior thyroid vessels are first clamped and divided at the upper pole. Hemostats are now applied to the large veins as they course from before backwards on the surface of the gland. In applying these clamps the amount of gland to be preserved is borne in mind (usually one-sixth) and that above the clamps cut away. Bleeding from the cut surface is controlled by an over stitch. The remaining steps of the operation are completed in the usual manner with the exception that all veins in the flaps are underrun with fine catgut at some distance from the flap-edge, and tied so that no catgut comes in the line of incision. The platysma and skin are united by two separate silk worm gut sutures introduced subcutaneously. The resulting scar is almost invisible.

There are several advantages of bilateral resection over unilateral lobectomy or unilateral lobectomy with partial resection of the opposite lobe. Minimum injury is done to the parathyroids. Absolute safety for the recurrent laryngeal nerve is assured. If for any reason further removal of gland should be indicated, such as for recrudescence of symptoms of thyrotoxic activity, or the rare but possible occurrence of malignancy, the one side could now be completely removed with an assurance that some portion of gland remained. It is a physiological fact that where there are paired organs, should one be removed the other undergoes hypertrophy. This, while desirable in a condition where one is normal, is what we wish to avoid in the case under discussion, and this end is best obtained by double resection. Finally, for cosmetic purposes, in the operation of lobectomy there is a well marked depression

on the side from which the lobe has been removed, and on the other side the portion of gland left produces an undue prominence, while in bilateral resection the neck is obviously symmetrical.

In 31 cases in which the operation has been done there have been no fatalities.—Author's Abst.

(THYROID) Diagnosis and treatment of hyperthyroidism (Sobre el diagnostico y el tratamiento del bocio exoftalmico y de los estados hipertiroideos). Marañón (G.), Revista Ibero-Americana de Ciencias Médicas (Madrid), 1917, ——, —. (June.)

See Endocrin. **2,** 343.

(THYROID) Mongolismus mit Myxoedem. Moro, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 536.

A short note. A child presented typical mongoloid eyes, hyperflexibility, aplasia of the thyroid, dry hair, obstipation and idiocy.—J. K.

(THYROID) Osseous demineralization and its treatment (La deminéralization osseuse et son traitement). Robin (A.), Bull. gén. thèrap. (Paris), 1920, **171,** 61-74.

The loss of mineral substances from the bones is attributed to infectious diseases, such as tuberculosis and syphilis, dyspepsias accompanied by marked hyperchlorhydria, undernutrition, lowered alkalinity of the blood and lesions of the nervous system. The treatment consists in furnishing the organism an excess of the mineral salts it is losing, not in the pure form but as contained in foods rich in the necessary elements; in diminishing the ingestion of acid producing substances; and among other medications giving 2 mgm. of desiccated thyroid gland twice a day. Tables are given of the calcium and magnesium excretion of several individuals.—F. S. H.

(THYROID) Medical treatment of goiter. Ryan (G.), Med. Rec. (N. Y.), 1919, **96,** 534-536.

A brief, readable, conservative article, but presenting no new data.—H. L.

(THYROID) Curative versus symptomatic treatment of exophthalmic goitre. Sajous (C. E. de M.), Med. Rec. (N. Y.), 1919, **96,** 536-541.

A very interesting contribution leading to the conclusions that the symptomatic treatment of exophthalmic goiter generally resorted to compromises the chance of the patient's recovery, by leaving unassailed the primary cause of the disease. Many patients are subjected to thyroidectomy, entailing risks and morbid after-effects, who could be cured by medical treatment did the latter aim to remove the primary cause of the disease and its morbid effects. The remote results of surgical treatment would be greatly improved were removal of the primary cause of the disease and its morbid effects first insured. All cases of exophthalmic goiter are due primarily to some toxin originating from some pathological process in one or more organs, either the tonsils, sinuses, nose, nasopharynx, teeth or gums, stomach, intestines, genito-urinary organs, the nervous sytem, etc. Even the cases due to emotional stress have as their primary cause toxic wastes formed in the cerebrospinal neurons subjected to stress,—cholin, phosphoric acid, and particularly neurin, a highly poisonous waste product. These poisons, by exciting the thyroid apparatus to supranormal activity, owing to the active part taken by this apparatus in the defensive functions, cause it to excrete excessively, thus producing an additional toxicosis. The thyroid hormone, particularly when produced in excess, taking part also in tissue catabolism, breaks down fats, including the fatty bodies in nerves and brain cells, thus accounting for the striking nervous phenomena of the disease. Exophthalmic goiter thus becomes the product of a vicious circle in which three toxins take part: the primary causative poison which excites the thyroid; the excess of thyroid hormone as second poison; the excess of catabolic wastes due to the thyroid hormone, as third poison. Timely removal of the disorder which produces the primary causative poison, by arresting the excessive thyroid activity, will thus prevent the triple toxicosis, and cure the disease. The after-treatment, some such as described above, to insure cure, must also aim to remove the effects of the poisons. "Symptomatic treatment" should be dropped as an empiric method unworthy of modern science. —H. L.

(THYROID) A case of functional chorea with hyperthyroidism (Un caso de corea functional con hipertiroidismo). Sanz (F.), Real Acad. Nac. de Med. (Madrid), 1919, ——, ——, (Feb. 22).

The clinical history is as follows: mother neurotic, father normal; one sister presents symptoms of nervousness; personal antecedents unimportant; first menstruation at fourteen years at which time the first symptoms of the disorder appeared,

which have increased and consist of irregular movements that are brusque, incoordinated and involuntary, involving different parts of the body and many ties. During emotional stress they are augmented. Accompanying the chorea is a goiter and slight tremor; tachycardia is absent. The author considers it a case of hyperthyroidism but not of exophthalmic goiter, since the ocular symptoms are lacking. [In the opinion of the reviewer, the author attributes too much importance to the mere absence of exophthalmos. It is only one of many manifestations of hyperthyroidism and is by no means the most frequent.]—E. B.

THYROID function as influencing growth (Influencia de la function tiroidea sobre el crecimento). Sanz (L.), Aragon Méd., 1919, ——, —— (Feb.).

The results of this study lead the author to the conclusion that the thyroid secretion acts directly on growth in contradistinction to the other glands of internal secretion, which apparently act indirectly. The principal point of influence is osseous metabolism and the activle principle is a specific iodine containing compound. The thyroidal alterations are accompanied by changes in other glands of internal secretion, particularly the hypophysis and gonads, which also add their quota to the growth processes. The climatic influence on growth is exercised through its modifying effect on the thyroid. All diseases which alter the nature of growth produce disturbances in the thyroid functions.—E. B.

(THYROID) Metabolism, report of a case. Schwartz (C. W.), Am. J. Roentgenol. (Detroit), 1920, **7**, 229.

A preliminary report on the case of a young man, twenty-seven years of age, who came to the hospital because of extreme nervousness and restlessness. He presented upon examination an enlarged thyroid gland, a loud bruit, tachycardia, exophthalmos, lid lag, tremors of the hands, sweating, and Hutchinsonian teeth, together with a positive Wassermann test and a markedly increased metabolic rate. In the course of three months, by means of a series of x-ray treatments, the technical details of which are given by the author, the rate was lowered 67 points.—J. F.

(THYROID) Aetiologie des Mongolismus. Stölzner, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 200.

The mothers of mongoloid children are often rather old or worn out by many confinements. In three cases observed by

Stölzner, the mother showed hypothyroidism. The author advises the administration of thyroid during pregnancy.

Homoplastic THYROID transplants. Swingle (W. W.). Anat. Rec. (Phila.), 1920, **18**, 263.

Experimental evidence is presented in support of the author's hypothesis that the long period of larval life of certain species of anurans (Rana catesbiana, for example) is due to the slow rate of thyroid development. Grafting the thyroid glands of advanced second-year tadpoles into small, immature first-year tadpoles produced rapid growth in the latter up to the stage of development shown by the animals from which the glands were obtained.—W. J. A.

(THYROID) A study of the distribution of iodine between cells and colloid in the thyroid gland. I. Methods and results of study of beef, sheep, and pig thyroid. Tatum (A. L.). J. Biol. Chem. (Balt.), 1920, **42**, 47-54.

When frozen section preparations of unfixed thyroid glands are floated in isotonic salt solutions the colloid separates out. Using this phenomenon as a basis of procedure Tatum prepared large amounts of sectioned material from relatively fresh glands and extracted with Ringer's solution and centrifuged. This was repeated and iodine determinations were made on the residual cell bodies, the whole glands and the extracts. There appeared to be a wide variation in the absolute amounts of the total iodine in the whole glands and cell masses. Nevertheless, the ratio of the percentage of iodine in the cells to the percentage of iodine in the whole gland was found to be a fairly constant value, and was considerably less than 40 per cent. From these results it is evident that iodine exists in both the cells and the colloid of beef, sheep and pig thyroid glands.—F. S. H.

(THYROID PARATHYROID) Tetanie-epilepsie. Tilling. Deutsche med. Wchnschr. (Berlin), 1920, **46**, 200.

There exists a close relationship between tetany and epilepsy. The author treated two cases with thyroidin (3 times daily with 1 gram) as indicated by Bolton and with parathyroidin (Freund and Redlich) without result.—J. K.

(THYROID) Diagnosis of Basedow's disease. Troell (A.). Hygiea (Stockholm), 1920, **82**, 33-45.

Goetsch's adrenalin diagnosis test was carried out on 6 Basedowians and 4 uncomplicated goiter cases with entirely satisfactory results.—J. A. H.

(THYROID HYPOPHYSIS OVARY) Remarks on the cure of various forms of headache and "faceache" by electrical methods. Hernaman-Johnson (F.), Practitioner (Lond.), 1919, **103**, 297-305.

As far as the ductless glands are concerned, the author refers to headache as a frequent symptom in exopthalmic goitre which disappears under suitable x-ray treatment. Disease of the pituitary gland may cause headache of a very terrible kind. A few cases, he says, are on record in which x-ray treatment of pituitary gland enlargement has produced benefit. He believes menstrual headaches to be due to ovarian hypersecretion and maintains that such headaches yield to x-ray treatment given with a view to reducing ovarian activity.

—H. L.

(THYROID) Changes in the larynx and trachea in benign goiter (Veränderung des Larynx und der Trachea bei gutartiger Struma). Wodak, Münch. med. Wchnschr. (Munich), 1919, **66**, 1365; Deutsche med. Wchnschr. (Berlin), 1919, **45**, 1400; Wien. klin. Wchnschr. (Vienna), 1920, **33**, 73.

In many cases of benign goiter there may be seen in the larynx and trachea changes of the nature of displacements, compression, distortions, catarrh of the mucous membranes and paralysis of the recurrent laryngeal nerve. The distortion is rarely described, but frequently occurs.—J. K.

(THYROID) A mentally deficient child with a protracted elevation of temperature. Wolf (G. D.), Med. Rec. (N. Y.), 1919, **96**, 880-883.

Report of a case presenting difficult problems of differential diagnosis, much improved by administration of thyroid.

—H. L.

THYROID and PARATHYROID tumors of the tongue. Wood (F. C.), Proc. N. York Path. Soc. (N. Y.), 1916, **16**, 84-89.

Wood describes briefly three cases of thyroid tissue masses occurring at the base of the tongue, in two of which were found small areas resembling parathyroid tissue. A brief reference is also made to other such cases reported in the literature.

These aberrant masses usually occur in the median line or near it at the base of the tongue. It is suggested that parathyroid tissue may in such cases as these arise from the second branchial pouches, as well as from the third and fourth, as normally.
I. M.

TISSUE EXTRACTS, Action of—upon coagulation of blood. Uchihara (K.), Taiwan Igakukai Zasshi, 1918, No. 182, 119-130.

The author isolated a globulin from extracts of different organs, and found that it accelerated the clotting of blood. He also isolated a nondialyzable albumin-like substance which hindered blood coagulation. This substance was always present in the same amount, while the amount of the globulin was variable. (Abstract in China Med. Jour.)—L. G. K.

(THYROID) Basedowism in a syphilitic family. Zeleneff (I. F.), Russk. J. Kozhn. i. Ven. Bolizen (Mosk.), 1916, **31**, 19-24.

In the cases studied Basedowism developed after infection with syphilis. Antisyphilitic treatment diminished the symptoms of Basedowism. Z. concludes, therefore, that the poison of syphilis has an etiological relationship to the symptoms of Basedowism.—S. H.

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ENDOCRINOLOGY

THE BULLETIN of the ASSOCIATION

for the STUDY of

INTERNAL SECRETIONS

OCTOBER-DECEMBER, 1920

EXPERIMENTAL RESEARCHES ON THE PITUITARY BODY

Diabetes Insipidus, Glycosuria and Those Dystrophies Considered as Hypophyseal in Origin*

Drs. J. Camus and G. Roussy

Professeur, agrégé, a la Faculté de Médicin de Paris

In recent years, notably before the War, we have carried out a series of researches on the pituitary body. These researches, undertaken without any preconceived idea, have furnished some results which have for the most part been published in various journals. It is of these results that we wish now to offer a succinct review.

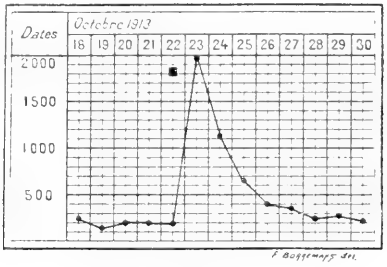
I. DIABETES INSIPIDUS AND THAT WHICH IS TERMED "HYPOPHYSEAL POLYURIA"

We must consider in succession the relation of polyuria to the removal of the pituitary body, the relation of polyuria to the lesions of the base of the brain, the site of the lesions which lead to polyuria, the interrelation of polyuria and polydipsia and the question of the regulation of water retention in the body.

1. *Polyuria and removal of the pituitary body.* In a very great number of hypophysectomies, partial or total, practised on the dog by the buccal-transpalato-sphenoidal route, we have

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

observed a marked polyuria. We were surprised at the outset of our researches at the copiousness of the polyuria. It even happened in the first two animals we operated upon that we could not measure the urine passed because we had placed under the cage receptacles of from only one to two litres and during the night these overflowed.



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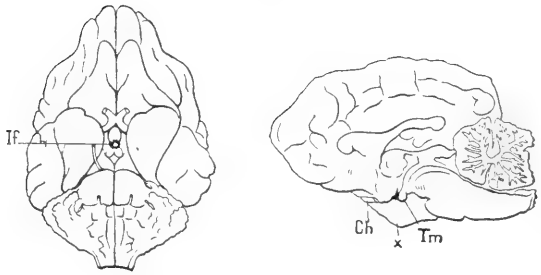


B C

Fig. 1. Female Dog Tigrette (weight 9 k.). Total extirpation of hypophysis Oct. 22, 1913, followed by profuse polyuria. Death, Dec. 26. Autopsy findings: Excoriation and dilation of the tuber at the border of the insertion of the stalk, the stalk itself has been removed; no trace of hypophysis in the sella turcica. On section a small fragment found in the cavity of the infundibulum at the right. The graph A shows the urine volume following operation on the 22nd; B, base of the brain showing infundibulum (If.) dilated; C, right hemisphere, inner surface; Ch, optic chiasma; T.m., mammillary body; X, lesion.

Thinking, at the commencement of our work, that the pituitary body was alone involved, we wished to begin by measuring the relative importance of the different parts of the organ in the production of the phenomena. But we were very rapidly brought to a realization that the key to the phenomenon is not to be found in an attenuation of the hypophyseal function. Contrary to the generally accepted view, these ablations—whether total or limited to one lobe—did not influence diuresis.

There follow, chosen from among the others, two examples which bring out this point. Of two hypophysectomized dogs there appears in the first (Tigrette) complete removal of the hypophysis resulting in a notable polyuria and in the second (Agrippine) a removal equally complete which does not give a trace of polyuria.

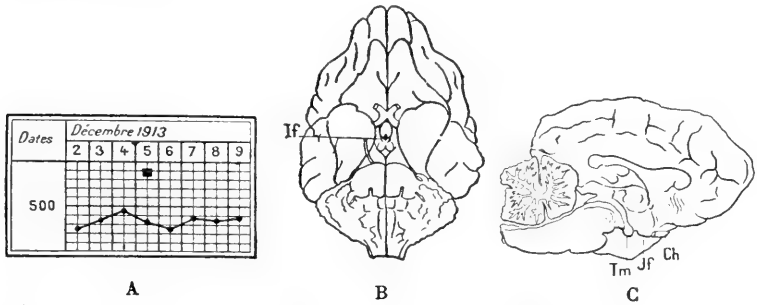


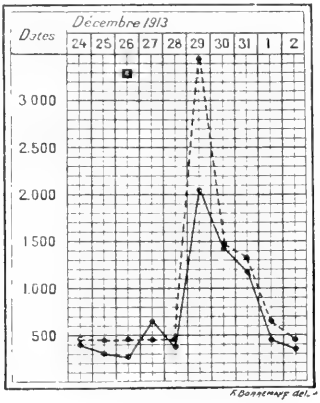
Fig. 2. Female Dog Agrippine (weight 7 k.). Total ablation of hypophysis Dec. 5, 1910. Polyuria followed. Animal killed Apr. 28. Autopsy showed stalk intact, infundibulum intact and not dilated, even constricted. Brain absolutely normal superficially at the base and upon median section. In the sella turcica no trace of hypophyseal tissue. Graph A shows the absence of polyuria; B, base of brain with infundibulum (If.) not altered; C, internal aspect showing integrity of the infundibulum (If.), of the chiasma (Ch.), and of the mammillary body (T.m.).

The autopsies showed that in the first case the base of the brain had been somewhat injured during the hypophysectomy, while in the second the brain was absolutely intact. This brings us to a consideration of our second question.

2. *Polyuria and lesions of the base of the brain.* Later, in evaluating the rôle played by lesions at that part of the base of the brain which borders on the pituitary body, we began injuring this region with a heated needle, meanwhile respecting the hypophysis itself. To do this we perforated the sphenoid with a gimlet. We have performed this operation successfully five times, each time with a very marked consequent polyuria—this despite an absolute lack of any change in the pituitary body, as shown at autopsy (Amilcar and Télémaque).

To exhibit the phenomenon even more evidently, we performed on each of two other dogs (Alexander and Annibal) two operations, separated by an interval of several weeks. In the first operation we removed the pituitary body, which ablation was followed by a passing polyuria. In the second operation, now that the pituitary could not be the cause, we injured the

base of the brain. A polyuria of equal intensity or even more marked than that after the first intervention, made its appearance.



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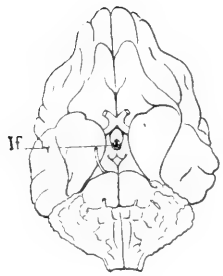

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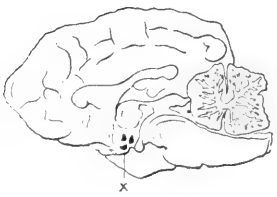

C

Fig. 3. Male Dog Amilcar (weight 11.2 k.). Puncture of the base of the brain Dec. 26, 1913. Following this, elevation of urinary output surpassing ingested water, which demonstrates that the polyuria is primary. Dec. 29, when the animal was allowed to drink as desired, there was noted a great polyuria and polydipsia. The dog was killed May 1. Autopsy showed infundibulum widely dilated and gaping. Upon median section small cicatrices of the former lesion seen in the infundibular cavity at the right. At the left the lesion is doubtful. The stalk is intact; the hypophysis is intact. In A solid line indicates urinary output; broken line, water ingestion. B, base of the brain with infundibulum (If.) dilated and altered. C, internal aspect of the right hemisphere with lesion showing at X.

In reality, as the autopsies showed, we injured the base of the brain in both operations—the first time involuntarily, the second time voluntarily.

The duration of this polyuria arising from a lesion of the base of the brain is variable—sometimes fleeting, at other times of a more permanent nature. We have seen it prolonged in one

dog more than 15 days (Attila); while in another it was extremely intense and lasted from the operation of October until May when the animal was killed (Moustachu). In this last dog we noted, for several hours after the puncture, a mild glycosuria, whereas the diabetes remained insipid for seven months. We believe that a diabetes equally marked and lasting has never previously been experimentally produced.

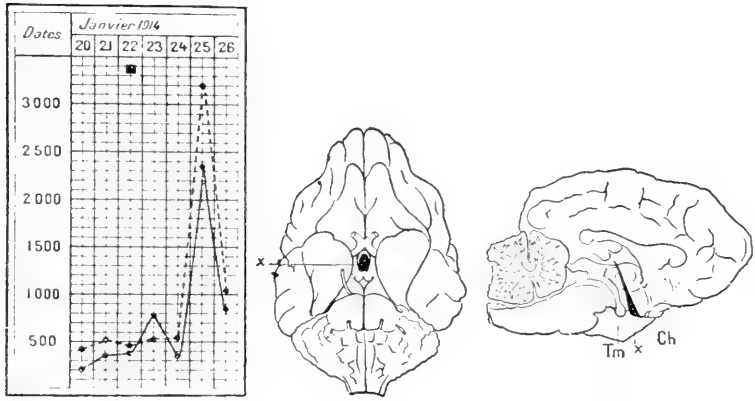

Fig. 4. Male Dog Télémaque (weight 11.7 k.). Puncture of the base of the brain on Jan. 22. Following this a marked elevation of the curve of urinary output is seen, which surpasses the quantity of water ingested (phenomenon identical with that observed in Fig. 3). Animal killed on May 5. Autopsy showed infundibulum gaping and altered. Within the brain substance a symmetrical lesion of the two hemispheres partially traversing the optic thalamus. Hypophysis and stalk intact. In graph A solid line indicates curve of urinary output; broken line, curve of water ingestion. B, lesion of the infundibulum at X. C, lesion X penetrating into the brain and passing between the chiasma (Ch) and the mammillary body (Tm.).

This experimental polyuria was not in the least modified in some animals on which, in the way of tentative therapeutics, we employed injections of pituitary extracts. We tried extracts of the posterior lobe, of the anterior lobe and of the whole gland —H. Carrion & Co. obligingly prepared these for us—and also the pituitrin of Parke, Davis & Co., all with no effect. These results gleaned entirely from our own animals do not confirm those of previous authors.

3. *Site of the cerebral lesions which determine polyuria.* A single glance over the figures we published allows a determination of what is important and what is accessory in the lesions that we produced. A comparative study of these figures, especially in conjunction with the urine charts, quite naturally forces

the conclusions of which we now make a résumé in a few paragraphs.

The lesion which determines polyuria in no way concerns the pituitary body. In five cases in which the experimental puncture has not touched the pituitary body, a consequent in-

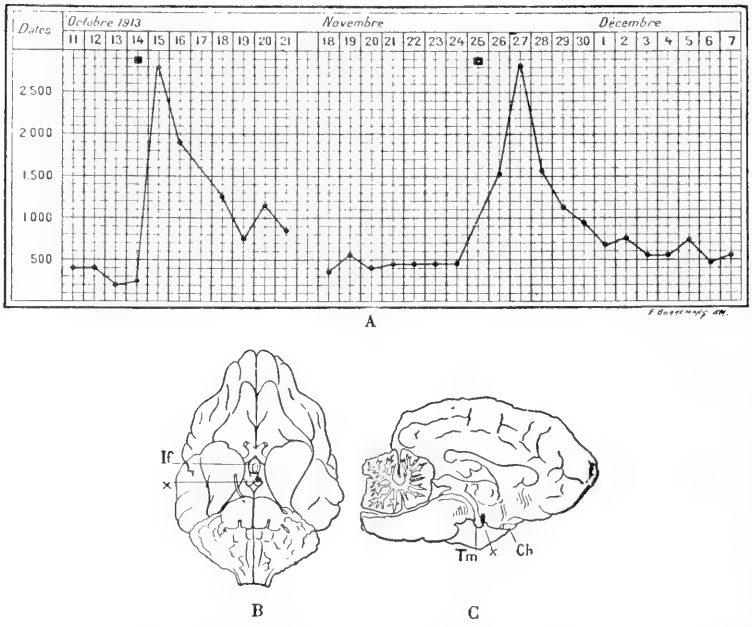

Fig. 5. Male dog Alexandre (weight 1.500 k.). Hypophysis extirpated Oct. 14, 1913, with resulting polyuria, as shown in graph A. On November 25 deep piqûre was followed by a longer lasting polyuria. The autopsy showed: infundibulum slightly dilated; posterior to this a lesion of the left mammillary tubercle independent of the infundibulum; upon median section a superficial lesion of the tuber penetrating 3 mm. and injuring the left mammillary body; in the right hemisphere a similar lesion but less discrete. In the sella turcica there remained a small fragment of the glandular lobe, verified microscopically. The graph A shows the curve of urinary output in the intervening days; B shows the base of the brain with the infundibulum (If.) dilated, and at X the lesion; C, the left hemisphere, showing at X the superficial lesion involving the mammillary tubercle (T.m.).

tense polyuria followed. The polyuria was neither more nor less marked when the pituitary body was involved in the lesion.

The total removal of the pituitary body, done without involving the base of the brain, does not result in polyuria (Agrippine). Nor does a previous ablation of the pituitary body hinder the production of polyuria if, in a second operation, the opto-peduncular region in injured (Alexander and Annibal).

As far as the production and the intensity of the polyuria is concerned, the depth of the puncture and the participation in it of the optic thalamus or of the peduncle seems quite without interest (Amilcar and Télémaque).

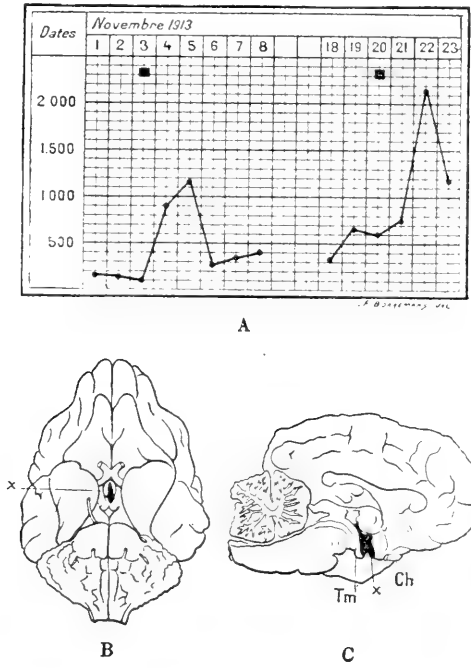

Fig. 6. Male dog Annibal (weight 11 k.). Extirpation of the hypophysis Nov. 3, 1913, followed by polyuria. November 20th deep piqûre was followed by a more marked polyuria. Autopsy revealed the disappearance of the stalk with no hypophyseal tissue in the sella; at the base of the brain the infundibulum gaping and greatly altered; upon median section a gross bilateral lesion extending in depth to the optic thalamus; chiasma intact; mammillary body altered at the left. The graph A shows the curve of urinary output; B, the lesion of the base is here somewhat extended (X); C, in the left hemisphere "X" shows the involvement posteriorly of the mammillary tubercle (T.m.).

The important fact is that a superficial lesion of the base of the brain, often involving only the surface and produced involuntarily in the removal of the pituitary body, is followed by polyuria.

In our animals it seems that the opto-peduncular region alone marks the zone within which a lesion is followed by polyuria. It lies at the level of the grey substance of the *tuber cinereum* in the vicinity of the infundibulum.

A lesion made in front of this zone at the level of the chiasm (Horace), or back of it at the level of the protuberance (Curiace), gives no polyuria.

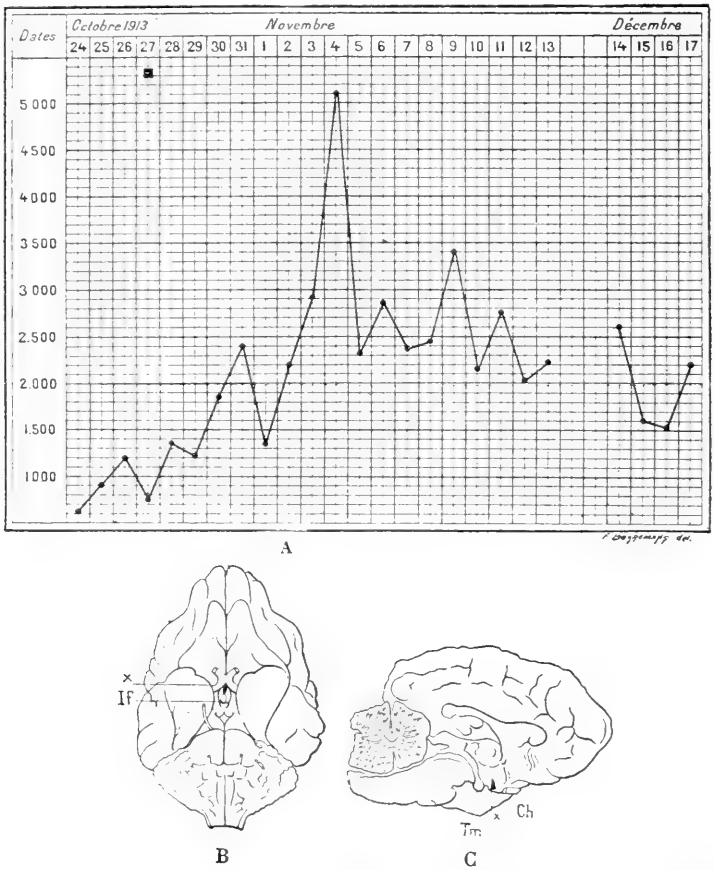

Fig. 7. Male dog Moustachu (weight 13 k.). Piqûre Oct. 27, 1913, and trephining of the sphenoid and penetration thereby of the hypophysis. A considerable degree of polyuria resulted and persisted for several weeks. Autopsy May 17 showed: infundibulum much dilated; anterior to the infundibulum and posterior to the chiasma a light colored nodule forming a projection; hypophysis small and atrophied (weight 0.20 grams); upon median section hemorrhagic linear scar (X) in the infundibular cavity. Graph A shows curve of urinary output; B, the lesion at the base of the brain at X; C, the dilated infundibulum (If.) and the lesion anterior to this at X.

4. *Correlation of polyuria and polydipsia. Regulation of the water retention in the body.* Along with the polyuria we observe, in the operated animals, a marked polydipsia. Is the polyuria primary or only secondary to the polydipsia? To an-

swer this question it is necessary only to put the animal on a constant water régime. That is, after the puncture in the opto-peduncular region we maintain for the animal a constant water intake.

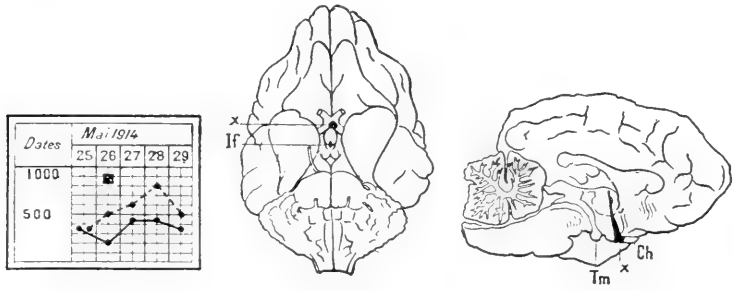

Fig. 8. Male dog Horace (weight 8 k.). A deep lesion made intentionally anterior to the hypophyseal region on May 26, with no polyuria following. Autopsy May 29: Hypophysis and stalk intact; lesion involving anteriorly the chiasma and penetrating to the anterior part of the left optic thalamus on both sides. In the graph A the solid line is the curve of urinary output, and the broken line the curve of water ingestion; B, base of brain showing normal infundibulum (If.) and at X the lesion involving the chiasma; in C lesion (X) is shown penetrating deeply.

This we have done with many dogs and we have seen the polyuria appear with no possibility of an increased water intake for the 24 hours. We even note an increase in the urine volume

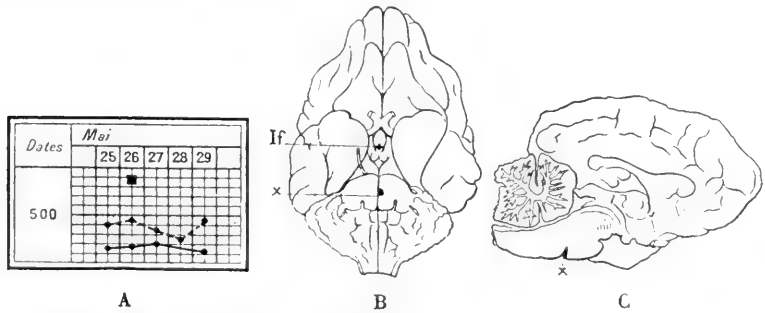

Fig. 9. Male dog Curiace (weight 8.5 k.). May 26 piqûre of the base of the brain made intentionally posterior to the hypophyseal region. No polyuria followed. Autopsy May 29: hypophysis and stalk intact; lésion posteriorly at the middle part of the protuberance and penetrating to the depth of 1 cm. In the graph A the solid line shows the curve of the urinary output, and the broken line the curve of water ingestion; B, the lesion shown at X in the protuberance; C shows superficial lesion at left.

to a point above that of the liquid intake. Under these conditions the water of the tissues diminishes and the phenomenon cannot persist for any length of time without some supplement

in the water given to the animal. If now we offer the animal water as he wishes, he repairs his losses and absorbs an enormous amount of water. Two of the dogs (Amilcar and Télé-

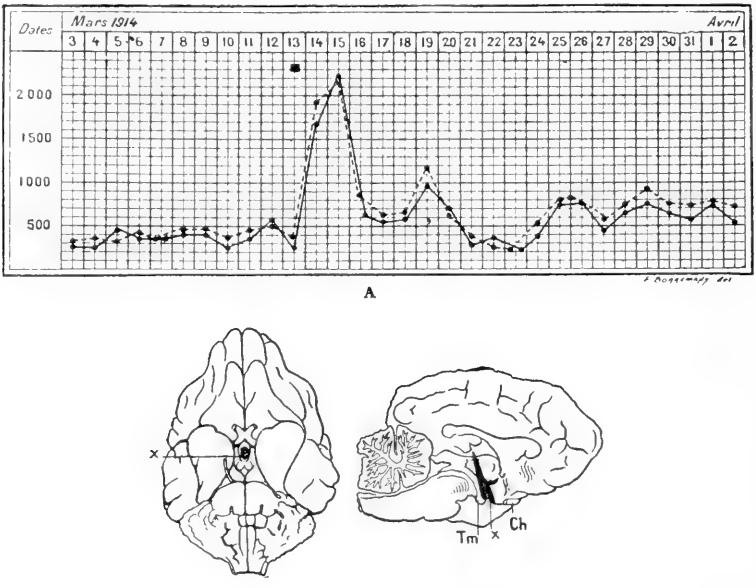

Fig. 10. Male dog Enée (weight 8.500 k.). March 13 experimental lesion in the optopeduncular region, followed by polyuria and considerable polydipsia but equal in degree, indicating no disturbance of water ingestion. The injection of glucose on the 7th and 23rd of March and of caffeine on March 25th gave insignificant result. Urea on the 11th had caused polyuria and on the 18th polydipsia also. Autopsy showed: Infundibulum dilated and altered; within the brain substance a large lesion involving posteriorly the optic thalamus at the left but extending to the right. The stalk is intact and the hypophysis definitely altered. In the graph A the solid line indicates the curve of urinary output and the broken line water ingested; B, lesion (X) of the infundibulum; C, lesion (X) penetrating deeply and involving posteriorly the mammillary body (T.m.).

maque) demonstrate these phenomena clearly—the polyuria following the puncture, then the polydipsia and marked polyuria. These facts allow us to consider that the polyuria is produced independently of the polydipsia.

When all of the animals have all the water they wish to drink, they do not react in identical fashion. Some repair exactly the water losses which the polyuria produces, others repair in excess, while still others repair insufficiently.

The dog Enée repairs her water losses perfectly; with her the regulation of water retention in the body is impeccable.

The dog Castor repairs in exaggerated fashion the losses of water which have been inflicted upon him. It seems that he drinks much more than he has need of, the urine volume being

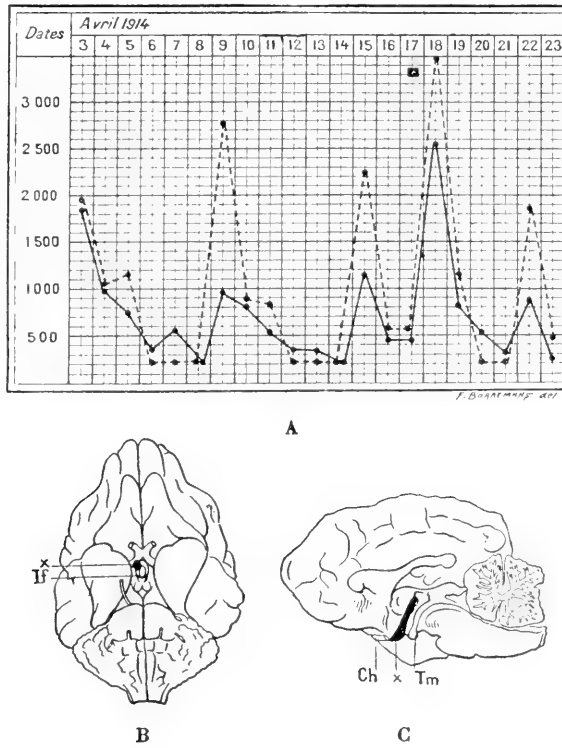

Fig. 11. A young male dog, Castor (weight 12.500 k.). April 17 experimental lesion in the opto-peduncular region, followed by polyuria and considerable polydipsia, but without parallelism, as in the case of Enée (indicating probably a slight disturbance of regulation connected with the youthful age of the animal). The first, second and fourth periods of augmentation of polydipsia were due to previous deprivation of water; the third was secondary to polyuria caused by cerebral piqûre. Piqûre Apr. 17, followed by considerable polyuria. Autopsy showed: infundibulum dilated; lesion anterior and to the right of this latter involving the optic tract; in the depths the large symmetrical lesion, more marked in the right, and reaching to the middle of the optic thalamus; stalk intact; hypophysis intact. In graph A the solid line indicates the output of urine, dotted line water ingested; B, base of the brain with infundibulum (If.) dilated and the lesion anteriorly at X; C, the lesion (X) in the right hemisphere.

secondarily increased. But this dog was still young and it is possible that in him the mechanism regulating the retention of water was functioning in some defective way. It is a classic notion that other mechanisms, other regulators of different func-

tions (circulatory, respiratory, thermic, etc.) comport themselves in imperfect fashion in young animals.

From this group of researches just summarized, there stand out the following conclusions:

(a) It is neither the injury to nor the removal of the pituitary body which leads to polyuria in the dog, but rather a superficial lesion of the base of the brain.

(b) This region corresponds to the opto-peduncular space. In the dog a lesion of this zone is followed by an abundant polyuria. The polyuria thus produced is much more marked and more lasting than that which can be produced in any other way—as by the injection of urea, glucose, caffeine or chloride of sodium or by preliminary water deprivation.

(c) This zone seems to play some part in the mechanism of the regulation of water retention in the organism. Lesions of this region—mayhap in accordance with their extent—are followed by a polyuria either with a parallel polydypsia which means, of course, that there is no trouble with the regulation, or by a polyuria without a consequent polydipsia, which is to say *with* disturbance of the regulator mechanism. Thus as to the production of polyuria we arrive at results sensibly the same as those we obtained in the study of glycosuria and the trophic genital troubles. Many authors have ascribed these phenomena directly to lesions of the pituitary body.

II. HYPOPHYSECTOMY AND GENITAL ATROPHY.

During some experimental researches on the pituitary body we observed, quite as a side issue, trophic troubles of the genital organs.

Our experience was gained from five dogs.

The first dog (Ecureuil), which had suffered a partial removal of the pituitary body, presented neither any modifications in growth, nor any genital atrophy. The second dog (Flick), after total or almost total removal of the pituitary body, has grown enormously—his weight almost doubling—but his genital organs are normal and function normally.

The third dog (Negro), after total or almost total removal of the pituitary body, appears to comport himself normally as far as concerns his development and genital organs.

The fourth dog (Narcisse), after partial removal of the pituitary body and extensive cauterization of the parahypophyseal region, has presented some modifications of the hind quarters and of the extremeties of the limbs with very marked genital atrophy. Obesity did not appear.

Finally in the fifth dog (Moustachu), which did not suffer a removal of the pituitary body but only a deep lesion of the surrounding region, marked polyuria and testicular atrophy developed almost immediately.

Of these five animals only the last two have presented any trophic troubles of the genital apparatus. In the fourth dog (Narcisse) we cauterized the region of the pituitary body and almost certainly we must have injured the neighboring parts since the animal developed difficulty in coördination and equilibration, symptoms which this dog alone, of all the great number we have worked with, showed. In the fifth dog (Moustachu) we purposely made a lesion of the base of the brain.

These experimental facts allow us to conclude that in the incidence of atrophy of the genital organs we are dealing rather less with any hypophyseal lesion than with trouble at some point in the base of the brain, the exact site of which remains yet to be determined with more precise methods.

As far as the obesity is concerned, it seems that it is not necessarily dependent upon the existence of genital atrophy and, moreover, that it is possible to see a breaking up of the "adiposo-genital syndrome." In this regard it is fair to question whether the adiposo-genital syndrome may not be due to lesions of separate centers—often affected coincidentally but not necessarily by the same process.

III. THE GLYCOSURIA OF HYPOPHYSEAL ORIGIN.

Our experimental researches on hypophyseal glycosuria may be separated under two heads: (1) those dealing with a spontaneous glycosuria consecutive to an operation on the pituitary body, and (2) those which deal with the tolerance of the operated animals for carbohydrates.

1. *Glycosuria observed after an operation on the pituitary body and the adjoining part of the base of the brain.* These researches on the glycosuria appearing spontaneously after opera-

tions on the pituitary body and the bordering region, included 45 dogs and 9 cats. In the 45 dogs, glycosuria was observed but 6 times. That is, in 39 cases the result, so far as the presence of sugar in the urine is concerned, has been negative.

We may make further subdivisions in these 39 cases. In 30 of the animals we have not produced any lesions of the base of the brain. In 14 of these 30, the ablation of the pituitary body seemed to us to be entire. It seems useless to discuss here the question of total removal, histologically speaking, and of remnant adherent hypophyseal tissue. At another time we will come back to this point. The only essential matter, as far as the glycosuria is concerned, is a profound blow to the pituitary body and, particularly, the removal of a fair share of the pars nervosa. Thus, we repeat, in 14 of our animals the removal seemed to us to be complete. In the 15 others the removal has been partial—often very considerable—and, for the most part of the cases, especially involving the pars nervosa.

In all these cases, let us repeat, we have not observed any glycosuria after the operation.

In 9 other dogs we have made, voluntarily or involuntarily, a more or less extended lesion of the tuber and of that region of the base of the brain bordering on the pituitary body.

In these 9 cases, 3 times (once partially and twice totally) the pituitary body was removed at the same time that we injured the base of the brain. In the 6 other cases, the base of the brain was wilfully injured, leaving the pituitary body untouched. In these 9 animals we did not observe any glycosuria.

The dogs which furnished these 39 negative cases represent every category. There were adult or aged dogs, dogs but a few weeks old and dogs in gestation. The phenomenon was thus not influenced by the animal's age, sex or physiological state of gestation.

This brings us to the 6 cases in which we have observed positive results. We may subdivide these as follows:

One time we were dealing with the apparently complete removal of the pituitary body in a dog in gestation. This dog has not as yet been killed and we do not know what the state of the brain is.

Twice the brain was manifestly badly injured.

Once we had cauterized the hypophysis and the neighboring cerebral region.

Once we cauterized the hypophysis with a red hot iron and it can scarcely be doubted that the adjoining regions were involved in this energetic procedure.

Once, finally, the removal seemed complete and the autopsy disclosed no lesion of the brain. In this case, however, the glycosuria was inconsequential.

How does the glycosuria show itself in these positive cases?

It appeared rapidly following the operative shock. It was always *light* and *fugacious*, disappearing in from less than 24 to 36 hours after the operation. It appeared quite independently of the polyuria which was often marked even without this glycosuria, as we have cited in numerous cases (Cf. Bull. Société de Biologie). The character of the food consumed prior to the operation seems to have had no influence on the appearance of the glycosuria.

Remember that of the 6 positive results in the 45 operations on dogs, *at least 4* showed lesions of the base of the brain.

In the cat after 4 out of 9 partial ablations of the pituitary body, glycosuria occurred—suddenly appearing and disappearing. Under our experimental conditions the glycosuria seems to be more easily attained in the cat than in the dog, but as yet we are unable to state any fixed rule as to its mode of production.

2. *Tolerance to carbohydrates on the part of animals deprived of the pituitary body—alimentary glycosuria.* We have given glucose, through an oesophageal tube, to some dogs totally or in part deprived of the pituitary body.

We determined the quantity of glucose which just produces glycosuria. Then, administering a slightly smaller amount of the substance, we injected into the animal an extract from the pituitary body (the posterior lobe, the total gland or only the anterior lobe). Thus, if we had found that 90 grams just gave a glycosuria, we administered 80 or 85 grams, injecting at the same time the hypophyseal extract.

Conclusions: a. The different interventions practiced on the pituitary body—partial removals of one or both lobes

or total removal—modify in appreciable fashion neither the tolerance to carbohydrates nor the appearance of alimentary glycosuria.

b. The injections of concentrated extracts of the posterior lobe, the anterior lobe or of the whole hypophysis, do not sensibly modify—in the animals operated on—the limit of tolerance to carbohydrates.

THE RELATION OF THE THYROID AND OF THE ADRENALS TO THE ELECTRIC CONDUCTIVITY OF OTHER TISSUES *

G. W. Crile, M.D., Cleveland, Ohio

The Thyroid—Osterhout has shown that iodin increases the electric conductivity of living vegetable tissue. In our laboratory in a research undertaken in collaboration with Miss

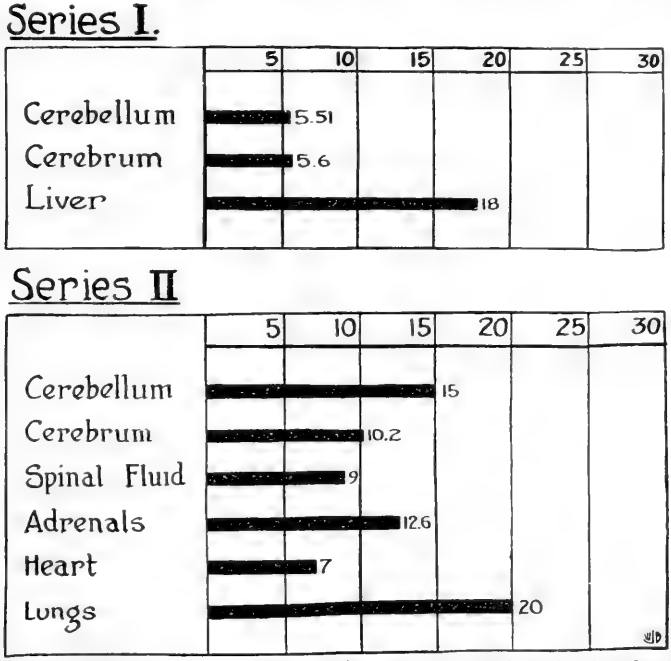

Fig. 1—Relative Percentile Increase in the Electric Conductivity of Various Organs and Tissues Produced by Iodoform averages from two series of observations.

Helen R. Hosmer and Miss Amy F. Rowland, we have found that the electric conductivity of the brain, the liver, the spinal fluid, the heart and the lungs, is increased in iodism produced by the injection of idoform into the peritoneal cavity (Fig. 1). A limited number of observations indicated that an

* Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

increased conductivity of the brain and the liver is an early effect of thyroid feeding. In exhaustion produced by thyroid feeding for prolonged periods the conductivity of the brain is decreased as in exhaustion from other causes.

The relation of the increased electric conductivity produced by iodin to the function of the thyroid gland becomes apparent when we consider that, as far as is known, the only function of the thyroid gland is to metabolize, to store, and to deliver iodin; and that the excessive administration of iodin will produce symptoms identical with those produced by abnormal amounts of thyreo-iodin manufactured by the thyroid gland. A limited number of observations indicate that excessive iodin and excessive thyroid activity alike produce increased sensitivity to adrenalin, increased metabolism, increased respiration, tachycardia, elevated temperature, with ultimate emaciation, delirium and death.

Iodin is an essential element in the normal functioning of the organism. Iodin is found only in traces in other tissues and organs of the body outside the thyroid. It is the function of the thyroid gland alone and it is the only proven function of the thyroid gland to take in iodin from the blood, to manufacture it into the compound in which it will be of the greatest use to the organism and to give it to the circulation as called for by the needs of the organism.

The normal activities of life in the normal individual are made possible by the amounts of iodin received from the thyroid. Abnormal amounts of iodin increase the activity of the organism as a whole. In the light of our experiments this increase may be interpreted as due, in part if not wholly, to the effect of iodin upon electric conductivity.

Exophthalmic goiter patients tolerate iodin poorly. If too much iodin or thyroid extract be given to a patient with simple goiter, exophthalmic goiter may be induced. Such cases are identical with exophthalmic goiter induced by any other cause.

On the other hand, if the thyroid gland does not metabolize sufficient iodin to meet the need of the organism there results a condition of subnormal metabolism in which the individual is dull, stupid, and more or less in a state of torpor.

The Adrenals—Our electric conductivity researches have shown that a single dose of adrenalin immediately increases the

conductivity of the brain. The administration of an excessive amount of adrenalin causes a decreased electric conductivity of the brain (Fig. 2). This action of adrenalin is probably due to its influence upon oxidation.

The immediate activating effect of adrenalin is most strikingly demonstrated in the reaction to the Goetsch test in cases of exophthalmic goiter.

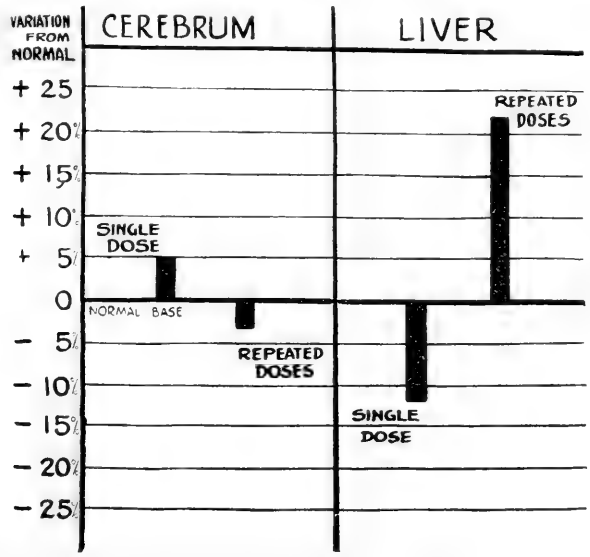

Fig. 2—Percentile Changes in Electric Conductivity Immediately After the Injection of Adrenalin and After Repeated Injections (Note Antithetic Effects on Brain and Liver).

If we accept the view of physicists and bio-chemists—notably DuBois-Reymond, Nernst, Bethe, Lillie, McClendon, Mathews, Osterhout, Loeb, Crehore and Williams, Ostwald, A. V. Hill, etc., that the functions of the cells of the organism relate to electrical processes, it would appear that the fabrication of electric energy within the brain cells is immediately due to oxidation; that oxidation in turn is facilitated by adrenalin; and that the passage of the electricity through the tissues is facilitated by thyreo-iodin.

The interaction of these two agents within the organism may be best demonstrated by a consideration of their relation to exophthalmic goiter .

The Thyroid and the Adrenals in Their Relation to Exophthalmic Goiter—Iodin increases the electric conductance of living tissue; increased electric conductivity is probably synonomous with increased permeability; increased permeability increases function.

According to Ashoff and Cannon stimulation of the nerve supply of the thyroid causes a discharge of thyreo-iodin; hence, we may suppose that the output of iodin is in part, at least, under the control of the nervous system. In exophthalmic goiter there is marked nervous activity, and we may suppose that the thyroid is under active stimulation. That this is the case is shown by the low iodin content of the gland in exophthalmic goiter. According to Cannon and others adrenalin activates the thyroid. We assume that the stimulated thyroid throws out large amounts of activating thyreo-iodin, which by so much facilitates permeability, hence increases activity of the body, including the activity of the thyroid itself and of the adrenals. Oxidation is the basic process in metabolism; adrenalin increases oxidation; iodin increases electric conductance, hence increases metabolism.

Therefore, through the mediation of the nervous system, a reciprocal interaction is established among the thyroid, the adrenals, and the nervous system. Iodin alone, adrenalin alone, thyroid extract alone, emotion, exertion, or infection alone, each causes a "Kinetic Drive" with phenomena similar to those of exophthalmic goiter.

If the foregoing interpretation be correct, then the drive of exophthalmic goiter should be diminished by lessening the activity of any of the three interacting organs—of the brain, by rest cure; of the thyroid, by its resection; of the adrenals, by their partial removal. Although evidence of the positive value of the last-named procedure is thus far incomplete, nothing in surgery is more striking than the immediate benefit of the surgical treatment of exophthalmic goiter.

It is of interest to note that the active principle of the thyroid secretion has been synthetically produced by Kendall; adrenalin is synthetically made and the generation of electric energy is a commonplace; hence, the equivalents of the activators of exophthalmic goiter, of emotion, of exertion, and of fever may be made in the laboratory.

SECONDARY SEXUAL CHARACTERISTICS AND ENDOCRINOLOGY

A. Pézard

(From the Laboratory of General Biology, Collége de France, Paris)

INTRODUCTION

The question as to the physiological conditions determining the secondary sexual characteristics has been for twenty years the subject of numerous and important researches. Not only do these characteristics form in themselves an imposing array, morphologic, physiologic and psychic, but it was early discovered that their relations, one to another, are particularly close. From the point of view of general biology the problem perhaps presents a more suggestive aspect: the characters in question which appear at the time of puberty and serve to give the animal its distinctive attributes, male or female, are more or less superadded or supplementary and can, better than any others, be eliminated without endangering the life of the subject. Their evolution and their suppression are quite accessible to scientific investigation; their study promises not only to afford specific data but also to throw a light on the general problem of morphogenesis. If, finally, it is considered that in certain species the secondary sexual characteristics are utilized for the determination of the race, it is seen that the problem, transcending its immediate interest, may lead us to the mechanism of the evolution of species. Such are the ideas which have inspired the present article. It is proposed to discuss the endocrine role of the testes of fowls and the deductions which may be derived.

I. HARMOZONE AND GROWTH

Secondary Sex Characteristics. It will at once be recognized that cocks afford particularly favorable material for such studies. Their secondary characteristics appear in great variety and in adults are easily perceptible grossly. Among such features are the great development of the comb, wattles and auricular appendages which, at puberty acquire a well-known redness; the ruffle of supple, tapering plumes about the neck *(camail)* and across the back *(lancettes);* the long and recurved caudal

plumes, large and small; spurs at the bases of the metatasals; —such are the morphologic criteria.

On the psychic side the array is not less varied: the strongly developed sex impulse leads to ardent regard toward the female and querulous intolerance toward male rivals; by lusty crowing and spirited strutting the emotions are given vent and victories announced.

Since these characteristics appear sharply at the time of puberty,—i. e., with the development of the testes,—biologists have not hesitated to postulate their dependence upon the sex glands. Castration experiments and the necessary control experiments, however, have failed wholly to justify such a generalization. It is true that if the genital glands are extirpated in young cocks the comb and wattles remain small, pale and rather bloodless; neither the amorous nor the combatative instincts appear and our animal maintains a demure silence. But on the other hand the spurs elongate in the absence of the gonads. As we have shown, they grow as rapidly as in the intact animal (1). There is no demonstrable relation between their development and the internal secretion of the male glands. Nor in the matter of plumage have we been able to establish any relation, either in the common variety of fowls which is raised about Paris or the Faverolles and Dorking races. It is true that Morgan, operating upon Seabright cocks (2), obtained an unexpected result,—the development of a magnificent male plumage of which the animals are normally destitute. This is an important fact to which we shall revert. In every case it is possible to recognize an influence of the testes upon only the erectile organs, the sex instinct and the voice. Every control experiment has remarkably verified this point of view. The most decisive, in the opinion of the writer, consists in ovariotomy of pullets, which has been carried out simultaneously by Goodale (3) and by me (4, 5). Deprived of the sex glands the young fowl rather soon undergoes a transformation and acquires the plumage and the spurs of the cock. The metamorphosis is definitive. Hens without ovaries, which have been kept for several years, have with each moult retained the male type of plumage, while their spurs have reached a cumbersome length (9cm.).

That the testes mediate their influence through internal secretion is demonstrated by two sorts of facts: (1) the characteristics abolished by castration reappear if one transplants into the peritoneum thin fragments of testes (Berthold, Foges, Pézard); (2) the same result is obtained by periodical injections of testicular extracts (Loewy, Pézard). We have personally employed in such experiments extracts from the glands of cryptochidic hogs which, it is claimed, are reduced to interstitial tissue only. Since, with several repetitions of the experiment, concordant results have been obtained, we must conclude that the testes elaborate an internal secretion with morphogenic role (harmozone-Gley) and that this harmozone possesses a physiologic specificity.

(*a*) *Law of Continuity.* These preliminaries having been established we reach now the vital part of the subject. In a remarkable report in 1913 Gley (6-p. 57) formulated a problem relative to the internal secretions in which endocrinologists have not failed to become much interested. "If one now considers but a single part of the developmental mechanism (the action of the internal secretion on development) it can be no better explained than by the idea that this development is arrested of itself at a given moment. Is it to be supposed that the interstitial tissue of the testicle—or similarly, any other organ, diminishes its functioning, reduces, for example, the amount of active substance which it sends to the organs on which it works? *But there is no proof that such functional diminution occurs,* and, moreover, these substances act in very minute doses, hence it is the absolute suppression of their functioning that would have to be supposed. The problem is pending."

Our experiments in post-pubertal castration allow the settling of the debate and the demonstration of the judiciousness of the reservations formulated by Gley.

If it is a fact that the endocrine function of the testicle stops at the moment when the secondary sexual characteristics, which are conditioned by its activity, have reached their complete development, the extirpation of the genital glands ought to be from this time on without effect on the animal.

Now that is not what occurs. If we castrate an adult cock at full sexual maturity, a few days later the sexual instinct and

the crowing definitely disappear. The erectile organs begin an immediate regression: they diminish in volume, grow pale, and finally acquire the reduced dimensions of the homologous organs of castrates. From the periodical measurements of the comb we have determined that the regression occurs with remarkable regularity, though this does not mean that the rapidity is constant. On the other hand, sections made of the erectile tissue show that the structure of this tissue has not been visibly affected, therefore the phenomenon should be imputed to a real regression.

We have carried out our experiments on cocks of different ages and have obtained the same results. Always, the regression of the comb is effected according to the same rhythm, going from the initial constant stage (sexual comb) to the final equally constant stage (capon's comb).

All these facts show clearly that the testicular function is constantly necessary for the maintenance of the erectile organs and the sexual instinct. Gley reasons correctly when he states that there is no proof of functional diminution. We can even say, in view of the uniformity of the results, that the testicular harmozone exercises a *sustaining action that is always equal.* It is true that the duration of the experimental regression of the comb is slightly increased with age, but we are tempted to see the explanation for this, not in the harmozone itself, but in a conditional property of the tissue.

We can further affirm that the internal secretion of the testicle disappears immediately after castration; that is to say, it does not outlast the ablation of the genital glands,—its action is *immediate.*

This was indicated by the manner of the beginning of the regression. We will state forthwith that all harmozonal persistence, after castration, would have as its result a more or less continued persistence of the characters it influences. Now what do we find? The regression of the comb immediately follows castration: the regression is maximum for the first few days at its beginning, a fact which is shown on the charts by a sharp fall in the curve. Thereafter the regression is retarded and, finally, the curve becomes horizontal. The regression is then at an end. Now the sharpness of the decline as established for

the beginning of the phenomenon is incompatible with the persistence of the harmozone. It must then be admitted that the harmozone is effectually destroyed in the blood. Moreover, we have established that for the injections of testicular extract to be efficacious they must be repeated very often, which indicates still further, a rapid destruction of the active product.

I conclude: The continuity of the endocrine function of the testicle is an indispensable condition for the maintenance of the conditioned characters. The morphogenic action of the testicle presents in addition a remarkable constancy which is dissembled by the arrest of growth in the adult.

It may be remarked in passing that the acquisition of these suggestive ideas is the consequence of two particularly favorable experimental conditions in our studies: on the one hand the possibility of measuring the comb, which permits a continuous cinematic study, and on the other hand the reversibility in the growth of that organ which makes significant the counter-proofs.

(b) Law of Minimum Efficacy. Observation shows that the glands of internal secretion are more than sufficient to assure the role that has devolved upon them. All biologists know that an insignificant fragment of the adrenal or thyroid preserves the animal from the consequences resulting from the complete extirpation of these glands. There is a luxus endocrine secretion, as there are digestive secretions in excess, as there is a margin of safety in respiration (6-p. 50). Is this so in the case of the testicle?

Two types of facts permit an affirmative answer: the frequently unsuccessful attempts at castration of cocks and the systematic experiments in testicular transplants. Minute fragments of testicles scattered in the peritoneum, far from the normal locus of the gland suffice to activate the development of true male characters and to assure their maintenance: such is the usual result.

In view of this effect, we have attempted to determine the mass of testicular substance below which the tissue is incapable of exerting its function. But apropos this subject a preliminary remark is necessary concerning the structure of the testicular nodules. These structures are highly variable and we classify them into three categories: (a) nodules having con-

served, even a year after castration, the normal aspect of the cock's testicle, seminal canals containing spermatids with almost no interstitial tissue; (b) nodules presenting the seminal canals degenerated and reduced to a few Sertolian nuclei scattered in an extremely vacuolated cytoplasm with interstitial tissue more abundant; (c) completely necrosed nodules, comprising degenerated seminal canals replaced by connective tissue in which interstitial cells are rare. The first two types alone are efficacious and it is with them alone that one can make weight comparisons.

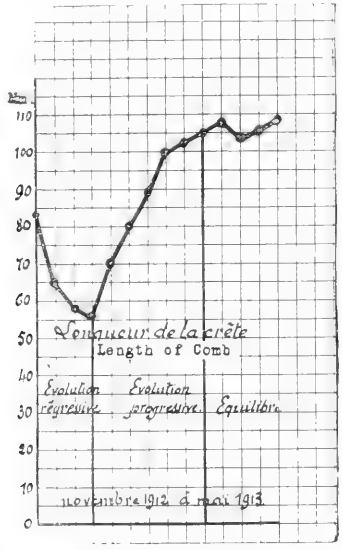

Fig. 1. Graph showing the changes in the length of the comb of a cock succeeding castration. A regressive stage is followed by a progressive stage and final equilibrium.

On the other hand an elementary precaution is imposed relative to the appreciation of the secondary sexual characteristics of a subject. *An isolated observation means nothing.* In order to judge of the state of these characters, a long continued cinematic study is necessary. For example, in fig. 1 are presented the data regarding a cock which we had castrated in November, 1912 and which had received at the same time some ovarian fragments from a hen. For a month the comb diminished, going from 84 mm. to 56 mm.; then suddenly the growth of the comb again commenced and from December to April the length increased

from 56 mm. to 108 mm. At autopsy we found a testicular nodule weighing 1.5 gm. An isolated observation would have made us consider the animal in December a castrate, in February an incomplete castrate, and in May a normal animal. So the characters should not be appraised until they have attained an equilibrium.

Neglecting this precaution, Foges (7), in a memoir relative to testicular transplantations in cocks, has reported results the interpretation of which is open to question. During the course of his study, carried out on 33 animals, he made but a single measurement the data of which, according to our mind, lead to a false conclusion. The data may be quoted:

	Comb		Wattles		Spurs
	Height	Base	Height	Base	Length
Control-cock	8	12	5½	2	2
Capon No. 1	4	8	2½	2	½

From this Foges concludes that in cock No. 1, which possessed two testicular nodules, the growth of the comb, wattles, and spurs, is diminished. And yet he has earlier admitted that in capons "the spurs can exist just as in the hens." In reality, animal No. 1 is probably a castrate the spurs of which have developed tardily.

Having made these reservations with regard to methods, we will again turn to the question of the transplant-bearing cock. In subjects presenting *characters in equilibrium* and with *functionating nodules,* we determine at autopsy the total mass of the fragments. We have found that these subjects can be divided into two groups: those that possess more than 0.5 gm. of testicular substance have the aspect of normal males; those that have less than 0.5 gm. are essentially castrates. The mean weight of the testicles being 15 gm. it is evident that the endocrine function of the testicle is assured when 1/30 of the normal gland weight is present. *The testicle does not deviate from the law of luxus secretion.*

(*c*) *All-or-none Law.* We are naturally led to an examination of the correlation that may exist between the mass of testicular parenchyma and the quantitative development of the conditioned characters, a correlation that is particularly interesting as we approach the minimal effective limit. If we consider the figures relative to those of our subjects the characters of which were in equilibrium, and to make the matter more clear, if we

arrange them in the order of diminishing size of the testicle and compare the weight of the seminal parenchyma in grams with the length of the comb in millimeters, we can establish a curve as shown in figure 2. The ordinates correspond to the succession of animals as in the table and the abcissae to the weight of the testes and length of the comb.

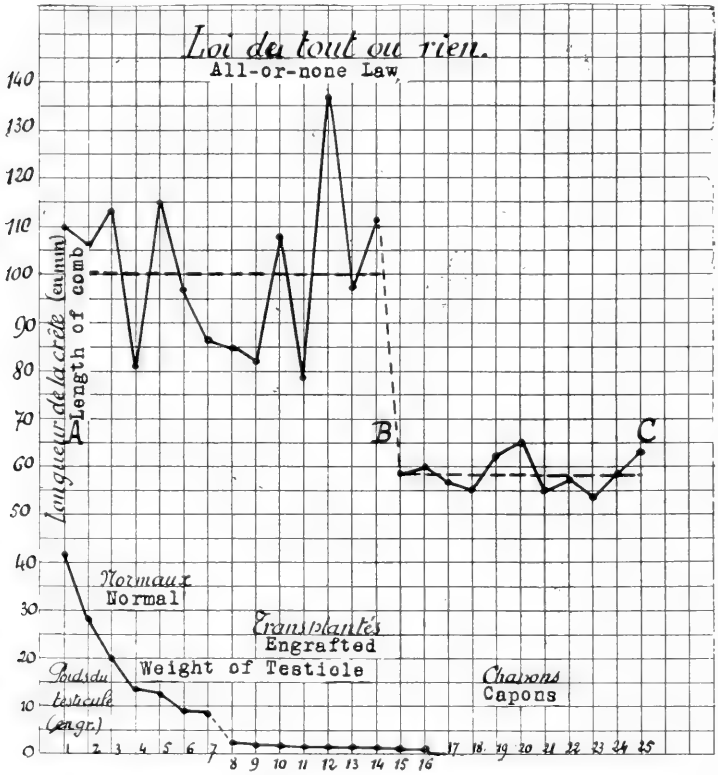

Fig. 2. Graph showing the length of comb as related to the weight of testicular tissue present in 25 cocks.

No.	Wt. Test.	L. Comb	No.	Wt. Test.	L. Comb	No.	Wt. Test.	L. Comb
1	42	110	9	1.5	82	17	0	56
2	28	106	10	1.5	40	18	0	55
3	20	113	11	1.0	78	19	0	62
4	14	81	12	1.0	137	20	0	65
5	12.5	115	13	0.7	97	21	0	55
6	9	97	14	0.5	111	22	0	57
7	8.3	86	15	0.1	59	23	0	54
8	2	85	16	0.1	60	24	0	58
						25	0	63

An examination of the chart shows clearly that there is no parallelism between the testicular weight and length of comb. In the part A-B of the curve which pertains to the cocks showing male characteristics, the curve is very high and presents variations; but these vary from one side to the other with a mean value of 100; they do not correspond to the variations of the morphogenic power of the testicles, but to racial characteristics, and are the result of the fact that the cocks to which they pertain are of different races. The part B-C of the curve which corresponds to the so-called neutral cocks, also shows variability but relatively less marked. Without doubt the variability again is to be ascribed to difference of races. The subjects fall in series with those of the region A-B and consequently are comparable with them; the mean of the second part of the tracing is 58.

At the point B the least efficacy is found; the curve here undergoes a sudden drop, passing from the level A-B to the level B-C. This turn of the curve and its obvious *discontinuity* seem to us, better than any reasoning, to show that the morphogenic effect of the testicle follows an *all-or-none law.* That is to say, *as soon as the functional threshold value is passed, whatever may be the mass of the active gland, a cock takes on as a whole its secondary sexual characteristics.* It appears that these manifestations can not be fractionated.

It would be interesting to determine if the moment these characters are started in their development in the cock is exactly that point when the testicle has attained this minimal weight of 0.5 gm. In this case the morphogenic action of the testicle would be at the beginning and throughout the sexual life a constant which directs the conditioned processes. There would result a great simplification in the study of the growth of the comb. Further researches should decide the question.

The all-or-none law carries another implication of general significance in relation to the factors operative in all conditioned growth. When one studies the morphology of the testicle of a cock, a uniformity of structure is found throughout the whole extent of the gland; moreover, this is maintained throughout the first years of life, from the third month on. Since the testicle is richly vascular, the conclusion is justified that the amount of the active harmozone thrown into the blood is proportional to the

amount of active parenchyma,—that is to say, in short, to the total weight of the gland (with the exception of the albuginous matter). If this harmozone actually constituted merely a substance promoting unrestricted growth, there is no reason to believe that the law of mass action would not obtain. The two curves in figure 2 would have the same trend, which is not the case. The observations cannot be interpreted unless one admits on the part of the harmozone a *stimulative action* upon a tissue the growth capacity of which is limited. This growth capacity which is a property of the conditioned organ represents, in these circumstances, the influential factor.

HARMOZONE AND EVOLUTION

(*a*) *The Sebright Breed.* In 1918 we wrote: "The theories of evolution presuppose the occurrence of progressive organic modifications which effect the transformation of the animal species through growth or atrophy of the organs. The environmental influence, the manner of living, the habits, constitute, outside of sexual reproduction, the possible causes of individual variations. One may well ask if the action of these different factors has no influence on the harmozones, the directors of the morphogenic processes. In fact an equilibrium can not be modified if something has not disturbed the cause operative in its maintenance; on the other hand, every cause acting on an endocrine gland is profoundly echoed throughout the entire organism."

This point of view has received confirmation through two observations as exact as they were unexpected. The first is related to the Sebright cocks, so well studied by Morgan.

Considered as very close to the original ancestral strain of the *Gallus domesticus* the Sebright variety differs from ordinary cocks by the racial characters selected from the secondary sexual attributes; they have neither hoods nor lancets; the recurved plumes hardly extend beyond the straight feathers of the tail. In fact so lacking are they in these male attributes that their plumage resembles more that of a hen. The wattles and the comb, however, are always of the characteristic male type. Now it is a curious thing that if a Sebright cock is castrated, there develops a rich male plumage, as has been shown by Morgan; hoods, lancets, and the curved caudal plumes elongate measureably; the animal loses its racial peculiarities and follows the

common law. It should be noted that in this circumstance the testicle, far from conditioning the male plumage, as has been previously considered, seems, on the contrary, to exert an inhibiting action similar to that of the ovary.

In the absence of histological studies of the testicles of the Sebright cock, in order to explain the plumage characters, we have thought of a state of false equilibrium, a condition which would be supplanted by castration or by a violent traumatism (1-p. 143). New studies advanced by Boring and Morgan (8) prevent us from attributing the cause of the anomaly to a somatic property of the cocks, and oblige anew a return to the conception of a conditioning by harmozone activity. In fact, on examining the structure of the testicles of the Sebright cocks, Boring and Morgan found a special type of cell which is not found in the testicles of other cocks. They are large elements with well defined margins, clear cytoplasm, nucleus more or less spherical, and forming more or less well defined islets in the interstitial tissue. Near them masses of yellow pigment were observed which suggested for the elements in question the name of luetin cells. Now the lutein cells are a normal part of the ovary of the hen (Boring and Pearl); we have described similar structures in the ovaries of the silver pheasant, *Euplocomus nycthemerus* (1-p. 116). Since these interstitial cells in the female ovary prevent the development of the male plumage, we believe with Morgan that the same is the case with the Sebright cocks. This now explains the assumption of the male plumage after castration.

It is certain that the special characters of the plumage of the Sebright cocks give to these animals an apearance such that one would think they are of a different species. These racial attributes strike the most casual observer much more than the histological structure of the gland. However, if one establishes a subordination of characters, as results from our studies on conditioning, one should admit that the presence of lutein cells is a dominating character, while the specialities of plumage constitute a subordinate character. From this, we must conclude that if, in the evolution of the *Gallus domesticus*, a *variation is produced at a given moment*, with regard to the plumage *it has been preceded, prepared, unloosed, by a correlative modification of the conditioned glands;* our hypothesis receives verification in an exact manner.

The zoologists ask a question here that can not be allowed to pass. Which is the primitive form, the structure of the testicles of the Sebright cocks, or the ordinary structure? It is customary to consider the Sebright cocks as being the older strain, on account of the simplicity of their plumage and because of their resemblance to the cocks of Asia. The conditions of breeding and selection have brought about the development of races having most luxurious male plumage, such as those of Japan, in which the tail has taken on an extraordinary development; this seems clear.

But the conclusions are reversed if one considers that castration causes the appearance in the Sebright cocks of the abundant plumage of the males. These animals possess then *in a potential state*, the same characters as other cocks, and an *added influence* has been necessary to prevent the development of these characters at puberty. From that point of view one should consider them as being more highly evolved. This notion of potentiality deserves to be retained when it is a matter of comparing racial characteristics; it forces us to revise our judgments based on simple morphological ideas. What problems still remain to be studied!

The Sebright cocks are not unique in the possession of simple plumage. According to Morgan and Boring, one finds in the Campine and Hamburg races cocks having plumage like that of a hen. In these species it is simply a matter of exceptional cases,—the majority of the males having normal plumage. Without doubt, no histological study has bound up these accidental variations with the structure of the genital glands, but it is allowable, in view of facts already acquired, to prophesy an accidental variation in the structure of the male glands. We would witness, if that view is correct, an actual transformation in the plumage equilibrium, a change brought about by a preliminary transformation of the conditioned gland. Intensive studies alone can definitely decide the question.

(b) The results of exclusive carnivorous diet in cocks and rats. One such mechanism is assumed in the supposition that the reproductive glands may be modified by the habitual causes of variation, alimentary regime, state of environment, etc. The time has come to examine the foundation of this allegation.

In a series of experiments carried on from 1901 to 1906, Houssay (9) studied the modifications produced in Gallinacea (cocks and hens) by an exclusive meat diet. Among the results obtained, the author noticed a reduction in the sexual dimorphism: progressive sterilzation, the cocks losing the fighting instinct, etc. Put in the presence of their rivals, certain meat-fed cocks appeared timorous and tried to hide; they did not resist, they were the attacked. More often, they were accepted by their normal companions who did not deign to pick a quarrel with them. We should add for the sake of completeness that the carnivorous régime did not produce constant results and that many cocks on this diet retained the aspect and functions of the normal bird. In all cases Houssay attributes the effect to a direct influence of the meat diet.

Pursuing the same line of thought, Paul (10) submitted several series of male rats successively to an exclusive meat diet. As controls, at the beginning of this regime he took rats that had just been weaned and castrated them; at autopsy he determined that the reproductive organs were little developed in comparison with those of the controls. The reduction affected the seminal vesicles, prostate and penis. Paul attributed the modification to a direct influence of the exclusive meat diet.

In the two cases it is interesting to call attention to the development of the testicles in the animals so modified. As far as the carnivorous cocks are concerned, we have determined, from the autopsy tables accompanying Houssay's memoir, that these glands had received a setback under the meat régime and had not developed,—at least in the animals having the castrate characters. The mass of glandular parenchyma in these various subjects varied from 0.7 to 0.2 gms. Among the meat-fed cocks which retained their sexual attributes completely, the figures are higher, varying from 1.9 to 42. gms. We call to mind here our conclusion relative to the potency threshold and the all-or-none law. A similar conclusion follows from the work of Paul, which is illustrated by two charts showing the reduction of the genital tract and the testicles; the male glands of the subjects submitted to the carnivorous diet are so small in comparison with those of the normal males that one would think them atrophied.

In one case as in the other, it is not expedient actually to attribute the non-development of these secondary sexual char-

acteristics to the direct action of the dietary regime. The truth is that the exclusive meat diet determines in the two species a slow intoxication, an abnormal chemical process, to which the genital glands are particularly sensitive; it has then produced the modifications *secondarily* consecutive to castration. These experiments prove, in our opinion, that the reproductive glands are capable of responding to a definitive chemical influence, even though the nature of the response is not such as to produce a new race.

In conclusion, the testicular harmozone holds as dependents a certain number of secondary sexual characters. Its action, which begins at puberty, presents during the sexual life, in the case of cocks, a *continuity* and a *constancy* that are really remarkable. It does not survive the ablation of the genital glands although a small amount of the glandular parenchyma suffices to assure the integrity of the function. Histological modifications of the gland are able, as in the Sebright cock, to induce modifications in the external characters and to determine the very different races. Finally, these glands are sensitive to the action of a dietary regime considered up to now as one of the primary factors in evolution.

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THE ORIGIN AND EVOLUTION OF THE INTERSTITIAL CELLS AND OF THE OVARY AND THE SIGNIFICANCE OF THE DIFFERENT INTERNAL SECRETIONS OF THE OVARY

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In the ovary two functions may be distinguished, one in relation to reproduction and consisting of the development of ova and the other referring to its role as an organ of internal secretions. From this point of view two sorts of histological structures are to be distinguished, the corpus luteum and the interstitial cells.

The corpus luteum was first recognized by Coiter in 1573, and the interstitial cells by Pflüger in 1863. Following Fränkel the reports upon the endocrine function of the corpus luteum have been almost innumerable. The functions of the interstitial tissue have been considered by Limon, Bouin, Fränkel, Regaud, Ganfini, Ancel and Bouin, Below, Graves and Felner.

According to our embryological researches, the corpus luteum has a dual origin from the connective and the epithelial tissue, this being the source of the theca and the membrana granulosa, respectively, from which the corpus luteum is derived. According to Sobotta and Cohn it is of epithelial origin and according to Guilera Molas it is of connective tissue origin exclusively.

Della Drips, who has studied the corpus luteum of the Spermophile, Citellus tridecemlineatus has noted that immediately after the formation of the corpus luteum there appear globules of protoplasmic secretion; these are colored red with the fuchsin-methyl green stain following fixation in Bensley's fluid. This latter is substituted by another secretion of lipoid nature; the latter is related to the post-partum retrogressive changes of the uterus.

In our preparations of the ovaries of rabbits and rats the red elements begin to appear as early as the membrana granulosa and discus proligerous stages of development. The secretory

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activity is manifested, therefore, before the production of the corpus luteum proper (Fig. 1). Our work shows also that the corpus luteum persists until after parturition.

We do not coincide in the opinion of Edem and Lokyer, Fränkel, Asher, etc., that the corpus luteum gives rise to menstruation. In short, the corpus luteum succeeds the rutting period, as demonstrated by us in the rabbit, by Della Drips,

Fig. 2—Microphotograph of the uterus of the rabbit during the rutting period, showing the characteristic modifications of the mucosa, the extravasation of blood and the blood-filled lacunae.

Donaldson and others in different animals; rutting is accompanied by phenomena analogous to menstruation. The accompanying microphotograph (Fig. 2) shows the details observable in the uterus of the rabbit during the rutting. Our work thus confirms that of Wallich. That the sanguineous discharge is to the exterior in women and the macaca is due principally to the anatomical circumstances of the presence of the type of muscular wall found in these primates.

During menstruation arterial hypertension frequently is seen whereas extract of corpus luteum produces hypotension. Such extract, futhermore, is of no utility in the treatment of precocious menopause and does not augment the menstrual flow. In cases of various women, we have noted, on the contrary, a diminution and retardation of the flow, confirming the observation of Epley, MacCann, Climenko and others. We accept as indubi-

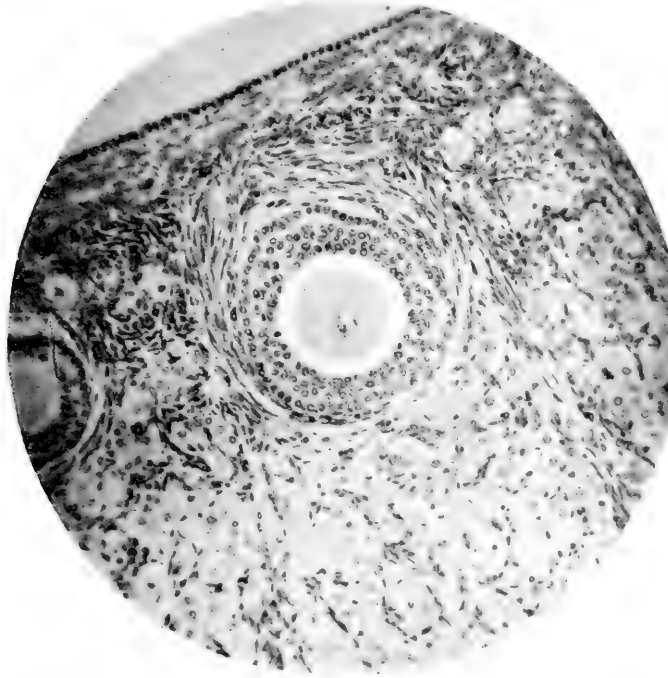

Fig. 3—Microphotograph of the cortical region of the rabbit ovary, showing an ovule developing and the interstitial cells, some with two nuclei and one in regression.

table that the secretion of the corpus luteum depresses menstruation, not by inhibiting any hormone secreted by the uterus but by its antagonistic action on the interstitial tissue of the ovary. We have studied the uterus in a great number of mammals and have never encountered any histological formation nor cytological process which would support the existence of a "myometrial gland" nor any definite evidence of internal secretion. We, therefore, take issue with Seitz and Wintz. That bilateral

ovarian extirpation suppresses menstruation is to be ascribed not to loss of corpus luteum but of the secretion of the interstitial tissue.

We have made studies of the interstitial cells, their embryology, evolution and endocrine function, arriving at the following conclusions: These cells may be considered as a constant formation in the ovaries of a great number of animals. The

Fig. 4—Microphotograph which shows the interstitial cells of the rabbit ovary. The chondrioplasts secrete lipoid material colored brown with osmic acid.

epithelial cells of the gonads which form a layer in immediate relation with the celom, multiply, invade the subjacent connective tissue, pass through the stages designated by Winewarter the "protobroca" and "deutobroca" and evolve in this manner: some pass through the well known stages to form oöcytes; others constitute the interstitial cellules. These undergo a process of phagocytosis encountered by us in the ovaries of the rabbit (Fig. 3) comparable to that described by the bota-

nists in the sexual elements and by Balfour and Lane-Claypon in other animals. Some of the cells are able to reach a stage analogous to that which precedes the formation of oöcytes, in the cells previously described.

The interstitial cells are the site of a cyclical phenomenon manifested principally by the evolution of chondriosomes. The mitochondria of these cells in which the hormones are elaborated

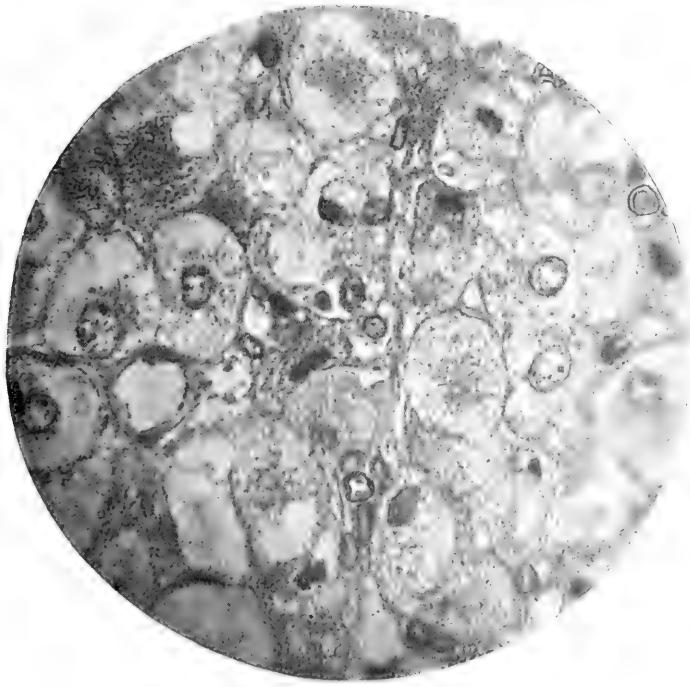

Fig. 5—Microphotograph showing the interstitial cells of the ovary during the dispersal of the chondriomites.

appear in the ovary of the fetus and undergo notable changes during the development of the animal. They are probably concerned in the appearance and conservation of the secondary sexual characteristics and especially the modifications characterizing puberty.

During menstruation in women, and in rutting, which is the equivalent of menstruation in animals, the activity of the mitochondria is clearly evident, characterized by the appearance of chondrioplasts, which in turn give rise to a substance

of lipoid nature that by osmic acid is stained a coffee brown (Fig. 4). At the termination of the rutting period the chondrioplasts give way to the smaller mitochondria and these form the starting point for a new secretory cycle (Fig. 5).

Of the two endocrine functions of the ovary, the corpus luteum mediates that having to do with the formation of decidual cells and the modification of the uterine mucosa which favor nidification of the ovum. If fecundation occurs the structure is transformed to the corpus luteum of pregnancy and alters the nature of its secretion. It assumes relations with the mammary glands and other endocrine organs. The secretion of the corpus luteum being, as previously mentioned, antagonistic to that of the interstitial ovarian cells, when the corpus luteum retrogresses or is experimentally suppressed, the action of the interstitial secretion is manifested. This secretion is the determining factor of menstruation; during the menstrual period the corpus luteum is either non-existent or in a regressive phase, while the interstitial cells manifest with maximum intensity the secretory phenomena. The ovarian congestion which coexists with menstruation favors the maturation of the graafian follicle. This ruptures and gives rise to a new corpus luteum which in turn depresses the interstitial secretion, causes the discontinuance of menstruation and thus again initiates the cycle previously described.

Fig. 1—Microphotograph of a preparation of the ovary of a rabbit. The chondriomites of the zona granulosa have been colored red directly from the slide by aid of the camera lucida. Fixation and staining by the methods of Bensley and Cowdry.

THE INTERNAL SECRETION OF THE TESTIS

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The researches of Mantegazza and Brown Séquard in the second half of the last century on the testis in order to determine if that gland produces an internal secretion which gives secondary characters to the male, opened the way for the study of the endocrine glands.

Although we know, if only imperfectly, the internal secretion of some of the ductless glands and we are able in certain cases, when the function is disturbed, to give treatment with success, the knowledge of the function of the sexual glands, although the first studied, is not even yet well known. This is due to the fact that though the anatomic and pathologic researches of Ancel and Bouin are arguments for the conception that the testis has an internal secretion, which is elaborated from the interstitial cells, the experiment did not give definite proofs.

Ancel and Bouin, after ligature and resection of the ductus deferens in the rabbit, obtained degeneration and atrophy of the seminal epithelium; the Leydig's cells remained without change. The animal kept the secondary sexual characteristics until the day that it was killed. Gosselin, Fabris and others, on the contrary, did not observe lesion of the testis from ligature and resection of the ductus deferens. Hence the conclusion as regards the internal secretion of the interstitial cells of the testis is not uncertain; the difficulty of solution of the problem is due to the disposition of the interstitial cells, which, as remarked lately by Cushing "is such as to make it impossible to observe the consequences of their ablation apart from the other cells of the organ."

Therefore, I believed it would be of value to repeat the study of the internal secretion of the testis and began the investigation herein described. The experiment of Ancel and Bouin was repeated, but with the rooster instead of the rabbit as the experimental animal. The rooster differs from rabbits in that it

has very marked secondary sexual characteristics: the comb, the spurs, the plumage, the sex instincts, the crowing and fighting tendency. After castration these characteristics disappear or become greatly modified. It is indeed easy to distinguish a capon (castrated rooster) from a rooster. If some time following the operation of ligature and resection of the ductus deferens the rooster, while alive, keeps all the secondary sexual characteristics of the male but the testes have become small and, on microscopic examination, atrophy of the cells of the seminiferous tubules is noted while the interstitial cells of Leydig show no lesion, one would be justified in agreeing with Ancel and Bouin that the interstitial cells have the function of internal secretion of the testis.

In addition to simple ligation of the ductus deferens a further experiment was made. Three or four months after the initial ligation, when atrophy of the cells of the seminiferous tubules had occurred, the testes were removed by a second operation. This amounted in effect to extirpation of the Leydig cells. Any changes in the secondary sex characteristics could then be ascribed to loss of these cells.

Fichera has found that castration in the rooster and in other animals produces hypertrophy of the pituitary body with increase of the eosinophile cells. Accordingly, in each experiment the condition of the hypophysis cerebri was observed. In the light of Fichera's results it would be expected that the pituitary body would remain normal after the first operation (ligature and resection of the ductus deferens with subsequent atrophy of the seminiferous tubules) and after the second operation (removal of the atrophic testis) it would become like that of the capon. Control observations were made upon normal roosters and ordinary capons.

Finally the experiment of Pézard and Lespinasse (the transplantation of testicular substance into the peritoneal cavity) was repeated in order to study the eventual change of the secondary sexual characteristic in comparison with the changes of the cells of the testis. In these experiments, also, the pituitary body of each rooster was examined.

The experimental series included many animals, because sometimes we observed reconstruction of the ductus deferens

after ligature and resection. In order to hinder this reconstruction as much as possible the vas deferens was dissected from the ureter for about 2 cm. and ligated at both extremities; at a point midway between the two ligatures a third knot was tied. The vas was then cut between the middle knot and that nearest the cloaca.

Fig. 1—Normal testis of cock. Note seminiferous tubules full of spermatozoa. The spaces limited between two or three seminiferous tubules show the interstitial cells. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

The tissue of testes and pituitary bodies for the histological study were fixed in formalin solution, in Zenker's, in Müller's or in Flemming's fluid; the sections were stained with haematoxylin-eosin, haematoxylin-Van Gieson, safranin-Flemming's, "thionine pheniquée" of Nicolle, and fuchsin of Altmann. Especial regard was paid to degenerative changes and chondriosomes as indicative of secretory activity.

A. THE INTERSTITIAL CELLS OF THE TESTIS OF NORMAL ROOSTERS

This series comprised 7 normal cocks. The testis in the rooster lies in antero-superior part of the peritoneal cavity in relation with the anterior-inferior surface of the kidney. It is an ovoid body of very large size considering the size of the animal; the average weight of the testis in a rooster of about 2½ Kg. is 10 grams. The spermatic ducts are two tortuous canals which extend from the epididymis to the cloaca, where they end. The vas deferens with its nerves and blood vessels follows the internal side of the ureter, and these structures cross the abdomen longitudinally.

The testis is made up of the seminiferous tubules and interstitial connective tissue. The interlobular or interstitial stroma contains groups of peculiar rounded polygonal elements, the interstitial cells. These are more frequent in the spaces limited between two or three seminiferous tubules, where there often is a small blood vessel. The interstitial cells sometimes do not show well defined limits. The nucleus has a spherical form and stains well. Some authors have studied the substances secreted from the testis, particularly the lipoids and pigments (Loisel, Pézard). Loisel says that the cells which lie in spaces between seminiferous tubules of the rooster secrete two kinds of pigments: "les unes, élaborent des pigments clairs, proviennent de l'ébauche germinale et doivent etre considérées comme des éléments soeurs de cellules germinatives; les autres élaborent des pigments foncés, insolubles, sont des éléments conjonctifs hypertrophiés apparaissant à une époque plus ou moins avancée de l'evolution du testicule. Il foudra donc sans doute reserver l'expression classique de cellules interstitielles pour désigner les éléments de la première categorie." I believe that one should consider the fat and especially the chondriosomes of the interstitial cells, because they give evidence as to whether the cells have secretory properties. The detection of the pigment in cells, when we are able to establish that they elaborate these pigments, does not demonstrate that the cells have a secretion.

I found in the interstitial cells of the testis of the rooster small and numerous fatty granules (safranin-Flemming method) and many small granules (mitochondria) well stained by the acid fuchsin with Altmann's methods. Rasmussen also found

mitochondria in the interstitial cells of the testis of the woodchuck.

B. THE PITUITARY BODY OF NORMAL ROOSTER AND CAPON

The pituitary body of the rooster (Piersol) consists of two distinct parts, the anterior and posterior lobes. The anterior part (glandular) constitutes the major part of the organ. It is surrounded by a fibrous capsule that is continuous with the thinner one inclosing the posterior lobe. We shall first consider the anterior parts. From the capsule extend inward fine processes which form a delicate fibrous reticulum; within the reticulum lie the cells. These are situated for the most part very close together and constitute a real cellular cord. Sometimes they are arranged almost like glandular tubules. The cells are apparently of two kinds: the chief cells which we can stain with basic dyes (only slightly with acid) and chromophile cells, which are larger and which have affinity for such acid dyes as eosin. The eosinophile cells in the hypophysis cerebri of the cock are generally very scarce. The blood vessels consist almost entirely of capillaries which lie in a mesh work.

The weight of the pituitary bodies of 7 normal cocks is recorded in Table 1.

TABLE 1.

	Age.	Body Weight.	Hypophysis weight, gms.	Weight of 2 testes, gms.
1	6 months	0.720 Kg.	0.11	2.16
2	6 months	0.600 Kg.	0.16	4.00
3	1 year	1.300 Kg.	0.13	9.00
4	3 years	3.200 Kg.	0.14	20.00
5	3 years	2.000 Kg.	0.12	16.00
6	3 years	2.600 Kg.	0.14	18.00
7	3 years	2.500 Kg.	0.18	16.00

The pituitary bodies of 4 capons were found to average heavier in weight than those of the roosters. The hypophysis of the capon is far richer in the eosinophile cells than that of the rooster; it is also more hyperemic. The data pertaining to this series are comprised in Table 2.

TABLE 2.

Weight of pituitaries of 4 capons:

	Age at Castration, mos.	Approximate Weight at Castration, Kg.	Weight of testes, gms.	Interval, months.	Weight at Autopsy, Kg.	Weight of Pituitary gms.
1	6	0.720	2.16	6	1.500	0.260
2	6	0.748	2.00	6	1.800	0.225
3	6	0.500	0.50	6	1.800	0.275
4	6	0.750	2.20	6	1.600	0.262

Castration then produces, as was observed by Fichera, a hypertrophy of the pituitary body and an increase of its eosinophile cells. But I believe, if the increase of the eosinophils in the gland signifies its greater activity, we could have eosinophilia also in other conditions. Indeed, I have found a certain degree of eosinophilia in the hypophysis cerebri of the 6th and the 7th roosters (the roosters were perfectly healthy) and Vassale found that the pituitary body of the puppy has more eosinophils than that of the adult. Therefore, perhaps, the eosinophilia may be related to the skeletal growth.

C. RESULTS OF LIGATION AND RESECTION OF DUCTUS DEFERENS IN ROOSTER

(I.) From a young rooster about 75 days old and weighing 0.550 Kg. was removed (June 4, 1910) the right testis (weight 1 gm.); the left spermatic duct was ligated and resected. The animal developed like a normal rooster. January 18, 1911, the animal (weight 0.950 Kg.) was killed. At the autopsy the left testis (weight 0.75 gm.) was found smaller and harder than the normal. In the epithelinin of the tubules degenerative changes were noted; the tubules were smaller than normal. In a few seminiferous tubules some spermatozoa still remained. The interstitial connective tissue was slightly increased and in this tissue the Leydig's cells were increased in number.

The pituitary body weighed 0.215 gm.; it was heavier than normal, but did not reach that of the capon. The quantity of the eosinophile cells in the pituitary was normal.

(II.) In a young rooster (weight 0.900 Kg.) about 6 months old (November 16, 1912), ligation and resection of

both spermatic ducts was carried out. The animal developed normally. June 18, 1913, the rooster was killed (weight 1.450 Kg.). At autopsy the right testis weight 3 gm., viz., less than the normal; the left testis was very small and weighed 0.20 gm. The pituitary body weighed 0.2 gm. The study of this experiment was interrupted; the microscopical examination of the testis and pituitary body was not made. It is included as showing atrophy of the testis.

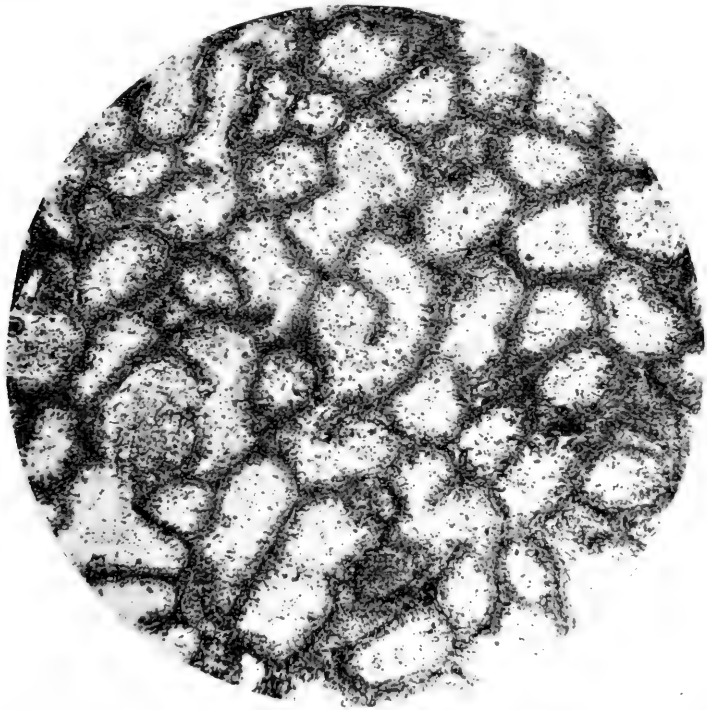

Fig. 2—Testis of cock, Series C, Experiment I, after ligation and resection of spermatic duct. Shows some spermatozoa in a few seminiferous tubules and degenerative changes in its epithelium, slight increase of the interstitial connective tissue and the Leydig's cells. Fixation, Bouin's fluid; staining, haematoxylin-eosin; magnification, 60 diameters.

(III.) In a young rooster (weight 0.850 Kg.), age 6 months (November 18, 1912), ligation of both spermatic ducts was carried out; they were not cut. The bird grew normally. June 18, 1913, the rooster, in good condition, was killed (weight 1.700 Kg.). At autopsy it was found that the ligature had yielded; the ducts were open. Together the testes weighed 5.25

gm. They appeared normal. The pituitary body weighed 0.215 gm. It was normal in structure.

(IV.) In a rooster one year of age (weight 2.050 Kg.) ligation and resection of both spermatic ducts was carried out (January 6, 1920). The animal recovered in a few days. February 29, 1920, the rooster (weight 2,400 Kg.) was in good health. A laparotomy was done and it was found that the left ductus deferens was reconstructed and its testis normal. The left testis was removed (weight 11.00 gm.). The right testis appeared small and seemed harder than normal; its vas deferens was also small. The animal recovered slowly. March 20th, the animal was well, but it seemed that its secondary sexual characteristics were less marked than normal. The crowing was not clear and strong. April 16th, the animal was in good health; a third laparotomy was made. It was very difficult to ablate the testis because the gland was sclerotic. It was removed in pieces. After the operation the rooster recovered in a few days, but at the same time it ceased to crow, lost its sexual instincts and the desire to fight.

The animal, when killed, weighed 2.530 Kg. The left testis (the first removed) was normal. The right testis (the second removed) showed: (a) the spermatogenetic cells with degenerative changes; (b) the Sertoli's cells normal; (c) a few spermatozoa; (d) increase of connective tissue and a slight decrease of Leydig's cells; (e) edema, hyperemia, lymphangitis and infiltration as in chronic orchitis. The loss of the left testis and the decrease of the Leydig's cells in right testis after the first operation may be the explanation of the diminished male instincts. The pituitary body weighed 0.23 gm. Microscopic examination showed a marked increase of the eosinophile cells.

(V.) Rooster, age about 3 years (weight 3.200 Kg.); January 9, 1920, both spermatic ducts were ligated and resected. The animal recovered in a few days; it remained male in its attributes. March 4th, the animal was in good condition. A laparotomy was done; the spermatic duct appeared small and almost empty. The testes were small, but the right testis was larger than the left. The right testis was removed. In one week the animal recovered and showed no changes in the secondary sexual characteristics.

April 8th, the animal (weight 3.100 Kg.), showing all the male characteristics, was killed. At autopsy the left testis (weight 2 gm.) was small and hard. The pituitary body weighed 0.18 gm. Microscopic examination of the right testis (which was removed March 4th) showed the seminiferous tubules smaller than normal; in the lumen were found a very few spermatozoa. It seemed that spermatogenesis had stopped. The spermatogenetic cells did not show important degenerative changes. There was marked hyperemia. The interstitial connective tissue was increased as well as the interstitial cells. The right spermatic duct contained no spermatozoa. The seminiferous tubules of the left testis were smaller than those of the right; nevertheless it was possible with careful search to find a few spermatozoa. Almost all of the spermatogenetic cells showed marked atrophy. The interstitial cells were slightly increased in number. The left ductus deferens was small; its epithelium was atrophic and no spermatozoa were found in the lumen. Very few eosinophile cells were found in the pituitary body.

(VI.) In a rooster age two years (weight 2.900 Kg.), on January 24, 1920, both spermatic ducts were ligated and resected. In a few days the animal recovered. March 30th, the rooster was quite well (weight 2,950 Kg.). The abdomen was opened and the right spermatic duct was found to be closed; it appeared greatly swollen; the left spermatic duct was reconstructed. We hoped to repeat the operation, but the rooster died.

At the autopsy the left testis (weight 11 gm.) appeared normal; the right, which had the duct closed, appeared the larger (weight 22 gm.). On microscopic examination of the right testis the seminiferous tubules appeared swollen with spermatozoa; the tunica albuginea was extremely extended. The spaces between the seminiferous tubules were large; there was edema in the testis. The pituitary body weighed 0.18 gm. The eosinophile cells were normal in quantity.

(VII.) In a rooster, age two years (weight 1.775 Kg.), on January 26, 1920, ligation and resection of both ducts was carried out. The animal recovered in a few days. April 22nd, the animal was in good health and had kept its secondary sexual characteristics and male instincts. A laparatomy was done; the

ducts were still obstructed and full of the testicular secretion. The left testis was removed (weight 11 gm.). The testis that remained appeared larger than normal. During the days following the operation the animal became very ill. It recovered slowly; but seemed to preserve its male instincts. It fought with other roosters, although very weak (May 5, 1920). On June 1st, the rooster had recovered, but it was yet weak. On June 3rd, it was killed.

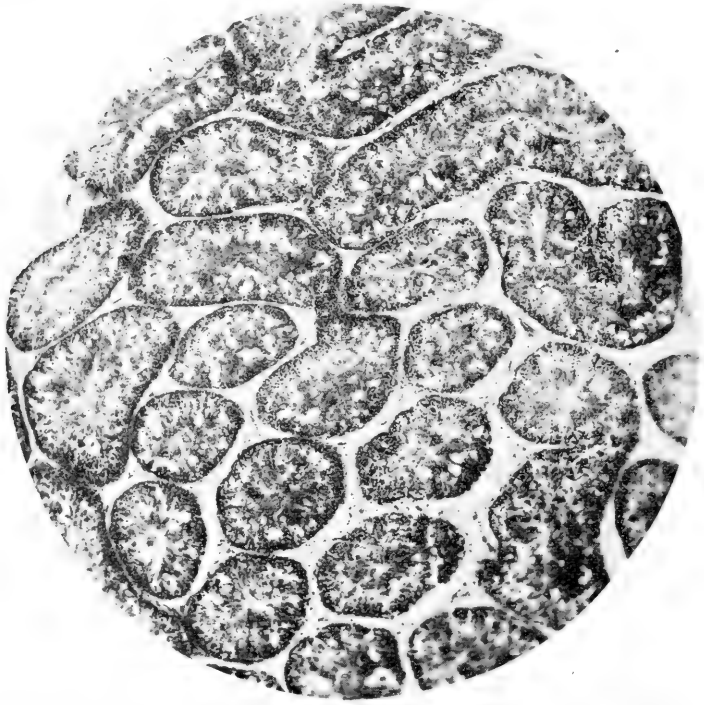

Fig. 3—Left testis of cock, Series C, Experiment VII., after ligation and resection of spermatic duct. Seminiferous tubules dilatated and full of spermatozoa; hydropic degeneration of the epithelium of the seminiferous tubules; interstitial connective tissue increased; Leydig's cells in normal number; edema. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

At autopsy the right testis was found very small and harder than the normal (weight 2.50 gm.). The pituitary body weighed 0.17 gm. Microscopic examination showed that the left testis, which had been removed April 22nd, had the seminiferous tubules dilated and full of spermatozoa of which many displayed degenerative changes. There was hydropic degeneration of its

epithelium; the interstitial connective tissue was increased; the Leydig's cells were normal in number; the organ was edematous. The right testis showed no spermatozoa in the seminiferous tubules, which were retained; the epithelium showed marked degenerative changes; there was a marked increase of the interstitial connective tissue and increase of the number of the Ley-

Fig. 4. Right testis of same cock as shown in Fig. 3. Note absence of spermatozoa in the seminiferous tubules and marked degenerative changes in their epithelium; marked increase of the interstitial connective tissue and increase of the number of the Leydig's cells. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

dig's cells. The epithelium of the vas deferens showed extensive degenerative changes and marked increase of the fibrous coat. The pituitary body showed an increase in the number of the eosinophile cells; this, of course, may have been due to the infection to which the rooster had been subject for a long period of time.

(VIII.) In a rooster, age about two years (weight 2.900 Kg.), January 27, 1920, ligation and resection of both spermatic ducts was performed. The animal recovered in a few days, but was always weak; it kept its secondary sexual characteristics. On February 22, 1920, it was killed (weight 1.650 Kg.).

Fig. 5. Testis of cock, Series C, Experiment IX, after ligation and resection of spermatic duct. Shows edema throughout the testis; hydropic degeneration in the epithelium of the seminiferous tubules, which are distended and full of very numerous spermatozoa; Leydig's cells normal. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

At autopsy no infection in the abdominal cavity was found. The cause of the weakness remained unknown. The testes were small; the right weighed 1.10 gm.; the left, 1 gm. The vasa deferentia were obstructed. The pituitary body weighed 0.15 gm. Microscopic examination of the testis disclosed albuminous degeneration and atrophy of the epithelium of the seminiferous tubules; no spermatozoa were present. A marked increase of the interstitial cells was found. The pituitary body was normal.

The atrophy of the testis was due probably more to the general condition of the animal than to the effects of the operation. But what is important from my standpoint is that the animal always preserved the male characteristics. For this reason the experiment is included in this series.

(IX.) In a rooster, age about three years (weight 2.700 Kg.), January 30, 1920, ligation and resection of the ductus deferens was performed. The animal recovered in a few days following the operation. The ducti deferentii were obstructed. During an attempt to remove a testis the animal died.

At autopsy it was found that each testis weighed 22 gm., and the pituitary body, 0.15 gm. On microscopic examination of the testis the following were noted: (a) edema in all testis; (b) hydropic degeneration (vacuolisation) in the epithelium of the seminiferous tubules; (c) very numerous spermatozoa in the seminiferous tubules, which were distended; (d) the Leydig's cells were normal. The pituitary body also appeared normal.

(X.) In a rooster about two years old (weight 2.900 Kg.), February 3, 1920, ligation and resection of the spermatic ducts was carried out. During the operation the right ductus deferens was accidentally ruptured near the kidney. It was not possible without risk of killing the animal to reach the duct again; it remained pervious so that the semen was poured into the peritoneum. In a few days following the operation the animal recovered. March 28th, the rooster was in good health. The right testis was ablated. The left testis felt larger than normal. The animal in the following days recovered and preserved completely its secondary sexual characteristics and instincts. The right testis was normal. On May 18th, during an operation for removal of the left testis, the rooster died. The testis was harder than normal; it weighed 12 gm. The pituitary body weighed 0.1 gm.

On microscopic examination the following observations were made: (1) the right testis was normal (the first removed and which had the vas deferens accidentally broken. (2) The left testis showed: (a) the seminiferous tubules swollen by spermatozoa; (b) hydropic degeneration of the epithelium lining the seminiferous tubules; (c) the lumen of the seminiferous tubules not distended; (d) the interstitial connective tissue in-

creased and the Leydig's cells more numerous than normal. (3) The pituitary body showed few eosiniphile cells.

The increase of the interstitial connective tissue explains why the left testis was harder than normal; probably this state represents the beginning of the sexual period, when the testis becomes atrophic because of the sclerosis of the interstitial connective tissue. (See Exp. I.)

(XI.) In a rooster about two years old (weight 2.320 Kg.), on February 11, 1920, ligation and resection of the spermatic ducts was done. The animal recovered in the days following. April 27th, the animal (weight 2.400 Kg.) was well. The peritoneal cavity was opened. The spermatic ducts were found to be reconstructed; the testes appeared normal. The left testis was removed; the right was distributed in peritoneum, divided in small parts. The animal died after two days, due to infection of the peritoneum.

On microscopic examination it was found that the pituitary body had numerous eosinophile cells. This eosinophilia might have been due to diminished testicular internal secretion (of the testes, one was removed and the other was spread in the peritoneum) or by the infection.

The foregoing data show that after ligation and resection of the ductus deferens we can have the following results:

1. The ductus deferens may be reconstructed (See Exp. IV, VI, XI; in Exp. III only ligation was done). In these cases we have no changes in the testis.

The ductus deferens may remain obstructed, but the consequences in the testis are not always the same: (a) sometimes following the operation the vas deferens and the testis increase in volume. After three months the testis may become enormous (See Exp. VI, VII, IX). On microscopic examination of the gland we find the seminiferous tubules greatly dilated and containing an extraordinary number of spermatozoa. Numerous spermatozoa are found in the vas deferens. In the epithelium of the seminiferous tubules we find hydropic degeneration. The interstitial connective tissue and Leydig's cells are normal or slightly increased; the testes are edematous throughout. To this first period succeeds a second (See Exp. I, II, VII, X) marked by increase of the interstitial connective tissue followed by

atrophy of the testis. After 4 or 5 months the seminal gland has become harder than normal and very small. On microscopic examination the seminiferous tubules appear small and the spermatogenetic function greatly diminished or almost disappeared.

At times, on the contrary, we have early atrophy of the testis. The gland becomes smaller and harder (Exp. IV, V, VIII); on miscroscopic examination we find the seminiferous tubules smaller and degenerative changes in spermatogenetic cells; few of these complete their cycle so as to become spermatozoa. The Leydig's cells, on the contrary, remain normal or increase in number. The time necessary to have these results varies within two or three months. I believe that the early atrophy seen in these cases depends upon the fact that during the operation the nerves which follow the vas deferens are injured. Marrassini, who obtained the same results in dogs by the ligation and resection of the ductus deferens, offers such a hypothesis. This author did not consider the consequences of the operation on the secondary sexual characteristics. Researches to establish the etiology of the different results will be undertaken in dogs in which it is easier to operate and to follow the consequences of the operation. But the important observations as regards the scope of the present study are that in no case in roosters after ligation and resection of the ductus deferens did there occur changes in the secondary sexual characteristics; in case of young animals development was normal (Exp. I, II). The observations of Ancel and Bouin in the rabbit are thus confirmed in the rooster. But the removal of the atrophic testes in which the Leydig's cells were in good condition (as confirmed by microscopic examination) caused in the adult animal a sudden cessation of crowing, a loss of the sexual instincts and of the desire to fight; I have observed no other changes.

The study on the hypophysis cerebri has shown that until the atrophic testis is removed, the organ in the rooster does not undergo the changes characteristic of castration (See Exp. I, II, V, VIII), but after its removal the pituitary body presents the same changes we have observed in the capon (See Exp. IV). Apparently then the hypophyseal changes are due to loss of the internal secretion of the testis. In the pituitary body of the

roosters of Exp. VII and Exp. XI the number of the eosinophile cells exceeded the normal, but was less than in the capon. In the pituitary body of normal roosters we can find sometimes, as we have seen, a certain degree of eosinophilia. Such eosinophilia can also be the consequence of infection from which the animals have suffered.

D. CONSEQUENCES OF THE TRANSPLANTATION OF TESTICULAR TISSUE IN THE ROOSTER

This research was undertaken to determine the eventual changes occurring in testicular tissue (particularly the Leydig's cells) transplanted in the peritoneal cavity and the relation of such transplantation to the secondary sexual characteristics and sex instincts. The operation was the removal of both the testes and the division of one into small pieces, which were scattered upon the peritoneum.

(I.) A young rooster about five months old, weighing 750 gms., was operated upon June 5, 1909. Complete removal of both the testes from their normal position was accomplished. The left testis weighed 1.5 gm. The right testis, which was about the same weight, was scattered about the peritoneum. The animal in the days following recovered, but crowed like a capon. On January 10, 1910, the animal, presenting the appearance of a capon, was killed. At the autopsy no trace of the testis was found in the abdominal cavity. The pituitary body weighed 0.230 gm. On microscopic examination the organ was found to present the picture typical of the capon.

(II.) A rooster weighing 2.017 Kg., about one year of age, was operated upon January 5, 1920. The removal of both testes was attempted. A small part of the left testis (weight 3 gm.) remained in situ (approximately 1/20 of the gland). The right testis was scattered about the peritoneum. In a few days following the operation the animal recovered. On March 1st, the animal, which now weighed 2.50 Kg., was killed.

Autopsy disclosed that the residue of left testis was in normal condition and two nodules of the testis which had been scattered about (right testis) had become adherent to the peritoneum. The pituitary body weighed 0.22 gm. On the microscopic examination the vestiges of the testis showed numerous spermatozoa in the seminiferous tubules and hydropic degenera-

tion of its lining epithelium; the interstitial connective tissue and its Leydig's cells were normal; some edema was evident.

The pituitary body showed an increase of the eosinophile cells. During the operation the rooster had lost almost all the left testis, and of the right, which had been transplanted, only a part remained grafted on the peritoneum. The microscopic examination showed no increase of the interstitial cells in the residue of the left testis nor in the transplanted testicular tissue. The small number of the Leydig's cells in the body of the animal can explain the diminished crowing and male instinct and the moderate hypertrophy and eosinophilia of the pituitary body.

(III) A rooster weighing 2.460 Kg., about two years old, was operated upon May 6, 1920, both testes being removed. The right testis was morcellated and scattered in the peritoneum. The left testis weighed 16 gm. In the days following the operation the animal recovered but lost the sexual and the fighting instincts. He never was observed to crow. On June 8th, the animal, in good condition, was killed.

At the autopsy no traces of the testicular substance were found. A few nodules adherent to the peritoneum were taken for histological study, but they were found to be made up of fat only. The pituitary body weighed 0.27 gm.

* * * * *

These experiments indicate that it is occasionally, but by no means always, possible to graft testicular substance upon the peritoneum. Where a successful graft is made the tissue after some time undergoes degenerative changes that involve all the elements of the structure. With the progress of the degenerative changes the sexual instincts diminish. Since the degenerative changes involve all the testicular substance it is not possible to distinguish clearly which of the two, Leydig's cells or epithelium of the seminiferous tubules, gives rise to the internal secretion. For this reason researches along this line were not continued.

Concerning the scientific question of the utility of the transplantation of the testis in old men, which, according to Stanley and Keller, produces in the body beneficial effects, I am of the opinion that exciting the sexual activities can produce only unhappy effects. The extinction of the sexual function in

old age is a physiological phenomenon accompanying the decay of the several functions of the body. The body organism is tired and if life is to continue there is need of rest and the conservation of the failing strength, which is not to be spent as in youth. Now it is notorious that sexual activity consumes much energy of the body, and wastes various substances, especially the lecithin, necessary to the nerve tissue. The consequences to the brain of sexual excess (v. Frankl-Hochwart) are well known and to create anew the sexual function by transplantation of the testes into the body, which has abolished this function because it has become old, is to contravene the normal laws of nature.

DISCUSSION AND CONCLUSIONS

The results of the work herein reported may be summarized as follows:

I. The testis has an internal secretion, which gives to the male the masculine sexual characters and sexual instinct and keeps the function of the hypophysis normal. This is well shown by the changes that come in the secondary sexual characteristics and in the pituitary body after castration and by the fact these changes do not come when there remains in situ or in the peritoneal cavity some part of the testis in functional condition. The nervous theory (Pflüger, Samuel) fails then, although some facts according to Luciani can find explanation on this theory which cannot find an explanation on a theory of internal secretion.

II. In the testis we have the spermatogenetic cells in the seminiferous tubules and the Leydig's cells in the interstitial connective tissue. Which of the two, then, produces the internal secretion? My researches indicate that the Leydig's cells have the endocrine function. This conception is supported by the following facts: (1) The Leydig's cells have the characters of secretory cells in that they elaborate fatty granules and mitochondria. (2) The animal remains normal even when we have marked atrophy of the seminal epithelium (See Series C, Exp. I, V, VII, VIII). (3) It is only when we remove the atrophic testis with the Leydig's cells then in good condition, that we have the changes that are noted after castration (See Series C, Exp. IV). (4) No facts exist which speak for the conception that the spermatogenetic cells exercise the endocrine function:

they complete a cytological cycle to become spermatozoa, which have merely the biological function of reproductive cells.

But the new information on the internal secretion of the testis that shows the effects of its abolition is very important not only for itself, but also because it shows that there exists through the internal testicular secretion a functional correlation between the testis and hypophysis cerebri. It lends support to the view that the pituitary body has the function of ruling the skeletal growth, and perhaps throws some light upon the obscure etiology of gigantism and acromegaly. In the acromegalic there is found marked hypertrophy of the hypophysis with eosinophilia of its cells and deficient development of sexual organs (Benda, Vassale, Cushing). But in the acromegalic the more important fact is that it is a lesion (hypertrophy, adenoma) of the pituitary body, whereas in the castrated it is the loss of the internal secretion of the testis, which secondarily produces hypertrophy of the hypophysis.

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EFFECTS OF X-RAY TREATMENT OF THE HYPOPHYSIS IN BRONCHIAL ASTHMA

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In the insufficiency of the endocrine organs the only therapeutic means, in use heretofore, with the exception of the casual treatment in specific cases, have been opotherapeutic substitutions. The results of such measures are at times wonderful, though often they prove disappointing, while the cause of failure can not always be determined. Long ago we thought of another way to correct endocrine insufficiencies through stimulation of the specific glandular elements; as a means to this end we chose deep radiations with x-rays.

Hitherto radio-therapy in endocrinology has been used only in destroying tissue, as in cases of exophthalmic goitre, in tumors of the hypophysis, etc. It remained to be seen whether, with lighter applications, the opposite effect could be reached of stimulating the gland cells to activity, or in other words if a *stimulating endocrine radio-therapy* were possible.

As soon as the necessary apparatus was available we tried the practical application of the principle suggested. The first treatment, made last January, was made in a case of dystrophy adiposo-genitalis.

The patient (B. P., a boy of 15) showed marked adiposity of the thighs, buttocks, mons veneris, breasts and inferior quadrant of the abdomen. His genitalia and secondary sexual characters were but slightly developed. The penis was 5 cm. in length and almost buried under the suprapubic fat; erections were infrequent and incomplete. There was no sexual tendency and no hair at the axillae, pubis and perineum. The voice was infantile. The body was underdeveloped; he was 1.49 m. in height and had short heavy limbs. Radiographically, no appreciable enlargement of the sella turcica could be detected. The patient had undergone several months of pituitrine and endospermine treatment with hardly any improvement; in one year

the penis had grown but 1 cm. in length and the height had increased only 2 cm. No hair had developed.

At the beginning of this year the patient had four irradiations of the hypophysis at intervals of one month. At every sitting three different fields were irradiated, one frontal and two temporal, for 36 minutes in all, at a distance of 45 cm., using an aluminum filter of 2 mm., S.E. 18-20 cm. and M.A., 3½. Twenty-five days after the first irradiation the pubis began to show hairs which gradually increased in number and length; the penis and testes increased in size, the penis in three months reaching a length of 8.5 cm. Erections became frequent and complete; the sexual tendency was accentuated. The height increased 5 cm. to 1.56 m., and the fat tended to diminish; the chest measurement dropped from 86 to 81 cm.

The irradiation treatment was also tried in a case of scleroderma. The patient, C. P., was a woman of 58. Her lesions, dating back two years, were especially conspicuous at the lower part of the thorax and superior part of the abdomen; the affected area extended like wide ribbons around the trunk, 10 cm. in breadth, with extensions upward to the breasts and downward to the pubis. Furthermore, there were oval and circular plaques, 3-5 cm. in diameter, on the breast, in the sternal region, the suprahyoid region, forehead and neck. The patient complained of diffuse pains in her body and limbs, great prostration, flushes of the face, slight tachycardia, anorexia, nausea, heavy feeling in the epigastrium and psychic sluggishness. Thyroid and hypophyseal treatment for six months had not modified either the general condition or the local lesions.

Then the patient underwent irradiations of the hypophysis as well as of the thyroid. Four treatments were given at intervals of about a month. Irradiation of the hypophysis was continued for 12 minutes in three different fields with the tube at 45 cm. distance, with a 2 mm. aluminum filter, S.E. 18-20, and with a current of 3½ ma. The thyroid irradiations lasted 5 minutes, with 2 mm. aluminum filter, S.E. 18-20, and current, 3 M.A.

After the second irradiation the cutaneous lesions began to change. The sclerodermic plaques of the breasts and suprahyoid region disappeared and the wide zone of affected skin, before shiny, copper-colored, thick and sticking closely to the under-

lying tissue, became pale, pink and thinner. It was possible to lift it in folds and the line of demarcation between the healthy and affected tissue became less apparent. The patient still complains of prostration and dyspesia, but the pains are greatly diminished, the pulse is slower and there is no more flushing of the face nor feeling of tension and weight in the abdomen. The psychic improvement is most marked.

Good results were also obtained in a case of Basedow's disease with two irradiations of the thymus. There was lessening of the tremor and the tachycardia (from 116-120 to 96-100) diminishing of the goiter (from 34 cm. to 31.1 cm) and subjective relief (15 minutes irradiation through 2 mm. aluminum filter, S.E. 20-22; M.A., 3).

Although in the above noted cases the effect has been satisfying, in other cases no defined result was obtained in regard to the fundamental lesion. A typical case of eunuchoidism in a patient of 26 was subjected to four applications to the testes and hypophysis and two to the thymus; a case of angioneurotic oedema of Quinke had three irradiations of the hypophysis and ovaries (in this case the general conditions improved and the menstruations became regular) and three cases of diabetes mellitus who had each four irradiations of the hypophysis and pancreas. In all these cases results were negative.

These negative results do not vitiate the principle predicated upon the positive results, and they should not hinder us from keeping on with the method. Other cases may improve under such treatment and, furthermore, given the delicate interweaving of mutuality, interference, antagonism and synergy existing between these glands, some modifications may be required, especially in regard to the Basedow cases and diabetes mellitus, which are now considered as pluriglandular syndromes.

It is also necessary to determine to what extent the irradiation may be used on the several glands to produce only the stimulating effect, a subject to be studied methodically and with prudence. Of course, there can not be obtained any stimulation whenever the tissue has degenerated to such an extent as to be no longer excitable.

We are sorry to have missed the opportunity of experimenting with irradiation of the hypophysis in diabetes insipidus, or of

the parathyroids in tetany maladies that seems especially to lend themselves to such treatment.

In view of the favorable results obtained by various observers in the use of pituitrin in asthma, irradiations of the hypophysis were tried in this disease. At each sitting three different fields were irradiated—one frontal and two temporal—for 12 minutes with aluminum filter of 2 mm., S.E. 18-20 cm. and 3½ M.A. current.

Case I. Frank G., 29 years old, a landowner, had been suffering from asthma for the past ten years. In the beginning the attacks lasted but a few minutes, coming on only once every 5-6 months. Since April of last year they had become very frequent—3 to 4 a day—so that the patient was hardly ever free from them and required 2-3 hypodermic injections every day of "asmolisina," which gave him some respite. Furthermore, every 7-8 days there were severe periods which lasted 8-10-12 hours when the patient was forced to keep absolutely immovable, since any slight motion increased the spasm and he had to take 10 to 15 or even 20 injections a day of "asmolisina." He is the brother of a physician and by him was brought to us to see if anything could be done for relief.

The patient is not tall, but appears very strong, and there is nothing abnormal about him but a decided emphysema, getting worse with the asthma. On May 15th the radio-therapeutic treatment was begun. He was given in all five treatments at 7-day intervals. Two days after the first irradiation one of his usual periods began, but it was milder and shorter, 3 to 4 injections of "asmolisina" a day being enough to allow him to go about. After this crisis there followed 8 days of complete relief from symptoms. A few days after the third irradiation a new crisis, but even milder than the previous one occurred. The attacks came on every other day, one to two a day; no "asmolisina" was required. This period lasted about a week, after which for 8 or 10 days he was well. Recently a few attacks have been experienced, but only at night and of very slight severity.

Thanks to the treatment the patient now secures sure relief from the "asmolisina," which before was only partially and slowly efficacious.

Case II. N. S. is a woman 37 years old. Her history is unimportant. Asthma has persisted two years. It began with brief attacks, 20 to 30 days apart. Since last November there have been 4 or 5 a week, lasting 3 to 4 hours. "Asmolisina" proved more dangerous than useful. The first irradiation of the hypophysis was given April 2nd and followed by four others eight days apart. From the first application the asthma ceased except for a very slight attack of a few minutes each.

Case III. U. R. is a boy 15 years old, a student. He is poorly developed, but nothing important was learned in his history. The first attacks of asthma began when he was 3 years old; they were short and infrequent. For the past 16 months they have occurred every 15 to 20 days and lasted 4 or 5 days.

Four weekly irradiations were given. Two days after the first a slight attack lasing two hours was experienced. On May 30th another attack occurred, but lasted only a few minutes. Since that time he has been well.

Case IV. L. M., a housewife, is 42 years old. No abnormality was found; her general condition was good. The last 15 months she suffered attacks of asthma, at first every 10 or 15 days, lasting an hour, then the last 6 months, every day and lasting 3 to 4 hours. Pituitrin hypodermatically did not help her.

Three irradiations were given, May 6th, 21st and 28th. During the treatment three slight attacks of a few minutes each were experienced. From May 27th on she has been well, except for an infrequent slight cough with mucous expectoration.

Case V. G. G. is a man of 34, an electrician. His family history is unimportant. He had lues when 15 years old. In November, 1917, he had pleurisy of the left side. He was poorly nourished, the pleurisy not being well cured. He had also pulmonary emphysema and diffuse bronchial catarrh. During the past year he has had attacks of asthma every morning. Each attack lasted about half an hour. Irradiations were given May 20 and 27. The attacks were reduced to only two or three a week and these were short and slight. The bronchial catarrh was not modified.

In these five cases the influence of the irradiations is clear. In the opotherapeutic treatment of asthma usually pituitrin and adrenalin are used together, therefore, whenever the stimu-

lation of the hypophysis proves insufficient one should try the stimulating irradiation of the adrenals also.

At any rate, the above noted cases clearly demonstrate the usefulness of the treatment; as regards the duration of the application and the persistence of the effects we need further experience. At the same time we need to make sure that the effect is really due to stimulation of the hypophysis or if there be other factors acting on the syndrome. We shall try to determine any such by looking for the effects of these slight irradiations on the endocrine glands, studying the functional changes as we can in the present state of science.

It will be worth while trying through the irradiations to study the glands in their functional aspects already known as well as any new phenomena, which may be evoked.

The field is large and full of promise. Even in the treatment of certain tumors, the development of which is influenced by endocrine glands the irradiation of these glands may conceivably prove useful.

The foregoing researches are reported in their incomplete form because we are forced to interrupt them for reasons not under our control and because of other studies that are being made in the same field.

Stettner in two cases of arrest of development in centres of ossification through the x-rays applied to the head and to head and neck had good results, which he attributes to an endocrine factor (hypophysis.) In asthma, Klewitz irradiated the anterior and posterior thorax in 18 to 20 fields, though without any beneficial effect. Stephan, on the basis of researches on the irradiations of the spleen thinks that such methods may be applicable wherever there is any obstacle to the cellular functioning and consequently in endocrine dysfunctions. Fränkel in a recent meeting of the German Radiological Society, talking of the stimulating action of very slight irradiations expressed a belief that such treatment might prove successful in endocrine dysfunctioning.

Precisely this hypothesis has been the starting point of our researches and the data herein repeated indicate the validity of the hypothesis.

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A FATAL CASE OF CARDIAC DILATATION WITH ASSOCIATED GASTROPATHY AND ENDOCRINOPATHY

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The subject of this report was a robust, vigorous young woman, a brunette, who married at the age of 19. She was the child of healthy parents and had enjoyed perfect health herself. About sixteen months after marriage she gave birth to a normal appearing nine-pound boy. At two months of age the child developed infantile eczema of an extreme type, which, after some weeks of varied treatment, responded quickly to thyroid extract. The eczema returned each time the treatment was discontinued.

At seven months it was decided to wean the child and thereupon developed violent and unconquerable fits of anger upon his part. They came on suddenly and were so noticeable that my attention was repeatedly called to the condition. Soon thereafter a gradual enlargement of the head, increased adiposity, changes in the appearance of the skin and lips made the diagnosis of cretinism positive. The thyroid treatment was again instituted, with a gradual recovery over a period of some months.

Soon after lactation had ceased, the mother went away for a visit but was brought back in five weeks in a most serious condition. This she reported had begun to develop before leaving. She had lost much weight, was weak and very nervous. Her pulse averaged between 120 and 160. She was dyspneic on the slightest exertion,—in fact, at this time was unable to leave her bed. Her urine contained a large amount of sugar and her thyroid was palpable. After eight weeks the sugar had disappeared, her pulse had decreased to between 80 and 90. Three months later she had about recovered from the acute hyperthyroidism but was constantly watched. She became apparently well and happy.

A year later she became pregnant and through the entire gestation enjoyed perfect health, as in her former pregnancy. A girl was born but was taken from the breast soon after birth because of the previous experience with lactation. This child has never developed any symptoms or condition suggestive of glandular disease.

Without going into all details, suffice it to state that the mother developed nervous symptoms soon after the birth of this latter child. The chief of these were referable to her stomach and associated with sudden increases of pulse rate. The attacks came on usually at night, without regard to food. She complained of fulness, pressure around the heart, dread of fainting and rapid pounding of the heart. The attacks becoming more and more frequent and beginning to tell notably on her weight, she was ordered to bed for a rest cure and a complete examination was repeated. The thyroid was palpable but not to the same extent as during her former illness. The cardiac outlines were normal. The blood pressure ranged from 122 to 105 systolic and 85 to 65 diastolic. The urine was negative, as was the blood Wassermann. There was no exophthalmus or any other goiter signs. Operative procedures were opposed for the time by the family in an effort to try out the medical measures; this procedure was agreed to by me. Two infected teeth and the tonsils had previously been removed, with improvement of the patient's general condition for a time. Chronic appendicitis had been discovered some months previously.

Ten to twelve weeks later she was out again and relatively well except for the occasional attacks with her stomach, giving rise at times to only a transient feeling of suffocation. Her pulse remained within normal limits.

A few months later an acute attack of appendicitis developed one night. A surgeon was called and the entire history reported. After due deliberation, on account of the suddenness, the severity of the attack and a 22,000 leucocytic count, she was operated upon that night. A purulent appendix of bad type was removed and drainage was instituted. For the next five days her recovery was exceptionally good. Her pulse never passed 84. She laughed and joked and desired food. On the morning of the sixth day I was hurriedly called. She was

cyanotic, with pulse of 120, diffuse apical impulse and left cardiac border outside the nipple line, indicating a condition of acute cardiac dilatation. Stimulants and minute care resulted in no improvement. She gradually grew worse and died at nine that evening.

DISCUSSION

The points presenting themselves in this history are the defective thyroid condition in the child, giving rise to a hypofunction as indicated by the eczema and cretinism; the relief with the administration of the gland but more marked relief upon cessation of the mother's milk. Striking also was the development of a hyperthyroid function in the previously normal mother upon the augmentation of her ovarian function and discontinuance of lactation. Again during pregnancy, when ovarian activity was in a depressed phase, her condition became normal in every way, only to be disturbed after parturition, when ovarain function was again stimulated.

In this connection I want especially to mention the gravity in prognosis, which is not sufficiently emphasized, in cases of so called functional heart conditions or in heart conditions without physical findings, in which gastric symptoms predominate. The feeling of fulness, pressure around the heart and suffocative influences often described as neurasthenic, especially when associated with any increase of the pulse beat, should be looked upon with alarm. In my experience, whether the patients are young or old, the majority of them sooner or later die suddenly. And then the thought arises whether or not many of the diagnosed anginas and even acute dilatations do not originally arise from thyroid intoxications which may or may not have been previously discovered.

525, The Woodward.

THE INFLUENCE OF THE THYROIDS ON THE FUNCTIONS OF THE SUPRARENALS

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CONTENTS

INTRODUCTION

An attempt to analyse the literature dealing with the influence of the thyroids upon the suprarenals reveals the presence of difficulties which are due to a variety of causes.

The dual nature of the thyroids and parathyroids was not always appreciated by the earlier investigators, and conditions following parathyroidectomy have been ascribed to loss of the thyroids alone. Less confusion has existed with regard to the suprarenals, where cortex and medulla are anatomically even more closely related than are the parathyroids with the thyroids. From the points of view of development, structure and functions, the cortex and medulla of the suprarenals are generally regarded as distinct organs, though the possibility of some physiological interdependence of both structures is not excluded.

Another difficulty lies in the fact that the medulla of the suprarenals is composed of cells which are not confined to this situation. The occurrence of aberrant glands as a fertile source of error in experimental work upon the thyroids and parathyroids has long been recognized, but too little attention has been given to the same difficulty in connection with chromaphil tissues.

Swale Vincent (69) has described the anatomical distribution of the chromaphil tissues in many species of animals, and it has been shown by Fulk and McLeod (21) that extracts of the retro-peritoneal tissues of man, the dog, cat, rabbit, white rat,

calf, sheep and pig have the same physiological action upon intestinal and uterine muscle as the active principle of the medulla of the suprarenal gland. The exact proportion which exists between the adrenalin content of the suprarenals and that of the other chromaphil tissues has not been ascertained, and is probably variable even in the same species of animal, but it is a factor which cannot be entirely disregarded.

Considerable doubt still exists as to the exact nature and extent of the rôle played by adrenalin in the physiological processes of the body. Following upon the earlier work of Cannon and de la Paz (8), Cannon and Hoskins (6), and Elliott (18), a tendency to exaggerate the influence of adrenalin has been followed by the opposite extreme. Stewart and Rogoff (64) in the course of a long series of carefully conducted researches find little evidence that secretion of adrenalin plays any important part in the ordinary mechanism of the body, and these authors believe that adrenalin is not indispensable. Gley and Quinquaud (26) have arrived at a similar conclusion. Cannon (5) gives excellent reasons for regarding the secretion of adrenalin as fulfilling an emergency function. The recent work of Kellaway (37) and Bazett (3) tends to support the earlier views that the secretion of adrenalin is not unimportant, and the "tonus" theory receives fresh support from Bazett's observations. The question cannot be considered as finally settled.

A due appreciation of the influence one gland has upon the functions of another is necessarily limited while we are still in ignorance of the exact functions of each of the endocrine glands. In experimental work and in disease, it is difficult to determine how far the changes met with are due to alteration in activity of any one gland. The picture which results is often a syndrome in which there is a disturbance of balance affecting many organs. An observed change in one gland may appear to be due to excess or diminution of function of another when the real determining factor lies in the disturbance of a third gland or series of glands, or in some general change of metabolism.

The literature relative to the action of the thyroids upon the functions of the suprarenals is not free from contradictory statements. Some of the discrepancies are explainable, others need the test of experience to prove which is true.

The present paper makes no pretence to be an exhaustive survey. The literature is widely dispersed, much of it is difficult of access, and valuable contributions may have been overlooked. It is hoped that a summary, however imperfect, will have some value in showing the general trend of opinion on the subject, and that it will draw attention to the more salient features which require further experimental investigation.

II. The Effect of Hyperthyroidism on the Size, Weight and Structure of the Suprarenals.

R. G. Hoskins (33) in 1910 fed 28 female guinea pigs with commercial desiccated thyroid in small doses for varying lengths of time. Pregnancy occurred in many of the animals, but in most cases the offspring were premature or born dead. In 21 offspring which survived, the suprarenals were smaller than in the young of normal animals of similar age, the average loss of weight being 53 per cent. No histological differences in pigment, mitoses, or proportion between cortex and medulla were noticed. Hoskins interpreted the results as indicating a reaction in the suprarenals of the offspring to an increase of adrenalin in the maternal blood brought about by experimental hyperthyroidism.

In a further series of experiments Hoskins fed young guinea pigs from the day of birth on small quantities, 5 to 15 mg., of desiccated thyroid, beginning with the lower dose and gradually increasing. At the end of 15 days the animals were killed and the suprarenals compared with those of normal animals of the same sex and age. The suprarenals of the thyroid-fed guinea pigs averaged 25 per cent. heavier than those of the normal animals. Hoskins recognized a source of error in the possible presence of toxic material in the desiccated thyroid, but in other respects his experiments were carefully and suitably controlled. His conclusions were that hyperthyroidism stimulates the suprarenals to hyperplasia.

Iscovesco (35) prepared an ether-soluble material from the thyroid glands, which, when repeatedly injected into rabbits produced in addition to changes in other organs a notable hypertrophy of the suprarenals in both sexes.

E. R. Hoskins (32) in 1916 published the results of a very careful and complete analysis of the effects of thyroid feeding upon the growth of the body and organs of the albino rat. He

obtained as a result of thyroid feeding an overgrowth in the absolute weights of the suprarenals of 14.5 per cent. in the younger females, of 16.1 per cent. in the older females, of 36.4 per cent. in the younger males, and of 38.1 per cent. in the older males.

Herring (27) employing rather larger doses of thyroid than E. R. Hoskins, obtained even greater hypertrophy of the suprarenals. For the male rat the increase in weight of the suprarenals averaged 56 per cent, for the females 41 per cent, the largest individual increase being 140 per cent in the male, and 94 per cent in the female. Herring pointed out that the increase is mainly one of cortex, though there is also some hypertrophy of the medulla as shown by the greater depth and extent of staining of the chromaphil material. Herring also drew attention to the hypertrophy of accessory suprarenals which takes place under the influence of thyroid feeding. These bodies are not merely cortical, but in the albino rat frequently contain masses of chromaphil cells.

Kuriyama (41) in 1918 failed to obtain the results of the previous observers. Working also with the albino rat he stated that "thyroid feeding of either short duration with large doses, or long duration with small doses, does not materially change the epinephrin content, nor the weight of the adrenals of medium sized albino rats."

Hewitt (31) has recently confirmed the results obtained by Herring and Hoskins, and brings forward evidence to show that in the young albino rat after the cessation of thyroid feeding there is a tendency with the subsequent growth of the animal for the suprarenals to regain their normal proportions.

Kuriyama's experiments are unsatisfactory in that he employed desiccated thyroid of unknown activity in doses which would be toxic if fully active. His animals were of widely-differing ages and weights; the male and female rats were grouped together. Further, the diet given, dog biscuit and lard paste, is not above the suspicion of being deficient in vitamine.

Desiccation, if not properly carried out, may injure the active principle of the thyroid. Gley (23) found that the activity of organic extracts diminishes rapidly the higher the temperature used in their preparation. Swale Vincent (68) has noted the possibility of impairment of dried extracts by methods which

decrease them. Hewitt (31) has shown that commercial preparations of desiccated thyroid vary greatly in activity.

According to Carlson, Rooks and McKie (9), many of the symptoms induced by thyroid feeding are caused by an excessive protein diet and are not specific. This objection was avoided by Hoskins in that he used very small doses of thyroid and gave similar amounts of thymus and other organs to his control animals. Herring employed fresh ox thyroid in his experiments and gave similar amounts of fresh ox flesh to his controls. In none of the control animals were the specific reactions of the thyroid-fed groups observed.

R. G. Hoskins, E. R. Hoskins and Herring all found that the reaction of the suprarenals to thyroid feeding is greater in the male rat than it is in the female. In the normal animal it must be remembered that the suprarenals of the male rat are lighter per unit body length or body weight than those of the female. The curve of growth, too, of the suprarenals differs considerably in the two sexes (Donaldson, 16). For these reasons alone male and female animals should be separately grouped for experimental work.

McCarrison (45) has shown that the absence of certain vitamines from the food induces hypertrophy of the suprarenals with loss of adrenalin. It is therefore of importance that all animals used for experimental work should receive both before and during the investigation a liberal supply of fresh and suitable food. It is also advisable that the thyroid-fed animals and their controls should be paired from the same litters to avoid as far as possible individual variations.

Cramer (12) has advocated the view that the cortex of the suprarenals, and particularly its zona reticularis, takes part with the medulla in the formation of adrenalin, and that the cortex and medulla are not functionally independent of one another. By a method of staining with the vapour of osmic acid he has demonstrated granules in the zona reticularis which appear to be of the same nature as the adrenalin granules. Cramer also finds that conditions producing overactivity of the thyroids increase the size of the suprarenals and lead to changes in the distribution of fat in the cortex, and to a diminuation of the adrenalin granules in the medulla. Such changes are, however, acute and were brought about by poisoning with β-tetrahydronaphthyla-

mine, a drug which Elliott (18) proved to cause a rapid discharge of adrenalin from the suprarenals.

There are very few references in the literature to the action of thyroid upon the cortex of the suprarenals. F. Munk (50) noticed a diminution of lipoids in the cortex of the suprarenals of animals which had been thyroid-fed.

The balance of evidence is in favour of the view that the administration of small doses of thyroid brings about hypertrophy of the suprarenals. The cortex of the gland is the part primarily affected, and the histological changes require further investigation. There is also some evidence that the medulla of the suprarenals and the chromaphil tissues generally, participate in the enlargement.

It is doubtful how far the hypertrophy of the suprarenals may be attributed to a direct action of the thyroid hormone upon these organs. It is possible that, as postulated by Eppinger, Falta and Rudinger (19), thyroid has a stimulating action upon tissues which produce adrenalin, but the relatively greater hypertrophy of the suprarenal cortex is more likely to be induced by indirect factors. The gross enlargement of liver, pancreas, heart and kidneys which occurs in thyroid-fed rats points to a general disturbance of metabolism which may be responsible for the condition. Further work is necessary to elucidate these changes.

III. The Effect of Hypothyroidism upon the Size, Weight and Structure of the Suprarenals.

Marinesco and Parhon (48) in 1908 studied the changes which take place in the fatty material of the suprarenal cortex in dogs deprived of their thyroids. They described two varieties of fat, and found that there was a notable diminution in the amount and size of the lipochrome droplets, more especially in the cells of the zona fasciculata. They regarded the cortex of the suprarenals as being especially concerned in the elaboration of lecithin and allied bodies, and concluded that this function is modified by thyroidectomy.

R. G. Hoskins (33) thyroidectomised newly-born guinea pigs, but found no subsequent change in the weight of the suprarenals compared with those of normal animals of the same age.

Lorand (44) stated that in senile myxoedema atrophy of the thyroid is followed by regressive changes in other organs of the body of which the suprarenals are examples.

Gley (24) found that the suprarenals of thyroidectomised rabbits are notably hyperthrophied and full of fat, but he regarded this condition, not as a sign of hyperfunction, but of degeneration of the cells in the last stages of myxoedema.

Herring (28) noted that in male adult rabbits killed from 30 to 73 days after thyroidectomy the suprarenals were lighter per unit body weight than were those of control rabbits of the same sex. The suprarenals were used for the determination of their adrenalin content so that no histological examination was made. The animals appeared to be perfectly healthy when killed.

F. W. Mott (49) in the investigation of the pathology of myxoedema described a case in which the suprarenals showed a marked diminution of the lipoid contents of the cortex. .

Cramer (14) stated that removal of the thyroid gland in rats and rabbits produces histological changes in the cortex which are, however, only slight, and appear to indicate a disturbance in the secretory mechanism of the gland rather than a deficiency in the formation of adrenalin.

The effects of hypothyroidism upon the suprarenals requires further investigation, and no definite conclusions can be drawn from the small number of observations quoted.

IV. The Effect of Hyperthyroidism upon the Adrenalin Content of the Suprarenals.

In estimations of adrenalin content, whether by physiological or chemical methods, it must be borne in mind that the chromaphil tissues not only produce adrenalin but have the capacity of storing it to a certain degree. Changes in the demand of the body for adrenalin may therefore influence the chromaphil tissues in several ways. There may be increased or decreased production of adrenalin with an effect upon the adrenalin load, depending upon the rate at which the adrenalin is given off to the blood. It follows, therefore, that the amount of adrenalin in the suprarenals is not in itself a true index of the activity of these organs. Its determination, however, may give some indication of the amount of production of adrenalin if the animal under experiment remains healthy, and if the adrenalin load be compared with that of a suitable control animal kept under identical conditions. Too much importance, however, must

not be assigned to the adrenalin load of the suprarenals, and its amount must be considered in relation to evidence of increased adrenalin in the blood. The whole question is so much complicated by factors at present unknown, or only partly recognized, that a safe deduction must of necessity be extremely guarded. With these reservations in view the evidence of the effect of hyperthyroidism upon the adrenalin load of the suprarenals may now be considered.

Herring (28) in 1916 found that the suprarenals of thyroid-fed cats, carefully minced and desiccated at 37° C, yielded a material which was more active when tested by Elliott's method (18) on the blood pressure of pithed cats than similarly desiccated suprarenals from the normal animals. By the subsequent employment of the chemical method of measuring adrenalin introduced by Folin, Cannon and Denis (22) Herring showed that the adrenalin content of the suprarenals of male and female cats is considerably increased by the prolonged feeding of these animals with small quantities of raw ox thyroid in addition to their ordinary diet. A histological examination of the suprarenals of the thyroid-fed animal further revealed that the cells of the medulla were closely packed with chromaphil material.

In a later paper Herring (27) extended his observations to albino rats. Male rats of the same age and as far as possible of the same litters, were taken in two groups. One group was fed on small amounts of fresh ox thyroid, the other group was kept as a control and fed with similar amounts of fresh ox flesh, the main bulk of the diet being in both groups a liberal supply of bread and whole milk. The adrenalin content of the suprarenals was estimated by the chemical method. It was ascertained that the amount of adrenalin in the thyroid-fed group was approximately 50 per cent. greater than in the controls. It was further noted that sudden death of the thyroid-fed animals was apt to occur even when the animals were putting on weight and apparently thriving. In all such cases the adrenalin content of the suprarenals was very high, and the condition was associated with a greatly hypertrophied heart and gross changes in other organs. In some of the thyroid-fed rats accessory suprarenals were found to be present and to contain chromaphil tissue in abundance.

In another paper Herring (30) dealt with the effect of thyroid feeding on the adrenalin content of the suprarenals of the female albino rat. It was ascertained that the suprarenals of the female rat normally have an adrenalin content nearly double that of the suprarenals of the male rat of the same size. The female animal is more susceptible to the administration of thyroid than is the male, and reacts in different ways. Some put on weight and remain healthy, and their adrenalin content shows on the whole a slight increase; other animals do not thrive and their adrenalin content falls.

Kuriyama (41) obtained no increase in the adrenalin content of the suprarenals of the albino rat on thyroid feeding. As already mentioned, Kuriyama grouped males and females, his experiments were few, and he employed large doses of desiccated thyroid of unknown activity.

It has been stated by Cramer (11) that external temperature has a considerable effect upon the adrenalin load of the suprarenals. Cold leads to a rapid exhaustion of the adrenalin store. Herring also noted that the mere separation of a litter of young albino rats into different cages adversely affected some of them. Experiments upon adrenalin content must therefore be attended by every precaution against outside influences, and the control animals should be of the same age and sex and preferably of the same litter, kept under conditions identical with those to which the thyroid-fed animals are subjected.

E. R. Hoskins (32) and Herring (29) have demonstrated that small doses of thyroid lead to striking changes in many organs. The hypertrophy of the heart and kidneys is greater than that of the suprarenals.

Kojima (40) and Herring (29) showed that the pancreas is also increased in size, and that this is not a mere matter of congestion is proved by Kojima's description of the numerous mitoses in the nuclei of the pancreatic cells brought about by the administration of small doses of thyroid. Herring came to the conclusion that hyperthyroidism stimulates the production of adrenalin, and that the enlargement of the heart and kidneys is a secondary phenomenon. The simultaneous hypertrophy of the pancreas was interpreted as being compensatory to the disturbance of carbohydrate metabolism associated with increased adrenalin formation. The results, whatever their explanation

may be, lend some support to the theory enunciated in 1908 by Eppinger, Falta and Rudinger (19). These observers as a result of experimental work, and from the consideration of the pathology of certain diseases, more especially myxoedema and exophthalmic goitre, formulated a general scheme whereby the interaction of certain of the ductless glands might be explained. Briefly they regard the glands as obeying the following laws:

I. Extirpation of a blood-gland has a two-fold result. First, a direct action through the loss of its specific secretion. Second, an indirect action through the disturbance of its metabolic relationships with other glands.

II. Between the thyro-parathyroids and pancreas, and between the pancreas and chromaphil tissue, there exists a mutual restraining influence, while between the thyro-parathyroids and chromaphil tissue there is a mutual stimulating influence.

III. Diminution or increase of secretion of one gland leads to over-action or insufficiency of another. For example, hyperthyroidism brings about a relative insufficiency of the pancreas and increased activity of the chromaphil tissue.

The laws enunciated by Eppinger, Falta, and Rudinger cannot be regarded as established, and they are obviously incomplete. They may, however, provide a working hypothesis to be confirmed or altered as experimental evidence dictates. The loss of balance of the ductless glands occasioned by the over- or under-activity of any one of them may ultimately be found to have its origin in changes in metabolism and the production in excess of toxic substances. The work of Noël Paton (55) and his co-workers on the relation of guanidine to tetania parathyreopriva, and of Kendall (38) is very suggestive.

V. The Effect of Hypothyroidism upon the Adrenalin Content of the Suprarenals.

Gley (24) in 1914 found that the suprarenals of dogs and rabbits previously thyroidectomised show no signs of any diminution of their adrenalin content when tested upon blood pressure. Extracts of the suprarenals of parathyroidectomised rabbits were sometimes a little less active than the normal, but in these cases the animals were suffering severely from the effects of the re-

moval of the thyro-parathyroids. Gley saw no trace of any specific action of the thyroids in maintaining the normal content of adrenalin in the suprarenals.

Herring (28) in 1916 noted that the desiccated suprarenals of thyro-parathyroidectomised cats yielded a material which was less active, when tested by Elliott's method on the blood pressure of pithed cats, than was similarly treated material from normal animals. In a further series of animals Herring, using the chemical method of estimating adrenalin, found that the loss of activity occurs only in cats suffering from tetany and obviously ill. In the rabbit, and in cats which show no symptoms, there is no decrease in the amount of adrenalin in the suprarenals. It would seem, therefore, that parathyroidectomy, and not thyroidectomy, is responsible for what loss takes place.

There is no evidence, then, that loss of thyroid in itself occasions any diminution in the amount of adrenalin present in the suprarenals. On the other hand the tetany and wasting which follow removal of the parathyroids are accompanied by loss of adrenalin from the suprarenals.

VI. The Effect of Hyperthyroidism upon the Adrenalin Content of the Blood.

Fraenkel (20) in 1908 attempted to measure the amount of adrenalin in the human blood by a physiological method. He adopted Kehrer's procedure, making the use of the isolated uterus of the virgin rabbit. By noting the response of the uterus to various dilutions of the blood of approximately normal individuals, and comparing the reaction with that produced by known dilutions of adrenalin, he claimed to have demonstrated the presence and measured the amount of adrenalin in human blood. Fraenkel also investigated the blood of individuals suffering from exophthalmic goitre and found in this disease a large increase in the amount of adrenalin. He regarded this increase as a compensatory mechanism on the part of the body against the lowered blood pressure brought about by increased thyroid secretion.

Bröking and Trendelenburg (4) in 1911 repeated the work making use of Laewen's method in preference to Kehrer's. They perfused the blood vessels of the frog's legs with known dilutions of blood serum from normal individuals and from patients

suffering from exophthalmic goitre. The results obtained by the constriction of the blood vessels were compared with those produced by known dilutions of adrenalin. Bröking and Trendelenburg estimated the concentration in normal human blood to be one part of adrenalin in from two to two and a half million parts of blood. In the blood of patients suffering from exophthalmic goitre they found from two to four times this amount of adrenalin.

Krause (42) noted that the enucleated eye of the frog showed dilation of the pupil when placed in the blood serum of patients suffering from exophthalmic goitre, a phenomenon which does not occur when the eye is immersed in the serum of healthy individuals. He also found an increase of adrenalin in the blood of animals previously injected with the juice obtained from the thyroid glands of patients suffering from exophthalmic goitre.

None of this evidence is satisfactory, for, as pointed out by Schafer (59), the physiological tests used for the estimation of adrenalin would also be given by pituitrin. There are other and more serious objections discussed by G. N. Stewart (62). The uterus alone does not furnish a suitable organ for the detection of adrenalin, and is particularly suspectible to the foreign proteins which exist in the blood of a different species of animal.

Stewart urged the necessity of control experiments in which the specific action of adrenalin in causing inhibition as well as contraction was made use of. He selected the rabbit's intestine as being best fitted to show the inhibitory action of adrenalin, and employing these tests in conjunction could find little evidence of the presence of adrenalin in human blood taken from the general circulation. In a later paper Stewart (63), using the same tests, found no evidence of adrenalin in the blood serum of a man suffering from Graves' disease.

The testing of blood for the presence of adrenalin by biological methods is complicated by the fact that a difference in action between blood plasma and blood serum has been alleged. O'Connor (52) believed that the coagulation of blood liberates substances in it having an adrenalin-like action. He found that blood serum causes a greater constriction of the blood vessels of the frog than does a citrated blood plasma. Trendelenburg (67), recognizing this possibility, changed his opinion as to the value

of his previous experiments, and gave a far lower estimate of the amount of adrenalin in the blood. Stewart and Zucker (66) investigated the action of blood plasma and serum under various conditions, and found that the increased action of serum is mainly confined to the blood vessels, and does not affect the uterus and intestine.

Similar objections apply to the use of the eyeball of the frog as a test for the presence of adrenalin in blood. Schultz (60) found it an unreliable method for detecting adrenalin in solutions where the amount present was much greater than could ever be the case with blood.

Ott and Scott (53) obtained an increase of adrenalin in the blood after the intravenous injection of thyroid extract. They made use of strips of the small intestine of the rabbit, the muscle of which responds specifically to adrenalin by loss of tone and inhibition of its rhythmical activity (Magnus, 47). But thyroid is not the only tissue extract which provokes increase of adrenalin in the blood. Ott and Scott found that extracts of parathyroids, pancreas, ovary and other organs have a similar action. Schwartz (61) had previously ascribed the increase of adrenalin after intravenous injection of animal extracts to the action of foreign proteins, and had shown that many substances can exhaust the adrenalin contents of the suprarenals when injected into the blood.

Gley and Quinquaud (25) obtained results similar to those of Ott and Scott. They took the blood from the suprarenal veins of dogs after the intravenous injection of extracts of thyroid and other organs. The blood from the suprarenal vein was then tested on the blood pressure of another dog. It was found that, while extract of thyroid increased the amount of adrenalin in the blood, it was no more active in this respect than extracts of liver and other organs. Gley and Quinquaud prevented the coagulation of the blood by the previous injection into the animal of Witte's peptone or leech extract so as to avoid the objections raised by O'Connor. It is quite possible that the injection of these materials had something to do with their results, for the reactions upon blood pressure which they figure are remarkably uniform in character whatever the nature of the extract used.

It cannot be said that an increase of adrenalin in the blood in hyperthyroidism has been satisfactorily established. Stewart and Rogoff (64) have shown that the amount of adrenalin in the general circulation is extremely small, and they regard its output as being dependent upon the integrity of the nerve supply of the suprarenals. In cats which had the right suprarenal excised and the left semi-lunar ganglion destroyed, the amount of adrenalin present in the circulation was still further reduced. Stewart and Rogoff estimated the amount in the veins of the suprarenals of these animals to be somewhere between 1 part of adrenalin in 300,000,000 and 1 in 700,000,000 parts of blood and in the general circulation to be at least 100 times less than this. The cats, nevertheless, remained healthy, and Stewart and Rogoff came to the conclusion that adrenalin is not indispensable to the body. The weight of evidence accumulated by Stewart and Rogoff is very great, but against it must be placed the fact that some of their results have not been corroborated by other observers whose methods would appear to have been equally careful. Kellaway (37), making use of the paradoxical pupil reaction in cats, found evidence of increased adrenalin secretion in anoxaemia after section of the splanchnic nerves. This did not occur after removal of the suprarenals, or only to so slight an extent as might be occasioned by the action of severe anoxaemia upon the extra-chromaphil tissue. If Kellaway is right, lack of oxygen would seem to have the power of increasing the output of adrenalin by a local action upon the denervated glands. It is quite possible that adrenalin secretion may also be regulated by hormone action. In this connection it is significant that Cannon and McKeen Cattell (7) have shown that the injection of small doses of adrenalin evokes an action current in the thyroids, and that a similar result follows stimulation of the splanchnic nerves, provided the suprarenals have not been previously removed. They further showed that the electrical changes in the thyroid are due to the stimulating action of some material, presumably adrenalin, carried to it in the blood stream from the suprarenals. It remains to be proved if the injection of thyroid can similarly provoke an action current in the denervated suprarenals.

VII. The Sensitizing Action of Thyroid upon Structures Stimulated by Adrenalin.

There is another aspect of the problem which has more experimental evidence in its support and about which there is less difference of opinion, namely, the sensitizing action of the thyroid secretion upon structures which are stimulated by adrenalin.

In 1911 Asher and Flack (2) showed that the thyroids produce an internal secretion which increases the excitability of the depressor nerve of the heart and the pressor effect of adrenalin upon the circulation. Stimulation of the nerves of the thyroid, or the intravenous injection of thyroid extract, greatly augment the activity of response to adrenalin. Stimulation of the thyroid nerves after extirpation of the thyroid has no such effect, and idio-thyrin was also shown to be inactive. Asher and Flack laid stress upon the nervous control of thyroid secretion, and upon the fact that the phenomena of exophthalmic goitre can be ascribed to the action of adrenalin upon structures which have been rendered more sensitive to it by hyperthyroidism.

Further work upon the same subject has been done by Asher (1) and his co-workers. Richardson (57) demonstrated that the isolated heart of the rabbit beats more rapidly and powerfully under the influence of adrenalin when perfused beforehand or simultaneously with extract of thyroid. Shigeshi Kakehi (36) obtained similar results, and found that the heart of an animal which had previously been thyroidectomised shows no difference in this respect from the heart of a normal animal. Levy (43) ascertained that stimulation of the cervical sympathetic nerve in cats augments the pressor action of adrenalin some 200 to 300 per cent, and that this effect does not follow if the thyroids have been removed. He also showed that the iodine-containing compound isolated by Kendall is effective in sensitizing the blood vessels to the action of adrenalin.

Oswald (54) stated that iodo-thyro-globulin increases the excitability of the vagus depressor and splanchnic nerves to faradic stimulation, and that the augmenting effect is in direct proportion to the iodine content of the material employed. Iodo-thyro-globulin from a case of Graves' disease had a similar influence.

Eiger (17), perfusing the blood vessels of the frog, demonstrated that, while extract of thyroid itself has no action upon them, it greatly increases their response to adrenalin. Eiger showed that the blood collected from the veins of the thyroid augments the effect of adrenalin, while that from other blood vessels has no such action. He also found that the blood of rats fed with thyroid, and the blood of patients suffering from exophthalmic goitre, have the same property of increasing the activity of adrenalin.

Santesson (58) claimed that the intravenous injection of various preparations of thyroid increases the sensitiveness of the rabbit to adrenalin. A greater rise of blood pressure is produced by the same dose of adrenalin if the animal is previously fed on thyroid or receives an injection of thyroid extract.

Schafer (59) was unable to confirm the results of Asher and Flack as regards the prior injection of thyroid extract in increasing the excitability of the cardiac vagus or depressor in the rabbit, cat, or dog. He found in the last two animals that the simultaneous injection of thyroid and stimulation of the depressor nerves produce a greater fall of pressure than that occasioned by either of these two alone. The increased depressor effect of the combination he regarded as the result of summation, for in the rabbit, where a slight pressor effect is sometimes produced by the injection of thyroid, the simultaneous injection of thyroid and stimulation of the depressor nerve evokes a smaller response than stimulation of the depressor nerve alone.

Dalman (15), while believing that the pressor effect of adrenalin is intensified by thyroid, looked upon its action as a mechanical one. He considered that thyroid promotes an absorption of fluid into the blood vessels from the lymph, thereby creating a condition favorable to an increased action of adrenalin.

There is, then, a large amount of evidence that the secretion of the thyroid has a sensitizing action upon the structures stimulated by adrenalin. The reaction is not necessarily a specific one. Kepinow (39) found that the pressor effect of adrenalin upon the circulation is intensified by the preliminary use of pituitrin, and that an augmentation of the reaction of the pupil is obtained in the same way. Cow (10) corroborated Kepinow's statement as regards the blood pressure, and further

showed that pituitrin activates the uterus to an increased response to adrenalin. Cow gave reasons for believing that this sensitizing action of pituitrin is exerted upon the peripheral mechanism of the sympathetic system but not actually upon the end organs. Further research upon these lines is clearly called for.

VIII. The Thyroids and Suprarenals as a Subsidiary Heat-Regulating Mechanism.

Eppinger, Falta, and Rudinger (19) discussed the possibility of adrenalin taking part in the regulation of body temperature. They noted that the injection of adrenalin causes a rise of temperature in normal, thyroidectomised, and depancreatised dogs. On the other hand, towards the close of life in dogs suffering from pancreatic glycosuria a decreased production of adrenalin is accompanied by a gradual fall of body temperature. They concluded that the secretion of adrenalin is an important factor in heat production.

This theory has been developed by Cramer (11) who regards the thyro-adrenal apparatus as a humoral mechanism supplementing the nervous one. Cramer believes that the thyroid hormone mobilises the liver glycogen by increasing the production of adrenalin and sensitising the sympathetic nerve endings. At the same time adrenalin constricts the arterioles of the skin thereby diminishing the loss of heat from the body. Cramer has adduced a number of experimental and pathological observations in support of this theory.

That some mechanism of this kind comes into play as an accessory factor in heat production is not unlikely. The stimulating action of thyroid upon metabolism is well known. Von Noorden (51) stated that "the thyroid acts upon metabolism as a pair of bellows upon a fire." McCarrison (46) said, "the thyroid gland is to the human body what the draught is to the fire." Herring (29) compared the action of the thyroid glands to the draught-regulating mechanism of a furnace.

Increased activity of the thyroid must therefore bring about a greater production of heat. The loss of glycogen from the liver may be simply due to the increased oxidation resulting from hyperthyroidism. The question of the action of adrenalin upon carbohydrate metabolism has received much attention,

and although having a distinct bearing upon the relations of the thyroids to the suprarenals, is far from being settled and is beyond the scope of this article. Even if it be admitted that hyperthyroidism stimulates the suprarenals to an increased production of adrenalin, its action upon other organs is greater. The liver and pancreas would appear to be more intimately concerned. A disturbance of thyroid secretion upsets the balance of many organs, all of which have to be taken into consideration in the interpretation of the picture which ultimately results.

IX. Summary.

There is much evidence, though not unanimous, that hyperthyroidism increases the size and weight of the suprarenals. The observations in this respect are confined to a few species of animals, chiefly the albino rat and it does not follow that a similar change takes place in all animals. In the albino rat the hypertrophy of the suprarenals is due mainly to an increase in the size of the cortex of the gland, the histological features of which have not as yet been investigated. The hypertrophy of the cortex of the suprarenals is associated with gross changes in other organs and in the general metabolism of the animal, and it is to these influences rather than to a specific action of thyroid that the cause may be attributable.

There is some evidence that hyperthyroidism does in the healthy animal increase the adrenalin load of the chromaphil tissues. The adrenalin load, however, is so easily altered by a variety of circumstances that it signifies little in itself. The alleged increase of adrenalin in the blood of animals suffering from hyperthyroidism is neither proved nor disproved. The evidence is untrustworthy. There is greater unanimity in ascribing to the thyroid hormone an activating influence upon the structures which are amenable to adrenalin. This sensitizing action of thyroid may explain the phenomena of Graves' disease which have been attributed to an increase of adrenalin in the blood. It does not exclude the possibility that an increased secretion of adrenalin may actually occur in this condition.

A specific action of thyroid in stimulating the secretion of adrenalin, and in sensitizing the structures amenable to its action, though not improbable is not satisfactorily proved.

Pituitrin has a similar action in sensitizing certain structures to the action of adrenalin, and further experimental work may extend the similarity.

Hypothyroidism is shown to have no effect upon the adrenalin load of the suprarenals, but here again no definite conclusions as to the absence of a specific stimulus can be drawn, for we know nothing about the extent of the requirements of the body for adrenalin in this condition.

The theory that one endocrine gland exercises a specific influence upon another only touches a part of the question. The changes in metabolism which occur when any gland is disturbed in function must have a widely-spread effect. Many of the metabolic changes undoubtedly take place in the liver, and it is unreasonable to suppose that this organ takes no active part in the problems presented by the ductless glands. Hyperthyroidism provokes such gross changes in the organs of the albino rat that one is drawn to look for the explanation of its effects in the products of a disordered metabolism. Noël Paton (56) has emphasized the importance of the endocrine organs as regulators of metabolism. The investigation of the substances normally formed in the body, and the influence which the ductless glands have upon them, provides a line of research which may eventually lead to the establishment of the endocrine glands as important factors in the regulation of the general metabolism of the body.

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THE FIRST CASE OF MYXEDEMA TREATED BY THYROID EXTRACT

To the younger generation of practitioners organotherapy is more or less a commonplace feature of every-day medicine. Its real development, however, has occurred entirely within the lifetime of this generation.

The first successful use of thyroid extract in the treatment of myxedema was begun in 1891 by Dr. G. R. Murray of Manchester, England. The recent death of the subject has impelled Dr. Murray to publish a recapitulation of the case (1).

"Mrs. S., aged 46, was shown at a meeting of the Northumberland and Durham Medical Society on February 12th, 1891. She had had a family of nine children, of whom six were living. At the age of 40 she had a miscarriage, after which she had menstruated once, at the age of 42. When she was 41 or 42 years of age her relations had noticed that she was becoming slow in speech and action, and she herself began to find that it required a great effort to carry on her ordinary housework. The features gradually became enlarged and thickened and the hands and feet increased in size and changed in shape, so that at the time of this meeting she presented the typical features of an advanced case of myxedema of at least four years' duration. After showing the patient, I stated my intention of treating her with thyroid extract, and described the principles upon which this treatment was based and the reasons for expecting that it would be successful. The treatment was not commenced until two months later, and the following note taken on April 13th, 1891, describes her condition at that time:

"She complains of languor, a disinclination to see strangers, and great sensitiveness to cold. The temperature is subnormal, and varies between 95.6° and 97.2° in the mouth. The pulse varies between 60 and 70. The face is blank and expressionless and the features are notably thickened. This change is well seen in the alae nasi and lips. The subcutaneous connective tissue of the eyelids is so swollen that she finds it difficult to look upwards. There is also considerable swelling beneath the eyes and of the cheeks. The hands and feet are both enlarged; the former have that peculiar shape which has been described as spade-like. The skin is very dry, there is no perspiration, and the superficial layers of the epidermis are continually being shed as a fine white powder. The hair is very fine in texture, and a considerable quantity of it has been lost. She is slow in answering questions; all her actions are slow and are performed with difficulty. The speech is remarkably slow and drawling and the memory is bad. No thyroid gland can be felt in the neck. The urine contains no albumin or sugar.

"The experimental nature of the treatment was explained, and the patient, realizing the otherwise hopeless outlook, promptly consented to its trial. In order to insure that the extract was properly prepared, the thyroid gland was removed from a freshly killed sheep with sterilized instruments and conveyed at once in a sterilized bottle to the laboratory, where a glycerin extract was prepared.

"In the treatment of this first case a hypodermic injection of 25 minims of the extract was given twice a week at first, and later on at longer intervals. The patient steadily improved and three months later, on July 13th, the condition was thus described:

"The swelling has gradually diminished, and has practically disappeared from the backs of the hands, the skin over them being now loose and freely movable. The lips are much smaller. The swelling of the upper eyelids has diminished so much that she can look upwards quite easily. The swelling beneath the eyes and of the cheeks has also much diminished. The face consequently, as a whole, has greatly improved in appearance and has much more expression, as many of the natural wrinkles, especially about the forehead, have returned. The speech has become more rapid and fluent, the drawl being scarcely noticeable at the present time. She answers questions much more readily, the mind has become more active, and the memory has improved. She is more active in all her movements, and finds that it requires much less effort than formerly to do her housework. She now walks about the streets without any hesitation, without a companion.

"She has menstruated normally during the last six weeks at the regular interval. For the last four weeks the skin has been much less dry and she perspires when walking. The hair remains as before. She is no longer so sensitive to cold. Unfortunately, owing to circumstances, a daily record of the temperature has not been kept, but out of four observations that have been made lately, about 11 a. m., three times the temperature has been 98.2° F. and once 97.4°.

"After this the injections were given at fortnightly intervals, and later on, when the oral administration had been shown by Dr. E. L. Fox and Dr. Hector Mackenzie to be equally efficient, she took 10 minims by the mouth six nights a week, so that one drachm was consumed in the course of each week. On this dose she remained in good health and free from the signs of myxedema. She continued to take liquid thyroid extract regularly until early in 1918, when it became difficult to obtain, so she was given dry thyroid extract. She enjoyed excellent health until early in 1919, when she died at 74 from cardiac failure.

"This patient was thus enabled, by the regular and continued use of thyroid extract, to live in good health for over twenty-

eight years after she had reached an advanced stage of myxedema. During this period she consumed over nine pints of liquid thyroid extract or its equivalent, prepared from the glands of more than 870 sheep."

1. Murray (G. R.). The life history of the first case of myxedema treated by thyroid extract. Brit. M. J. (Lond.), 1920, (i), 359-360.

ENDOCRINOLOGY IN RETROSPECT AND PROSPECT

With this issue ENDOCRINOLOGY completes its fourth year of publication. While the retrospections of a four-year-old may not be regarded as highly portentous, something of value may be deduced from the consideration of even this brief experience.

The declared central purpose in the organization of the Association for the Study of Internal Secretions was "to correlate the work and interests of physicians and students engaged in the study of internal secretions and, by concerted effort, to broaden knowledge in this field." The constant aim of the editorial staff has been to coöperate to the best of its ability in the realization of this aim.

Starting with no resources but an idea and the enthusiasm of its proponents, it was expected that progress would in any case be somewhat slow. Almost as soon as the journal got under way, however, it had to encounter the vicissitudes of war. A large proportion of the active men upon whose support reliance was placed either entered directly into military service or assumed such heavy duties in connection with the war that little time and energy were available for the Association and its journal. That the infant survived this trying ordeal seems a surprising manifestation of innate vitality.

Not only, however, was the preoccupation of its supporters a handicap to the Journal, but the disorganization of medical and scientific activities throughout the world also proved a seriously disturbing factor. The supply of original articles for publication was reduced almost to the vanishing point and the periodical literature from which abstracts are derived became difficult to secure. Many journals suspended

publication and those which continued publication in many cases reached the abstracters only irregularly. In fact, many library files are still incomplete for the period of the war. Partly on this account, hundreds of articles published in the past three years remain yet to be abstracted.

Three plans for dealing with the current literature have been entertained. The first of these is to collect the literature in abstract form, as it appears. The publication of this material affords a cross section of the literature for the given period. If adequately presented, such a cross section should exhibit in a colorless way both the virtues and defects of this literature. That various palpable absurdities have thus been presented for the consideration of the readers is fully realized.

As regards articles of dubious value, the policy of most abstract journals is to pass them over without notice, in the hope of their relapsing promptly into oblivion. In the meanwhile, however, the titles have been catalogued in the more complete bibliographic journals and they remain, to the thorough student, at least, a factor that must be taken into account. For example, an author proposes to bring up to date the literature on a given point. From the bibliographic journals he secures a list of references to all sorts and conditions of articles. Frequently none of these can be discarded without at least cursory consideration. If the articles were all available in adequate abstract form, those of no permanent value could at once be dismissed from consideration. For this reason, it is felt that the re-publication of even so-called trash is of constructive value. Accordingly, the policy is to abstract "all the endocrine literature since 1916."

Not the least of the difficulties encountered in carrying out this plan resides in the scientific conscience of the abstracters. In each case the aim has been to secure the services of men of well-balanced critical judgment. Such men have a readily understood hesitancy to attach their initials to material of dubious significance, even as reporters.

So much for the first plan. It represents to a considerable extent merely a preliminary process.

A second plan is to collect the literature on given topics, irrespective of date, and to publish this material as a series

of synthetic reviews, in which each article is critically evaluated by a competent authority. Only a beginning has been made toward the evolution of this plan. It amounts to a presentation of the literature—to carry out the morphological simile—in reconstruction.

A third plan is to collect in abstract form and publish in chronological sequence the literature on select topics—to present this literature in longitudinal section. Obviously, the literature on some topics, for example, Graves' disease, would not lend itself to such treatment. That on other and less extensive topics might, however, be thus presented and a great deal of work be saved upon the part of those having occasion to review such material. So far it has not been practicable to proceed with this plan.

A fourth plan, also, namely, to supply translations or abstracts of less accessible individual articles to our members and subscribers, has had to remain one for future development.

At this time it may not be amiss to point out that the limiting factor is solely the elementary one, an inadequate budget. One of the leading scientific societies is said to expend approximately $50,000 a year upon its abstract journal alone. The actual realization of the maximum possibilities for usefulness in an abstract and bibliographic service might exhaust an even larger budget. There is readily accessible the most complete collection of the current literature on medicine and medical sciences in the world. Translators and abstracters are also obtainable. Salaries alone are lacking.

A rapidly growing subscription list is an encouraging indication of the future possibility of augmenting the usefulness of the Association and its journal. The time, however, would seem to have arrived when, in recognition of their place as educational institutions, associations and journals of this sort should be supported by considerable endowments. When the needs and possibilities of such are realized and adequately presented, doubtless such endowment will be forthcoming.

So much for the matter of second-hand dealings with the literature. As regards original material, the endeavor has

been and will be to publish at first hand a considerable proportion of the best articles appearing in the field of Endocrinology. Articles of wide interest and such as summarize the results of extensive studies are especially to be desired. The coöperation of the entire membership of the Association is needed to make the most of this phase of our activities.

With the beginning of Volume V, the Journal will appear bimonthly. The material to be presented is constantly increasing in amount, and bimonthly issues will perhaps be of more convenient size than would quarterly. It is hoped that this consideration, together with that of more prompt publication of original articles and abstracts, will compensate for the additional effort and financial outlay involved.—R. G. H.

LE SYMPATHIQUE ET LES SYSTEMES ASSOCIES. By A. C. Guillaume, with preface by Pierre Marie, Paris, 1920. Masson et Cie., 160 p.

In view of the close relationships between the autonomic nervous system and the endocrine functions this book will be of interest to endocrinologists generally. In addition to introductory and concluding sections the volume consists of six chapters, taking up, respectively, the morphophysiologic conception of the autonomic system, the connection of this system with the organic processes, the pharmacologic relationships, the syndromes due to selective excitation of the system, clinical "vagatonia" and "sympathicotonia" and the pathological connections of the autonomics with the "organic" and "animal" systems. The morphologic relationships are brought out in a series of unusually comprehensible diagrams. In the section on pharmacology the author goes, in the interest of philosophical gratification, considerably beyond the limits of safety. He postulates a function for the suprarenal cortex bearing the same relation to the parasympathetic system as does the medulla of the gland to the sympathetics. "Hormone x" in this case is cholin. The pancreatic secretion is alleged to have a somewhat similar function to that of the suprarenal cholin. He also oversimplifies the equasion in assigning to the thyroid hormone merely a selective affinity for the sympathetic fibres rather than regarding it as a general cell stimulant. On the whole, the book, while illuminating and full of useful data, must be read somewhat critically. The data are largely derived from other compilations.—R. G. H.

BEITRAEGE AM SCHILDDRUESENFRAGE (THE GOITER PROBLEM). By Otto Bayard. Basel, 1919. Benno Schwabe & Co., 42 p.

The author likens goiter to beriberi, in that both may develop when patients go from one country to another, owing to differences of food encountered. He considers goiter as a deficiency disease, iodine being the lacking factor. Especially during youth the organism needs a large amount of iodine. The less iodine in the food the larger is the thyroid. In Kiel, situated at the seaside, the average thyroid is smaller than in Berlin. In Berlin it is smaller than in Munich. The size of the gland in Bern is larger than in Munich. The greater the distance from the sea, the larger the size of the thyroid.

The iodine has to be fixed in the cells of the body and the author believes (though why is a mystery) that it is fixed only in the nucleus. He applies Ehrlich's side-chair theory of anti-

toxin formation to the thyroid problem. In youth the cells have more receptors for thyrjod (the name the author gives to the active principle of the thyroid) than in advanced age. Therefore, during life the cells gradually lose these thyroid receptors. When the function of the thyroid is diminished there will be too small an amount of thyroid to saturate all receptors and some receptors which do not get saturated, disappear. When this happens during youth the cells come to have only the number of receptors that they otherwise have in more advanced years. Therefore . . . cretins have an oldish face and make an oldish impression. This conception, to the reviewer, seems downright fantastic.

As a prophylaxis against goiter the author recommends that the public be restricted from using salt for cooking except such as has been supplemented with potassium iodide (5-10 mg. to 5 k. of salt).

On the whole the book, while full of original ideas, contains so many unproved assertions as to demand a highly critical attitude upon the part of the reader.—J. K.

(IL PROBLEMA DELLA SONNO. LE AZIONI ORMONISCHE REGOLATRICI DEL FENOMENO.) SLEEP AND ITS HORMONE REGULATION. By Prof. Mario Barbara. Palermo, 1920. Scuola Tip. Boccone del povero. 39 p. 8°.

The author postulates as the essential feature in sleep an alternation of anabolic and catabolic predominance due in turn to alternately preponderating activity of "excito-anabolic" and "excito-catabolic" hormones. The problem as previously regarded is thus translated into newer phraseology.—R. G. H.

DIE REIZTHEORIE UND DIE MODERNEN BEHANDLUNGSMETHODEN DES DIABETES. By Priv. Doz R. Kolisch, Berlin and Vienna, 1918. Urban und Schwarzenberg. 152 p.

The question whether diabetes is caused by increased formative or diminished oxidation of sugar has given rise to an enormous literature. Claude Bernard was the first who considered increased formation as the cause. In Germany this theory was not accepted and well known specialists like Külz, von Noorden and Minkowski wrote against it. Kolisch was one of the first authors in Germany to support in his "Reiztheorie," the view of Claude Bernard. "Diabetes is caused by increased formation of sugar in the tissues. This is due to abnormal stimuli; these stimuli may be toxic or nervous." Though in the begin-

ning this theory received little credence, modern research has more and more supported it.

In this little book Kolisch describes his theory and discusses the literature pertaining to it. The best treatment is to try to diminish the abnormal stimuli by rest. Therefore, it is necessary to give as little food as possible to the patient, and not only to restrict the carbohydrates but also the protein. The influence of opium on glucosuria is very clear, considered from this point of view: it diminishes the irritability of the overstimulated nerves.

It is unfortunate that the author has written the last five pages of this book, wherein he discusses the Allen treatment in a way to indicate that he scarcely knows even the most fundamental things about it. Except for this last chapter the book is excellent and may be warmly recommended to those interested in the history of research in the field of diabetes.

Some figures quoted from the mortality statistics of Vienna are used by Kolisch as evidence of the value of under-nourishment in the prevention of death from diabetes.

DEATHS FROM DIABETES IN VIENNA, AND TOTAL MORTALITY

	Total Mortality		Cause of Death: Diabetes	
Year	Civilian	Military	Civilian	Military
1913	32,130	184	337	2
1914	31,480	1,788	292	2
1915	33,052	3,966	265	6
1916	33,494	4,137	265	15
1917	40,260	5,871	194	15

—J. K.

ABSTRACTS

ADRENAL insufficiency and war (L'insuffisance surrénale et la guerre). Agnel (E.), Thèse de Paris, 1918-19, **143.**

The importance of adrenal insufficiency in the pathology of war is discussed by Agnel. Its chief causes are overwork, wounds and infections of various kinds, of which the most important are dysentery, malaria, tuberculosis and various intoxications, such as food poisoning, alcoholism, chloroform, arsenobenzol, antityphoid and cholera inoculation and gas poisoning.—Med. Sc. Abst. & Rev., **2,** 133.

(ADRENAL) Recovery from Addison's disease. Anon. Lancet (London), 1920, **(i),** 923.

This editorial is devoted to the description of a case of Addison's disease ending in recovery. It was described by Giraudeau in his inaugural thesis (Paris, 1919-20, No. 31). Death occurred from cancer of the stomach eleven years later, when the autopsy findings confirmed the original diagnosis. Scar tissue was found in the right suprarenal, indicating the occurrence of inflammation many years previously. The nature of the lesion could not be determined. There was no evidence of tuberculosis or syphilis in the other organs. The case was treated with suprarenal extract for about six months, during which time all symptoms disappeared. Therefore Giraudeau concludes that in cases in which generalized and transient suprarenal incompetence is the result of a localized inflammatory lesion treatment may be effective, whereas it is of no avail in caseous tuberculosis of the suprarenals.—L. G. K.

ADRENAL extract as emergency medication in Erb's myasthenia during severe attacks (L'extrait surrénal total, médication d'urgence dans la myasthenie de Erb an cours des accidents graves). Marie (P.) & Bouttier (H.), Bull. et. mem. soc. Méd d. hôp. (Paris), 1920, 3. s., **44,** 575-581.

Report of a case of Erb-Goldflamm's myasthenia improved by the intramuscular administration of extracts of the whole adrenal gland.—F. S. H.

ADRENALS, Note on the development of — in the hedgehog (Note sur les développement de la surrénale du béris-

son). Célestino da Costa (A.) Compt. rend. Soc. de biol. (Paris), 1920, **83**, 878-879.

Of embryological interest.—T. C. B.

Grave ADRENAL insufficiency during influenza (Dos casos de insuficiencia suprarrenal grave durante la gripe). Clemente (M.), Siglo Med. (Madrid), 1919, **66**, 1057-1060.

Two cases are described. The suprarenal insufficiency was indicated by marked asthenia, vomiting, diarrhea, small pulse, extreme hypotension, lividity of the nose and extremities, Sergent's white line—in short, a syndrome amounting precisely to collapse with retention of the mental faculties. Energetic treatment with adrenalin by mouth and hypodermatically resulted favorably. [The abstractor has noted in various fatal cases of this type in the Hospital Gral at Madrid, that the adrenals were the site of well-marked lesions.]—G. M.

(ADRENAL) Addison's disease in a girl of thirteen years, death, autopsy (Maladie d'Addison chez une fille de treize ans, mort, autopsie). Comby (J.), Arch. de Méd. d. Enf. (Paris), 1917, **20**, 28.

Report of a characteristic case with caseation of both adrenals. Of interest because of the age.—C. H. G.

(ADRENAL) Association of a marked pigmentation and lichenous growth on the buccal mucosa during the course of an evasive adrenal insufficiency (Association d'une pigmentation considérable et d'un lichen de la muqueuse buccale au cours d'une insuffisance surrénale fruste). Crouzon & Bouttier, Bull. et mem. Soc. d. med. hôp. (Paris, 1920, 3. s., **44**, 67-71.

A detailed case history unamenable to abstracting.
—F. S. H.

(ADRENALS) Treatment of tuberculosis with adrenochrom (Adrenochrombehandlung der Tuberkulose). Diesing, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 598-599.

Adrenochrom is an extract from adrenals, made with alcohol, ether and benzine and containing adrenalin, sulphur and phosphorus. It is injected in doses of 0.2-0.5 cc. of 1:1000 solution. Adrenaline dilates the pulmonary vessels; sulphur diminishes the amount of oxygen in the lungs; phosphorus increases the formation of connective tissue. The author saw

splendid results in tuberculosis of the lungs and recommends it also in surgical tuberculosis.

[No histories of patients are reported; the article gives the impression of an advertisement rather than a report of serious pharmacological work.]—J. K.

ADRENAL-vascular syndrome (El sindrome suprarreno-vascular). Duran, La Clinica Contemporánea, 1918, ——, ——. Symptomalogical description without significant data. —E. B.

(ADRENAL) Chemical and morphological studies of cholesterin and cholesterin esters in normal and pathologically altered organs (Chemische und morphologische Studien über das Cholesterin und Cholesterinester in normalen und pathologische veränderten Organen). Fex (J.), Biochem. Ztschr. (Berlin), 1920, **104**, 82-174.

The free and combined cholesterin varies but slightly from the normal in the liver or kidneys in various pathological conditions. The free cholesterin of the adrenals shows no significant variations from the normal but the combined cholesterin esters vary greatly. These variations are attributed to a normal physiological fluctuation rather than to a pathological increase.—F. S. H.

ADRENAL apoplexy in small children (Nebennierenapoplexie bei kleinen Kindern). Friederichsen (C.), Jahrb. f. Kinderh. (Berlin), 1918, **87**, 109.

Friederichsen emphasizes the importance of adrenal hemorrhage and consequent acute adrenal insufficiency in the study of adrenal function and pathology. He reports two cases of patients, aged 3 and 10 months, respectively, and cites twenty-eight more from an extensive review of the literature. The majority of the cases occur in well developed, previously healthy children under one year of age. The onset is acute, with a cry and often with vomiting. There is a rapid development of cyanosis and pallor without dyspnea or pulmonary symptoms. The temperature is high, 39-41° C. The pulse is small, feeble and very irregular. Physical examination shows a normal heart and lungs. Cyanosis of the extremities rapidly appears and several hours after the onset and shortly before exitus it is replaced by a purpuric efflorescence. This begins as numerous dusky red petechiae, which rapidly spread and become confluent if not well nigh universal. Exitus occurs

six to twenty-four hours after the onset. Post-morten examination shows cutaneous and adrenal hemorrhages. The primary cause of the adrenal hemorrhage is unknown, though the author states that the acute onset and fever suggest an overwhelming infection. The clinical picture is similar to that following adrenal extirpation in animals, and the author believes it to be determined by an acute adrenal insufficiency. The purpura is secondary to this latter, perhaps as a result of a loss of peripheral vascular tone with consequent stasis. The author draws an interesting analogy between the purpura and the bronzing in Morbus Addisoni. The prognosis is determined by the degree of disturbance of adrenal function and two cases are cited in which old adrenal hemorrhage was found at autopsy. Adrenalin therapy is indicated.—C. H. G.

(ADRENAL) Case of malignant adrenal cortex tumor with metastasis in the liver (Ein Fall von maligner Nebennierenmarkgeschwulst mit diffuser Metastase der Leber). Fujimori (Yuhei), Verhandl. d. japan. path, Gesellsch. (Tokyo), 1916, **6,** 187.

An autopsy report. The subject was a woman of 35. The metastatic growth had completely infiltrated the liver, which was enlarged to a weight of 745 grams.—R. G. H.

(ADRENALS) Plethysmographic exploration of the blood circulation in the suprarenal capsule (Exploration plethysmographique de la circulation sanguine dans la capsule surrénale. Hallion (L.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 335-336.

Description of a plethysmograph for studying the circulation in the adrenals.

(ADRENAL) A case of congenital sympathetic neuroblastoma combined with Addison's disease in a child (Ein Fall von Neuroblastoma sympaticum congenitum, combiniert mit Morbus Addisonii bei einem Kinde). Hertz (P.) & Secher (K.), Jahrb. f. Kinderh. (Berlin), 1918, **87,** 367, 1pl.

A case report with a record of complete clinical and pathological findings.—C. H. G.

(ADRENALS) The functional connection between the suprarenal cortex and other glands of internal secretion, in white rats. Hewer (Evelyn E.), J. Physiol. (Lond.), Proceedings 1920, **53,** xcvii-xcviii.

A preliminary communication. Both feeding and inoculation experiments are being carried on. The work is not complete.—T. C. B.

(ADRENAL) On the suprarenal glands in congenital syphilis. Jubo (M.), Verhandl. d. jap. path. Gesellsch. (Tokyo), 1919, —, 59.

The author concludes that there must be some relation between congenital syphilis and status thymicolymphaticus since in both cases similar alterations are found in the suprarenals, which are characterized chiefly by hypertrophy of the cortex and incomplete development of the medulla.—E. V. C.

The ADRENALS and pathology of war (Les glandes surrénales en pathologie de guerre). Loeper (M.) & Oppenheim (R.), Rev. gén. de path. de guerre (Paris), 1916-17, **1**, 123-141.

A somewhat extensive review of the voluminous French literature on the etiologic and therapeutic aspects of the suprarenal glands. The authors believe that the glands play an important role in muscular fatigue, exhaustion, and in the reactions to traumatism, infectious diseases, specific vaccinations, toxins and poisons. In short, one gathers that, in the minds of the authors, bodily weakness and adrenal deficiency are approximately interchangeable terms. In accordance with this conception, adrenal medication is extensively indicated. In more severe cases adrenin in doses of 3-4 mg. hypodermically or intravenously is recommended. In less severe cases adrenalin, 20-40 drops daily, by mouth, is advocated. Glycerine extracts of adrenal substance administered hypodermatically, are said to be remarkably efficacious in grave infections. In delayed convalescence, asthenia and chronic depression desiccated adrenal substance is used. It is reported that adrenal opotherapy has been largely employed among soldiers in accordance with the foregoing principles and much service thereby rendered.—R. G. H.

(ADRENAL) The so-called post-mortem suprarenal softening. Materna (A.), Arch. f. path. Anat. etc., (Berl.), 1920, **227**, 235-265.

Mild grades of central softening are commonly found in the adrenals. Most often it is associated with acute infections such as sepsis, pneumonia and intestinal inflammations. There is increase in weight, lymphocytic infiltration, hemorrhages,

edema and necrosis. In the cortex there is frequently pigmentary degeneration and rapid disappearance of lipoidal material.—Chem. Abst. **14**, 2023.

ADRENAL cortex tumor in a woman with virilism (Tumeur de la couche corticale de la capsule surrénale droite observée chez une femme et ayant provoqué l'habitus masculin). Mauclaire (P.), Bull. et Mem. Soc. de Chir. de Paris, 1920, ——, —— (May 25); Abst., Arch. méd. Belges, **73**, 263.

Mauclaire adds another case of virilism of suprarenal origin to those recorded in the literature by Appert, Launois, Auvray and Tuffier, Quinby, Thumin, Glynn and others. Mauclaire's case was that of a woman of 38, who, for the previous six years had noted the development of a tumor of the abdomen. During this time her menses became suppressed and her facial appearance altered to a masculine type. Her body, neck and chest became covered with hair. Her breasts atrophied and the feminine, rounded form of the body was transformed to the muscular male type. At operation a tumor was found in relation with the inner border of the right kidney. Histological examination showed it to be of suprarenal origin.
—R. G. H.

(ADRENAL) Pigmentation of the limbus corneae in Addison's disease (Über Pigmentation des Limbus Corneae bei Morbus Addisonii). Meesmann, Deutsche Med. Wchnschr. (Berlin), 1920, **46**, 644.

Demonstration of a case of Addison's disease in which there were not only the well-known pigmentations of the conjunctivae but also a closed ring of pigment on the limbus corneae. The pigment was situated in the middle and deep layers of epithelium. The walls of the lymph vessels were filled with pigment.—J. K.

ADRENAL insufficiency following the injection of novarsenobenzol in recurrent fever. Remarkable effects of adrenalin in this and another case, showing syndrome of toxic hemiparesis of like origin (Insuffisance surrénale aigue consecutive a l'injection de novarsénobenzol dans la fièvre récurrente. Effets remarquables de l'adrénaline dans ce cas, ainsi que dans un syndrome d'hémiparésie toxique de même origine). Monziols & Collignon, Bull. et mem. Soc. med. d. Hôp. (Paris), 1920, 3. s., **44**, 214-215.

The administration of 1 mgm. adrenaline is systematically followed out by the authors to counteract the symptoms

of adrenal insufficiency after the giving of 0.3 grams novarsenobenzol for recurrent fever. Uniformly favorable results are reported. The case of hemiparesis was similarly cured by the injection of 3 mgm. adrenaline the first day and 1 mgm. on each of the three succeeding days. The cause of the adrenal insufficiency is attributed to the rapid destruction of the spirochetes by the arsenical treatment and the resultant liberation of a large amount of toxins. These overpower the adrenals so that their detoxicating function can not operate to an adequate extent and symptoms of insufficiency result. Adrenalin is assumed to tide the patient over this period until his suprarenals are again able to cope with the conditions.

—F. S. H.

ADRENAL changes in experimental scurvy (Uber die pathologischen Veränderungen der Nebennieren bei experimenteller Barlowscher Krankheit nebst Gewichten einiger endokrinen Drüsen bei derselben). Morikawa (Y.), Osaka Igakkwai, 1920, **19,** 9.

The author has found the following changes in the suprarenals in experimental Barlow's disease in guinea pigs: (1) Increase in weight, (2) Increase in lipoidal content of the cortex, (3) Reduction in amount of doubly refractile fat, (4) Distribution of the lipoid in the zona fasiculata in three layers —an outer rich in lipoid, a middle poor in lipoid and an inner rich in lipoid. He concludes that this hypertrophy, which is similar to that found in polyneuritis gallinarum, indicates that the absence of a necessary vitamine is also an etiological factor in Barlow's disease.—E. V. C.

ADRENALS, Development of—in man (Considérations sur les capsules surrénales ou cours du développement chez l'homme). Mutel, Compt. rend. Soc. de biol. (Paris), 1920, **83,** 357-360.

An embryological and anatomical consideration of the causes of variation in the right and left glands. Non-proportional growth, fixity of the vascular pedicle and displacement of the neighboring organs are the three causes of the variation.—T. C. B.

ADRENALS, The smooth muscle fibers of the central vein of the— (Les fibres musculaire lisses de la veine centrale surrénale). Peindarie (J.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 958-960.

Description of a system of smooth muscle fibers connected with the central vein of the suprarenal and its principal affluants. The author thinks these muscular formations play an important role in the physiology of the gland. Emotive adrenal discharge appears to be only the result of general vaso-constriction of the veins, collectors of the secretion, which are compressed and emptied of their contents. This is said to invalidate the seductive hypothesis of Cannon.—T. C. B.

(ADRENAL?) Premature sexual development. Phillips (J.) & Lambright (G. L.), Arch. Ped. (N. Y.), 1920, **37,** 282.

The authors report a case of a girl seven years old who was 4 feet, 4 inches tall and weighed 73½ pounds. She gave a history of having been a robust child who developed unusually large breasts at the age of two years, pubic hair at five with well developed genitals. Between the ages of three and four years she was seized with convulsive attacks which gradually increased in severity; these resembled epilepsy, being ushered in with a cry, followed by clonic and tonic contractures of the right side of the face and extremities. Menstruation was established with an increase in the severity and frequency of these attacks. Examination showed a premature sexual development in that she presented pubic hair, axillary hair, breasts and broad pelvis, all of normal adult size. Her mentality was below par. The bones of the right side of the face and the femur were large. The authors give a short resume of the literature on the subject. No tumor was noted. X-ray examination of the skull and the sugar tolerance test were both negative. Because of the negative skull picture the negative sugar tolerance test and the absence of any definite pituitary or pineal pressure symptoms, the authors by exclusion take the case to be one of involvement of the adrenal cortex.

—M. B. G.

ADRENAL insufficiency, influenza and manic-depressive psychoses (Grippe, insuficiencia suprarrenal y psicosis maniacodepresiva). Rossi (Santín C.), Anales Fac. de Med. (Montevideo), 1919, **4,** 801-812.

Nine cases are reported in which manic-depressive psychoses developed during the weakness following influenza. The weakness was interpreted as indicating suprarenal deficiency. Similar evidence of the same sort was noted in cases of six other manic-depressives who had not had influenza. Adrenalin treatment proved beneficial, i. e., the patients' condition improved while they were receiving the drug. On this

basis a far-reaching theory is elaborated to the effect that the data reported lift the veil of mystery from this type of psychosis, indicate the etiology and point out the therapeusis.
—R. G. H.

(ADRENAL THYROID) Influenza as a pulmonary necrotic alveolitis involving the endocrines. Sajous (C. E. de M.). N. Y. Med J. (N. Y.), 1920, **111**, 837-846.

The Pfeifer bacillus upon reaching the alveoli of the lungs finds all suitable conditions for growth and develops colonies which arrest the function and cause necrosis of the alveoli. The alveolar lesions interfere with the respiratory processes of the system at large, thus causing asphyxia of all organs, including the adrenals, whose hormone enables the hemaglobin to be converted to oxyhemaglobin and sustains the tone of the arterioles. The thyroid exerts powerful influences on the general metabolism and its secretion and iodine are physiological constituents of an active factor in the systemic defense against infections which acts by sensitizing pathogenic bacteria to phagocytosis. It also facilitates the proteolytic activity of the enzymes, which serve to destroy or, rather, digest, bacteria. Hence, prophylaxis against influenza may be established by the inhalation of iodine fumes, by therapeutic doses of strychnine, which excites the adrenals, and by thyroid gland to increase general opsonic and phagocytic activity. The active treatment of influenza consists of absolute rest, calomel and salines, deep inhalation of iodine fumes and salicylates. When the temperature is down strychnine and adrenal preparations may be freely given.—H. W.

(ADRENAL-GONAD) Early development of the secondary sex characters in a two-year-old girl following a hypernephroma of the right kidney (Frühzeitige Entwicklung der sekund. Geschlechtecharaktere bei einem zweijahrigen Mädchen infolge einer Hypernephroms der rechten Nebenniere). Schiff (E.), Jahrb. f. Kinderh. (Berlin), 1918, 87, 519.

A clinical and pathological case report. The child was adipose, with marked hypertrichosis, the pubic hair being especially well developed. The breasts were normal. The sella was slightly enlarged. The histological examination showed the endocrine organs to be normal. Clinical differentiation from Frölich's syndrome was simple owing to the palpable abdominal tumor.—C. H. G.

ADRENIN. Pathological physiology of— (Contribucion al estudio fisiopatolojico de la adrenalina). Sepúlveda V (H.), Inaug. Dissertation, Santiago de Chili, 1917.

To determine the concentration of adrenin in the blood the author used the following technique: To 4 or 5 cc. of a 5 per cent solution of mercuric nitrate in N/10 silver nitrate in a tube graduated in small units blood serum is added drop by drop until there is complete precipitation. This requires 1 to 2 cc. of serum. The mercury salt forms a white gelatinous and the silver, a whilte caseous precipitate. This is filtered off. The filtrate is transparent or slightly opaque. To this is added, drop by drop, standardized permanganate solution until a light rose coloration is produced. By this technique the author determined a maximum value of 0.30 gms. per mil. of adrenin in normal adults. Determinations were made on ten subjects who were not fatigued. In subjects who were ill the quantity of adrenin averaged in general less than 0.30 gms. per mil. The determinations appeared to have considerable prognostic value. With findings of less than 0.12 gms. the prognosis is very grave; from 0.12 to 0.20, it is doubtful; above 0.20, the majority of the patients recovered.—J. R. P.

(ADRENIN) On the permeabilitv of the placenta for adrenalin in the pregnant rabbit and albino rat. Shimidzu (Yoshitaka), Am. J. Physiol. (Balt.), 1920, **52,** 377-394.

In multiparous animals there may be several fetuses of both sexes in one uterus; one pregnant animal, therefore, incloses several hormone systems. In deciduate animals these systems are separated by the placenta, and the question arises whether the placenta is permeable to these hormones. The aim of the present experiment is to learn whether adrenalin administered to a pregnant animal will increase the adrenalin in the fetus. Rabbits and albino rats were used. The conclusion is that the placenta is impermeable to adrenalin, to the extent at least, that we cannot increase the adrenalin of the fetal blood by subcutaneous injections of the drug into the mother.—T. C. B.

(ADRENIN) Essentials in measuring epinephrin output, with further observations on its relation to the rate of the denervated heart. Stewart (G. N.) & Rogoff (J. M.), Am. J. Physiol. (Balt.), 1920, **52,** 521-561.

A further reply to Cannon with protocols of experiments and a full discussion of the results. The paper should be read

in the original for numerous details. It is contended that the acceleration of the denervated heart by asphyxia cannot be taken as an index of increased epinephrin output; it may be obtained and may not be diminished after the adrenal veins have been ligated, after complete isolation of the adrenals from the circulation, and after complete removal of the adrenals. When it does not occur it is due to deterioration of the animal. There is no good evidence that asphyxia causes augmentation of epinephrin output by a direct action on the cells of the adrenal medulla. Opening of the abdomen does not interfere with the acceleration caused by asphyxia. The catheter method of estimating changes in the rate of epinephrin output is defective in principle. It can only measure changes in concentration. The fundamentally correct method is to collect the blood and assay it.—T. C. B.

(ADRENIN) The relation of the epinephrin output of the adrenals to changes in the rate of the denervated heart. Stewart (G. N.) & Rogoff (J. M.), Am. J. Physiol. (Balt.), 1920, **52,** 304-363.

A lengthy article in which the authors describe experiments showing that acceleration of the denervated heart is not a reaction by which the rate of epinephrin output can be measured. Clipping off the adrenal vein has no effect on the heart reaction caused by sciatic stimulation, although it markedly diminishes or abolishes reactions which are known to be genuine reactions to epinephrin. Acceleration of the denervated heart on sciatic stimulation is well obtained in cats which have had one adrenal removed and the nerves of the other sectioned, and also when both adrenals have been removed. The reaction is well obtained after opening the abdomen as in the operation for a cava pocket. When the reaction disappears after the removal of the adrenals it is not because of the absence of increased epinephrin discharge on stimulation of the sciatic, but for other reasons, such as deterioration of the animal which interferes with the reflexes involved in the reaction or with the capacity of the heart to accelerate its beat.

—T. C. B.

ADRENALIN and guanidin. Preliminary communication. Burns (D.) & Watson (A.), J. Physiol. (Lond.), Proceedings, 1920, **53,** xcix-c.

In the course of investigation on the action of guanidin on the neuro-muscular mechanism of mammals the adrenalin blood pressure reaction was used as a measure of sympathetic

irritability. The injection of 1 cc. of 1.7 per cent guanidin hydrochloride into the jugular vein of the cat produced no effect on the carotid pressure. Three minutes later 1 cc. of 1/1000 adrenalin caused a slightly supranormal rise of pressure which was sustained for at least double the normal time. A nerve-muscle preparation was subjected to a bath of 1/100,000 adrenalin, then 0.02 per cent guanidin hydrochloride, and again to adrenalin. On stimulation with a minimum break shock the contraction was supranormal in extent, duration and rapidity of onset. The guinea pig's uterus showed similar effects.—T. C. B.

(ADRENIN PITUITRIN) Experimental studies on the effect of anesthetics in shock. Cattell (McKeen), Am. J. Surg. (N. Y.), 1920, **34**, 89-91.

As an incidental part of the work, the effects of adrenin on the heart of animals in shock under ether anesthesia, were studied. After an overdose of ether certain animals were resuscitated by adrenin. It was found that this resulted in a marked lessening of the sensitiveness to ether, due to an influence exerted apparently on the heart, since stimulation of the peripheral blood vessels with pituitrin produced no such decrease of sensitiveness to the anesthetic.—R. G. H.

(ADRENIN) Attempt at poisoning by adrenaline (Tentative d'empoissonnement par la solution a adrenaline 1/1000e). Grasset (R.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 981-985.

The attempt to commit suicide by drinking 15 grams of adrenaline solution (1:1000) proved abortive, although two hours or more elapsed between time of the ingestion of the drug and medical treatment.—F. S. H.

Influence of ADRENIN on heat regulation (Über die Wirkung der Adrenalins auf die Warmeregulation). Kondo (S.), Acta Scholae Med. Univ. Imp. in Kioto, 1919, **3**, 169-205.

The author finds that adrenalin only brings about an increase in body temperature when it is administered in large amounts either subcutaneously, intravenously or intraperitoneally, and further, that when the vagi are treated with atropin or are sectioned this increase in temperature is inhibited. He is of the opinion that these observations indicate the existence of a double innervation: a sympathetic poisoned by adrenalin and a parasympathetic poisoned by atrophin.

Intra-cerebral injection of adrenalin increases the temperature only slightly after thyroid extirpation.—E. V. C.

ADRENIN medication in the persistent vomiting of pregnancy. (Vomissements incoercibles de la grossesse et médication adrénalique). Rathery (F.) & Bordet (F.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 778-784.

A report of a case of persistent vomiting in pregnancy of two months, during which the patient suffered from inanition and dehydration, accompanied by acidosis. After two or three days of treatment by injections of adrenaline in large amounts of normal saline, the symptoms ceased and did not reappear when the drug was withdrawn. The rapidity of the action of the drug is to be noted. The doses used were: First day, 0.5 mgm. subcutaneously; second day, 1 mgm. subcutaneously and 1 mgm. ingested; third day, same dose; fourth day and following seven days, 1 mgm. ingested. The increase in weight was very rapid and at the rate of one kilo per day for nine days. The medication used was not the extract but adrenaline; it did not cause glycosuria.—F. S. H.

ADRENIN, The behavior of the blood pressure curve after—injection in children with various pulse qualities (Über das Verhalten der Blutdruckkurve nach Adrenalininjektionen bei Kindern mit verschiedener Pulsqualität). Schiff (E. R.) & Epstein (B.), Jahrb. f. Kinderh. (Berlin), 1920, **91**, 128.

The authors found that children with normal pulse quality react to adrenalin with a marked blood pressure increase. On changing from the upright to the horizontal posture the blood pressure is unchanged. Pale children with pulse of poor volume and tension but without appreciable vaso-lability react with a minimal blood pressure increase or none at all. On lying down the blood pressure increases 20-30 cm. of water. Pale children with pulse of poor tension and volume, with apparent vaso-lability, show a prompt but very slight blood pressure increase and no change upon standing or lying down. The response found in the latter two groups is rather uncritically ascribed to a functional inferiority of the vascular system leading to a defective response to stimulation of the vasomotor innervation.—C. H. G.

(ADRENIN) Circulatory disturbances in the acro-contractures. Direct muscular adrenalinization and electric reactions (Troubles circulatoires dans les acro-contractures. Adrénalization musculaire directe et réactions électiques).

Sicard, Roger & Simom. Bull. et mem. Soc. med. d. hôp. (Paris), 1917, 3. s., **41,** 811-814.

The injection of adrenalin directly into the living muscle substance results in fibrillary contractions and hyperexcitability to both mechanical and electrical stimulation.—F. S. H.

A case of general, absolute ALOPECIA of emotional origin (Un caso di alopecia generale assoluta do origine emotiva). Todde (Carlo), Riforma med. (Napoli), 1920, **36,** 382-383.

The A. reports a case of a soldier of 34 who had previously been wounded and then released from the service in Italy, only to be called again to the colors and sent to France, where he had to stand a week of bombardment from airplanes. After this trying period he began to lose his hair, at first from the exposed parts, afterwards from the whole body. He had never before had any infection or skin disease except phlectenular conjunctivitis, but was of lymphatic constitution. The family history indicated hereditary nervous taint and the subject presented certain symptoms suggesting exophthalmic goiter. His case was accordingly classified as an endocrine disturbance and he was put under treatment of pluriglandular therapy. Boschi has reported the case of a woman whose hair dropped out after severe emotional stress but reappeared under thyroid treatment.—G., V.

AMAUROTIC FAMILY IDIOCY, or infantile amaurotic idiocy. Epstein (J.), Med. Rec. (N. Y.), 1920, **97,** 224-227.

Epstein reports five cases of this unusual disease. "It may not be impossible that the much wanted etiology will ultimately be found in some abnormal action or reaction in the endocrine group which has a profound influence over the general metabolism and the life history of the nerve cells. But, at present, there is no evidence of an endocrine pathology in infantile amaurotic idiocy."—H. L.

Endocrine factors in bronchial ASTHMA (Endokrinen Grundlagen des Bronchialasthmas). Curschmann (H.), Deutsch. Arch. f. klin. Med. (Leipzig), 1920, **132,** 362-378.

Asthma may be related to and caused by endocrine disturbances, though medical men rarely think of this fact. The author observed two cases of intermittent Graves' disease. Each time the symptoms reappeared the patient had attacks of asthma. That there exist relations between asthma and the parathyroids is well known. Attacks of asthma with symp-

toms of tetany (so-called broncho-tetany) have been repeatedly described. These cases are cured by calcium, which is a specificum against tetany. Whether the adrenals are related with asthma is not known. Real asthma during Addison's disease has never been described. Hyperfunction of the adrenals is only observed as sympathicotonia in Graves' disease. In these cases asthma has never been observed. The ovaries have an influence as is proved by the asthma beginning in the menopause. The author describes one case (which does not prove much.—J. K.). In another case asthma regularly returned during menstruation. Relations between asthma and the testicles are not known. It is possible that the hypophysis has an influence. A case is described in which diabetes insipidus and asthma developed at the same time. Post-mortem examination disclosed a tumor of the mediastinum with metastasis in both adrenals, hypophysis, lungs, kidneys and spleen. The author believes that these facts may prove of great importance in relation to treatment. In cases in which asthma begins in the menopause, the ovary should be treated. When there is hypothyroidism, thyroid may be given also. Curschmann has seen no good results with hypophysis medication in asthma, though it has been recommended by Borchhard.
—J. K.

CAROTID GLAND, Adenoma of the— Reid (M. R.), Johns Hopkins Hosp. Bull. (Balt.), 1920, **31**, 177-185.

Not of immediate endocrine interest.—R. G. H.

CORPUS LUTEUM in neurological practice. Climenko (H.), N. York M. J. (N. Y.), 1918, **109**, 302-305.

See Endocrin., **3**, 1-15.

CORPUS LUTEUM, The nausea and vomiting of pregnancy. Davis (C. H.), Wisconsin M. J. (Milwaukee), 1920, **18**, 513-518.

No beneficial results followed the administration of corpus luteum in cases that gave a history of ovarian insufficiency and abortions.—H. W.

(CORPUS LUTEUM) Experimental histological studies on the origin of the corpus luteum. Hirose (T.), Tokyo Igakkwai, 1920, **34** (No. 2).

Mention is first made of the two conflicting theories regarding the origin of the lutein body. According to the first

(Sabotta), the lutein cells arise from the granulosa; while according to the second (Johann), they become differentiated from the cells of the theca interna. The author used the following criteria for differentiating between the corpus lutein cells and the theca lutein cells: (1) Relation to the connective tissue, (2) location in reference to the hyaline limiting membrane, and (3) fate of the granulosa cells. He used as material the ovaries of 16 rabbits taken from 5 hours to 21 days after copulation, and of 10 pregnant and 16 non-pregnant women. He concluded that the lutein cells of the corpus luteum and the interstitial cells arise from the cells of the theca interna. The paper is well illustrated and a good deal of literature is reviewed.—E. V. C.

(CORPUS LUTEUM) War amenorrhea (Über Kriegsamenorrhöe). Köhler (H.), Zentralbl. f. Gyn. (Kiel), 1919, **43,** 359-368.

A clinical report of four cases of amenorrhea in which microscopic examination of the ovaries led the author to the conclusion that the "war amenorrheas" are primarily due to disturbances of nutrition which in turn cause a lack of functioning of the corpus luteum.—F. S. H.

(CORPUS LUTEUM) Preservation of the procreative function in women. Langstroth (F. W.), N. Y. Med. J. (N. Y.), 1920, **111,** 982-986.

Langstroth cites an instance of a woman who suffered one or two severe headaches each month, similar headaches following the administration of corpus luteum preparations. The author believes this subject had an anaphylactic reaction to her own corpus luteum secretion. Extensive surgical repair work was done but the headaches continued.—H. W.

CORPUS LUTEUM extract in vomiting of pregnancy. Quigley (J. K.), N. Y. State J. M., 1919, **19,** 306.

Data reported elsewhere. See Endocrin., **4,** 115.

The DUCTLESS GLANDS and constitutional diagnosis. Gutman (Joseph), Med. Rec. (N. Y.), 1920, **97,** 558-561.

"In the interpretation of a case from the constitutional standpoint several fundamental facts concerning the functions of the ductless glands upon which the study of human constitutions is based must be borne in mind: (1) The effect of the

inherited powers of the endocrine system upon the development of the individual; (2) their control of all metabolic processes of fundamental importance; (3) their domination of all vital functions occurring during the three cycles of life; (4) their co-operative method of functioning and intimate relationship, and (5) the consequences resulting from a derangement of their functions or of glandular dyshormonism." Gutman agrees with Fraenkel's classification of endocrine constitutions: the thyrotrope, adrenotrope and pituitotrope, and the mixed types. The subject in case of each type is peculiar in build, height, skin, hair, mental capacity, character, ambition and predisposition to certain diseases. "Whether an individual is to be tall or short, lean or corpulent, graceful or awkward is all dependent upon the peculiar reaction of the different glands individually and collectively." The author believes the cardiovascular, gastrointestinal, vasomotor, respiratory, sexual and other systems fully subservient to the glandular hormones. According to Gutman every functional expression is not an accident but a corollary of endocrine expression.—H. L.

Further development of an interesting case of ERB-GOLDFLAM'S DISEASE and remarks on the nature of this disease (Ulteriore decorso di un interessante caso di morbo di Erb-Goldflame ealcune considerazioni sulla natura di questa malattia). Capezzuoli (Cesare), Riv. crit. di clin. med. (Firenze), 1920, **21**, 97-114.

After a detailed report of a case the author insists on the desirability of further study of this disease on the basis of endocrine dysfunction (pluriglandular), as it seems justified from the frequent accompanying lesions of the thymus, of the thyroid, hypophysis and parathyroids. Its being found often mixed with other endocrine syndromes as well as its familiar type and the usual determining causes give a new weight to his hypothesis. In other words, he considers the syndrome as an individual idosyncrasy to abnormal products of endocrine dysfunction, sufficient to bring about the disease in hypersensitive subjects.—G. V.

(DWARFISM) The metabolism of a dwarf. Talbot (F. B.), J. Am. M. Ass. (Chicago), 1920, **74**, 1225.

A basal metabolism study of a dwarf boy. He was seven years of age, weighed, clothed, 12.6 K. (normal weight for boy of seven years is 21.9 K.) and was 91.5 cm. in height (normal, 114.3 cm.) The author found that the total metabolism for

twenty-four hours was 780 calories as compared with an average of 900 calories for a normal boy of the same age. This is almost within the normal limits of variation. When the total calories for twenty-four hours were compared with those of boys of the same weight, it was found that he was producing more than the average (780 against 675). This is slightly above the possible variations from the normal. When his metabolism was considered from the viewpoint of unit of body weight, it was found to deviate markedly from the normal. His calories showed an increase of 45 per cent (58 calories per Kgm. against 40 for a normal boy of the same age) and his metabolism per Kgm. of body weight, an increase of 13.7 per cent above the normal. His metabolism per unit of body surface was 12 per cent higher than that of normal boys of the same age and 11 per cent higher than that of normal boys of the same weight. There was no clinical evidence of any disturbance of the glands of internal secretion.—F. C. P.

(DIABETES) Experiments on carbohydrate metabolism and diabetes. I. Intravenous glucose tolerance of dogs. Allen (F. M.) & Wishart (M. B.), J. Biol. Chem. (Balt.), 1920, **42**, 415-458.

The paper forms the first of a series concerning the endocrin function of the pancreas. The results reported are generally in harmony with those of other workers and demonstrate that in dogs rendered diabetic or near-diabetic by partial depancreatization there occurs a reduction of sugar tolerance, although marked exceptions occur. Extensive tables are given in lieu of protocols.—F. S. H.

Experiments on carbohydrate metabolism and DIABETES. II. The renal threshold for sugar and some factors modifying it. Allen (F. M.) & Wishart (M. B.), J. Biol. Chem. (Balt.), 1920, **43**, 129-147.

Extensive experiments on dogs, either completely or partially depancreatized, demonstrate that a diminished renal permeability for glucose in the sense of a raised threshold is definitely proved as the rule in diabetic animals. As the same rule holds for the great majority of human diabetics, this demonstration furnishes one more point of similarity between the experimental and clinical conditions. Various possible causes for the elevation of the threshold are discussed. The prolonged excess of sugar in the blood may be an important factor, but some considerations seem to oppose it. Certain observations suggest that high fat diets may raise the sugar

threshold in diabetes even without acidosis. The renal function may be affected by various extraneous causes, of which the elevation of the threshold by epinephrine is one interesting example. No interrelation of the renal and pancreatic functions is demonstrable in the sense of an increased readiness of sugar excretion even in totally depancreatized animals. An elevation of the threshold seems to be connected particularly with severity of the diabetes, but a teleological interpretation of this as a protective mechanism for saving sugar to the body is considered dubious—F. S. H.

(DIABETES) Estimations of sugar in the blood in the diagnosis and treatment of diabetes. Cammidge (J. P.). Practitioner (Lond.), 1920, **104**, 114-130.

The author describes the methods of Lewis and Benedict, Folin and Wu, and his own for estimating quantitively the sugar in the blood. He emphasizes the range in sugar values which lie within normal limits, 0.06 to 0.14 per cent, and how such variations depend upon the nature of the food and the time after a meal the determination is made. The blood sugar curve in diabetes is similar in form to the normal, but it has a wider time relation and attains a greater height as a rule. In severe cases a permanent hyperglycaemia is established and the percentage of sugar in the blood never drops within normal limits, even after a night's fast. In a normal person the difference between the percentage of sugar in the blood two hours after the sugar has been swallowed and when fasting should not exceed 0.01 per cent. A study of over 700 cases of diabetes induces the author to believe that there is no constant blood-sugar level for the appearance of sugar in the urine in quantities recognizable by ordinary test; and also that there is no definite relationship between the percentage of sugar in the blood and either the percentage or total amount of sugar excreted by the kidneys. Hyperglycaemia may exist without glycosuria and is sometimes the cause of boils, carbuncles, sciatica. Patients with a permanently high blood sugar may pass comparatively little sugar in their urine, while, in some instances, a normal, or even a subnormal, blood sugar curve may be associated with frank glycosuria. In either condition, examination of the urine alone does not give a correct picture of the case, and, if it is not checked by blood sugar estimations under controlled conditions, may readily lead to mistakes in diagnosis and treatment. As a rule, young diabetics have a lower threshold point for clinical glycosuria than those of middle age, and the threshold rises with advancing

years. It is, therefore, important that the presence of even small amounts of sugar in the urine of persons of middle age should not be dismissed as of little significance, unless a series of blood tests have shown that their tolerance for carbohydrates is not seriously defective. Hyperglycaemia may exist without clinical glycosuria, that is with an insufficient percentage of sugar in the urine to give the ordinary tests for sugar. The reverse condition, glycosuria with a normal or subnormal percentage of sugar in the blood, is not as uncommon as is generally supposed. Twenty-five per cent of obese people have hyperglycaemia without glycosuria. Cases of glycosuria with normal blood sugar are either examples of latent diabetes or renal diabetes. The former group, Cammidge believes hepatic in origin; the latter, a congenital abnormality depending upon abnormal permeability of the kidneys for sugar. He reports a unique instance of renal diabetes in father and daughter. He considers a low blood sugar content in ordinary diabetes as a good sign even when a large amount of sugar is being passed in the urine. Such patients become sugar free more rapidly and ultimately acquire a comparatively high tolerance. He believes that hyperglycaemia even without glycosuria is more readily controlled if the fat content of the diet is materially reduced. He writes: "Permanent success in the treatment of diabetes can only be secured by keeping the blood sugar curve within normal limits, even though more severe restriction of the diet may be necessary to attain this end than is required to keep the urine sugar free." He considers a high blood sugar level with no glycosuria more serious than a low blood sugar level with moderate glycosuria. Hyperglycaemia occurs in other conditions than diabetes. In nephritis its presence is a serious omen and indicates a speedy termination. High blood sugar curves are frequently encountered in carcinoma and hyperthyroidism.

—H. L.

(DIABETES) The prevention and treatment of diabetic coma. Cammidge (P. J.), Lancet (London), 1919, **(i)**, 60-64.

The author maintains that acidosis can no longer be accepted as the sole cause of diabetic coma, but that it is often an associated or merely an incidental phenomenon. The failure of alkali therapy has been one of the main stumbling-blocks in the way of a general acceptance of the acid intoxication theory. Coma is rather to be considered as the consequence of auto-intoxication, but the available evidence suggests that it is a toxemia resulting from the general failure of metabolism occurring in diabetes, instead of from a specific toxin

originating in a break in the chemistry of the body in one particular direction. It is likely that coma is produced by several toxins of different origin acting together. Probably toxic substances resulting from abnormal protein metabolism are responsible for a part of the symptomatology of diabetic coma. A deficiency of inorganic salts may also be a factor. In order, therefore, to prevent coma the diet must be arranged in such a way that: (1) The patient's tolerance for carbohydrate, fat and protein is not exceeded; (2) the total load of food is within his metabolic capacity; (3) the diet is correctly balanced; (4) a sufficient supply of inorganic salts is provided. If coma has already developed absolute, rest in bed is essential. The bowels should be cleared by enemata. The diet should consist of 2 ounces of lemon juice and 7 to 8 ounces of potato or 2½ to 3 ounces of oatmeal taken in the form of gruel, in small quantities, at 3 to 4 hourly intervals over the 24 hours. As much liquid as possible should be administered. If speedy improvement does not occur alkaline injections should be tried. Massive doses, controlled by repeated examinations of the blood or by estimations of the alveolar CO_2 are necessary. Cardiac stimulants are advisable at an early stage.—L. G. K.

Syphilitic DIABETES due to sclero-gummatous pancreatitis (Diabète syphilitique par pancréatite scléro-gommeuse). Carnot (P.) & Harvier (P.), Bull. et mem. Soc. med. de hôp. (Paris), 1920, 3. s., **44.** 71-76.

Clinical and post-mortem report of a case of diabetes in a syphilitic due to gummous lesions of the pancreas. The subject, a woman of 53, had shown symptoms of neurosyphilis and diabetes for about two years. The urine had been abundant and had contained from 66 to 72 gms. of sugar per liter. Death was due to pneumonia. The pancreas was found to be transformed almost entirely into a sclerogummatous mass. The authors regard this as the first reported case of diabetic manifestations due unquestionably to syphilitic lesions of the pancreas. Four other cases from the literature are cited but in these autopsy showed only ordinary sclerosis of the pancreas. —F. S. H.

DIABETES A Roentgenologic study of the gastro-intestinal tract in—; a report of seventy-two cases. Case (James T.), J. Am. M. Ass. (Chicago), 1916, **67,** 858-861.

Case found that in diabetes gall bladder involvement is very common. The stomach empties with unusual rapidity.

Duodenal stasis is rare but illiac and low grade colonic stasis is very common.—R. G. H.

(DIABETES) The amount of tissue hydration in diabetes mellitus (Le taux d'hydration des organes dans le diabete sucré). Chauffard (A.), Brian (Mille. P.) & Jacobs (J.), Bull. et mem. Soc. med. de hôp. de Par., 1918, 3. s., **42**, 49-51.

From a comparison of the water content of the tissues of a normal (?) individual with the tissues of one dying in diabetic coma and one having diabetes but dying of tuberculosis, the authors are of the opinion that among diabetics it is only those dying in coma who give evidence of tissue dehydration as the result of the pathological processes. [See also Chauffard, Endocrin., **4**, 144.]—F. S. H.

DIABETES MELLITUS, The limitation of starvation in ——. Edgar (T. W.), N. Y. Med. J. (N. Y.), 1920, **111**, 803-806.

Starvation of diabetics will cause a loss of sugar in the urine, but at the same time it results in the production of acidosis and ketonuria. The prevention of acidosis, therefore, is the logical treatment of this disease. This is accomplished by alkinization and a diet sufficient to maintain weight. The Edgar serum which "contains the internal secretion in hormone form" is capable of increasing the carbohydrate tolerance of certain cases from 25 to 60 per cent and arrest the progress of the disease. The serum is obtained from rabbits after they have undergone a series of maneuvers calculated to activate the various endocrine organs to augmented activity.—H. W.

(HYPOPHYSIS) Diabetes insipidus after meningitis serosa (Diabetes insipidus in Anschlusz an Meningitis serosa). Foerster (A.), München. med. Wchnschr., 1920, **67**, 694-696.

Report of a case. Subcutaneous injection of extract of the posterior lobe of the hypophysis gave temporary improvement. The most active drug is pituitin; less action was seen from pituglandol. Hypophysin had no effect whatever.—J. K.

(DIABETES) Transitory glycosuria of renal type. The relation between renal diabetes, phlorizin-glycosuria and diabetes mellitus (Transitorische Glykosuria mit renalem Typus. Das Verhältnis des renalen Diabetes zur Phlorizin Glykosurie und zum Diabetes mellitus). Galambos (A.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 600-602.

No new facts. A case is reported of a young man with a transitory renal glycosuria. The amount of carbohydrates ingested had no influence on the glycosuria. The amount of blood sugar was normal. Only when glycose was given or phloridzin was injected was the quantity of sugar in blood and urine increased for a short time. It is sometimes very difficult to differentiate renal glycosuria from ordinary diabetes. The author observed a case of classical renal glycosuria with acidosis.—J. K.

(DIABETES) Epileptic attacks during diabetes with acidosis (Crises épileptiques au cours d'un diabète avec acidose). Guillain (G.), Bull. et mem. Soc. med. de hôp. (Paris), 1920, 3 s., **44**, 808-810, Abst., Prog. Méd. (Paris), 1920, **35**, 302.

A case report. The case is reported of a patient who, during the course of two months, developed acute diabetes with polyuria, polydipsia, polyphagia and emaciation. During this time he suffered numerous epileptic attacks with left hemiparesis, the crises coinciding with marked acetonuria. The convulsive attacks were highly characteristic, with contracture, biting the tongue and incontinence of urine. They ceased after several days' intensive alkaline treatment; at the same time the hemiplegia receded. This hemiplegia was no doubt of toxic cortical origin. The Babinski sign was consistently negative.—R. G. H.

The history of DIABETES mellitus. Horwitz (P.), N. Y. Med. J. (N. Y.), 1920, **111**, 807-812.

An interesting survey of the history of diabetes mellitus. —H. W.

DIABETES, Advantages of class instruction in the treatment of—. Janney (N. W.), N. Y. Med. J. (N. Y.), 1920, **111**, 806-807.

The treatment of diabetes should consist of immediate attention and the education of the patient to appreciate his condition and care for himself. Where possible, classes of instruction are of decided benefit in the handling of such cases.—H. W.

DIABETES and exopthalmic goiter (Diabète et goitre exopthalmique). Labbé (M.), Bull. et mem. Soc. med. d. hôp. (Paris), 1919, 3 s., **43**, 955-962.

The non-fortuitous coincidence of diabetes and exopthalmic goiter is well brought out by the author's description and discussion of 5 cases in which the two disorders occurred in the same individual. In one of his cases the woman developed goiter at 20; glycosuria became installed at 50, and at 54 the symptoms of severe exopthalmic goiter developed and the diabetes became aggravated. Each time there was a hyperthyroid attack, with tachycardia, the sugar content of the urine and blood ran up high, scarcely modified by dietetic measures, but subsiding with the paroxysm of hyperthyroidism. He cites Manby, Lancereaux and others' reports of instances of diabetes in some members of a family and exophthalmic goiter in others. All types of diabetes apparently may occur with exophthalmic goiter, but in general they seem to be more resistant to treatment than do the ordinary uncomplicated cases. Hereditary influences seem to play a part and the disorder easily runs into an acidotic condition which may be associated with the disturbed nitrogen metabolism of the goitrous. Therapeutically the medicaments, such as quinine and salicylate, which act against the goiter, also retard the glycosuria. In two of the cases cited iodine treatment was successful; at the same time that the palpitations and tachycardia subsided, the glycosuria also decreased. Labbé is of the opinion that the diabetes of Basedow's disease is probably the result of a functional disturbance of the thyroid.—F. S. H.

(DIABETES) L'épilepsie acidosique. Labbé (M.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44,** 810-811; Paris Méd., 1920, **10,** 354-358.

Report of 4 cases of diabetes in which epileptic seizures occurred accompanied by acidosis, together with a discussion of the literature. Labbé concludes that diabetic epilepsy is a manifestation of acidosis. In cases of acidosis in which there is no cause for assuming uremia or any other intoxication, occasionally epileptiform seizures develop which it seems justifiable to associate with acid intoxication. They are localized or general, and are followed by loss of consciousness, either transitory or prolonged. They may precede diabetic coma, or appear after the diabetic coma has begun, or occur long before coma sets in.—F. S. H.

Experimental pancreatic DIABETES after partial pancreatectomy. Langfeldt (E.), Acta Med. Scand. (Stockholm), 1920, **53,** 1-192.

This number of the journal is devoted exclusively to an account of Langfeldt's two years of researches on the develop-

ment of glycosuria in dogs of different ages after partial pancreas ablation. In order to make the metabolism of the animals more like the human metabolism, the dogs were fed on carbohydrates without meat for a long period of time before the operations. Four dogs, prepared in this way, were operated upon. The tolerance for carbohydrates was tested, giving glucose by mouth; normal dogs of the same litter served as control animals. Two of the dogs were operated, when 3-4 months old, 8/9 and 7/8 of the pancreas, respectively, being removed. For 3 months after the operations the tolerance decreased; then it increased and reached that of the control animals. Six to eight months later the tolerance gradually decreased and the dogs developed chronic diabetes. When 8/9 of the pancreas was removed in a fully grown dog, glycosuria developed immediately after the operation. In the last dog operated on as a puppy, 6/7 of the pancreas was removed. The tolerance was repeatedly tested; it was not decreased until one year after the operation. Different portions of the pancreas were removed in different cases, but with no change in results. The chronic diabetes of the dogs showed close resemblance to the human type, the symptoms being polydipsia, polyuria, loss of weight, ketonuria, albuminuria and cataract. The D:N ratio was relatively high and the nitrogen excretion in hunger, low. The ketonuria reached a considerable degree. The diabetic dogs died 8 and 13 months, respectively, after the operations, while the others were killed when the tolerance decreased. In the diabetic dogs no islands of Langerhans were found at autopsy, but they were intact in the animals without spontaneous glycosuria. The findings thus confirm the preponderance of the pancreas in all diabetic phenomena. It appears to have a catalytic action. When the sugar content in the blood reached a higher level than 0.19 per cent, glycosuria followed. Duration of the high sugar content was of greater import than higher concentrations for shorter periods. The article is in English. The autopsy findings are illustrated by 12 photomicrographs. A bibliography of 167 titles is included.—K. M.

DIABETES, The relation between creatinuria and acidosis in—(Forholdet mellem Kreatinuri og Acidose ved Sukkersygen). Lauritzen (M.), Ugesk. f. Læger, (Copenhagen), 1919, **81**, 1595-1605.

After a résumé of the literature of this subject and a description of the technique he has adopted, Lauritzen gives details of several cases of diabetes illustrated with charts, in

which he analyzed the daily excretion of nitrogen, creatin, and ammonia. The first case showed that the excretion of creatin followed a curve parallel with that of the excretion of ammonia. Only during two "hunger days" did these two curves fail to run parallel. This parallelism of the creatinuria and ammonia excretion was also observed in several other cases. In one case the acetonuria and diaceturia were greatest when the creatinuria was at its highest. Lauritzen suggests that the curves of creatinuria and ammonia excretion ran parallel because the diabetic diet affected acidosis and creatinuria in the same way. When, in slight cases of diabetes, creatinuria appears before acetonuria, this, he suggests, shows that restriction of carbohydrates in the diet leads to creatinuria more readily than to acetonuria. He believes that there is insufficient evidence for assuming that acidosis per se leads to creatinuria in diabetes. It is more probable that faulty carbohydrate metabolism is the common cause of both these conditions. He dismisses as untenable the hypothesis that the creatinuria of diabetes is due to incomplete conversion of creatin to creatinin, with consequent excretion of creatin in the urine.

Probably the demonstration of creatinuria before the development of acetonuria will prove of little value in connexion with the early diagnosis of a pre-comatose state, for its onset is indicated by symptoms easier to gauge than creatinuria. But it may be of benefit to the diabetic that creatinuria is combated, for if it is protracted it may contribute to weakness of the muscular system. And, as these investigations show, creatinuria can be controlled by the same dietetic treatment that reduces acidosis. The degree of creatinuria is of prognostic significance: if it is considerable and continuous, it is of bad omen.—Med. Sc. Abst. & Rev., **2**, 296.

DIABETES, coma as a cause of death in ——. McCay (D.), and others. Indian J. Med. Research (Calcutta), 1919, **7**, 22-80.

The absence of acidosis during the course of the treatment of diabetes and even in terminal coma indicates that coma as a terminal phenomenon in diabetes as found in India is unlike European diabetic coma. It is probably uremic. McCay gives evidence that without true nephritis, simple albuminuria may lead to fatal uremia. For comparison blood analyses of 25 normals were made. In 10 walking cases of simple glucosuria without albuminuria somewhat higher values were found for non-protein N (N. P. N.), urea and the ratio N. P. N.:total N.

In 45 cases of albuminuria without glucosuria and 26 cases of albuminuria with glucosuria a retention of urea or other N. P. N. and an increase in the N. P. N.:total N. ratio were found. Blood phosphates were normal and but slight changes occurred in blood alkalinity, as determined by Wright's method, in 71 cases but anti-diabetic treatment (milk and green vegetables) assisted in the elimination of N-waste products. In 25 cases of uremia and severe kidney involvement there is a still greater retention of N. P. N. with or without increase in urea. The N. P. N.:total N ratio in severe cases was from 1:5 to 1:15. A retention of phosphates and a decrease in blood alkalinity were also observed in severe cases. In uremia of chorea, anuria from whatever cause, and eclampsia, the retention of N. P. N., urea and phosphates and the decrease in alkalinity were marked. Acetone was found in the urine and blood of some cases but not of others just as ill. In 13 cases in the terminal stages of diabetes as seen in India, diacetic acid and acetone were generally absent. Positive results of other workers using the $FeCl_3$ test are due to the alkaline condition of some urines. Acidosis and diabetic coma practically do not occur in India, but the terminal coma in India is uremic and not diabetic. The fundamental derangement of the kidneys that accompanies diabetes is the important factor leading to coma and death. Typical "air hunger" is never found among natives. Two cases of diabetes among Europeans had "air hunger" and acidosis.—Chem. Absts., **14**, 2368.

The treatment of DIABETES in India. McCay (D.) and others, Indian J. Med. Research (Calcutta), 1919, **7**, 81-147.

The incidence of diabetes among the indolent well fed classes; its comparative rarity among working classes; and the fact that meat-eating Mohammedans living under otherwise identical conditions with the Hindu, escapes, while his indolent, sugar-sodden companion develops the disease, all point to causative influence exerted by the ill effects of a prolonged and excessive, one-sided carbohydrate dietary. There is an apparently close association between the one-sided carbohydrate type of diet and decreased HCl of the gastric juice, fermentative dyspepsia, oxaluria or renal calculus, hyperphosphaturia and glucosuria. The oxaluria is a sign of gastro-intestinal catarrh that often precedes glucosuria. The evidence points to a slow atrophy of the pancreas. The authors confirm the fact that extracts of liver and trypsinogen lessen the excretion of sugar for short periods, and found the rice, soy bean and oatmeal cures worthless. In hundreds of cases

they found no starvation period necessary, and in Indian diabetes could always clear up the sugar excretion and lower the blood sugar by removal of carbohydrates from the diet. Patients rarely die from diabetes as found in India and it seldom passes into the graver forms of the disease. Reduction of the carbohydrate intake is practically never followed by severe acidosis. A trace of acetone may occur in the urine; diacetic acid was never found in thousands of analyses; the NH_3 of the urine remains constant.—Chem. Abst., **14**, 2369.

Treatment of DIABETES with caramel (Beiträge zur Behandlung von Diabetikern mit Karamel). Reimer (Georg), Deutsches Arch. f. klin. Med. (Leipzig), 1920, **132**, 219-240.

Caramel is very useful in the treatment of diabetes; it has a caloric value, it does almost never produce glucosuria and it diminishes acidosis. Some persons cannot take it, however, because they get diarrhea. It has an especially good influence in young patients. It should be taken over a period of several days, 100-200 grams daily in coffee, pudding or alcohol. Vegetables and fat may be given at the same time. It is better not to give other carbohydrates or proteins on caramel days.
—J. K.

DIABETES, The importance of renal function in —— (Die Bedeutung der Nierenfunktion in der Zuckerkrankheit). Schirokauer (H.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 791-793.

It is a well known fact that hyperglycemia can exist without glycosuria when the kidneys are not permeable to sugar. Von Noorden has written that often when a diabetic develops Bright's disease the glycosuria disappears and the diabetes is cured. This is, of course, not true. Diabetes is not glycosuria. Glycosuria is only one of the symptoms of the disease. On the other hand, an increased amount of blood sugar without glycosuria may occur without diabetes in cases of chronic nephritis with increased blood pressure. In cases of hypertension without pathological changes in the kidney the blood sugar may be increased also. All glands of internal secretion have an influence on carbohydrate metabolism. Perhaps the kidney itself has an internal secretion. The author cites some experiments from the literature to support this view. Hence it is possible that the kidney has an influence on sugar metabolism. It will be necessary to include in experimental and clinical work on diabetes a study of the changes in the kidneys

and of the influence of the kidneys on carbohydrate metabolism.—J. K.

DIABETES und syphilis. Simmonds, München. med. Wchnschr. 1920, **627,** 734.

The author made postmortem examinations in 300 cases of diabetes. In 20 cases syphilis was found, but only in 3 did there exist syphilitic changes of the pancreas.—J. K.

The drugless therapy of DIABETES. Stark (H. S.), N. Y. Med. J. (N. Y.), 1920, **111,** 800-803.

The use of opiates and drugs in general is condemned in the treatment of diabetes. Endocrine gland therapy is useless; their failure to remove or alleviate the symptoms is the best possible argument to disprove the influence of internal secretions in the causation of the disease. A consideration of dietary measures is given for the treatment of diabetes.—H. W.

(DIABETES) Coma diabeticum during pregnancy (Ueber Coma diabeticum bei Schwangeren). Umber (F.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 761-763.

Patients with diabetes very rarely become pregnant. The author describes two cases of women in whom the diabetic symptoms regularly increased during menstruation. Both died in coma during the fourth month of pregnancy. No abortion took place. In a third case a woman with diabetes innocens became pregnant and died in the sixth month, in coma. In this case the woman during coma was delivered by caesarian section of a child that lived less than 24 hours. The blood sugar percentage of the mother during coma was 0.437, and that of the child only 0.091 per cent. [Carlson has found that in partially pancreatectomized animals glycosuria may be in abeyance during pregnancy and the animals kept in fairly good health, but succumb to diabetes after parturition].—J. K.

(DIABETES) The treatment of a mild case of diabetes mellitus. Woodyatt (R. T.), J. Missouri State M. Ass. (St. Louis), 1920, **17,** 227.

A practical talk at a meeting of the St. Louis Medical Society, stressing the importance of the educational phase in the treatment of diabetic patients in securing the best average of results in a large number of cases of all classes and illustrating a specific manner of teaching a patient of the dispensary class.—Author's Abst.

(ENDOCRINE FUNCTION TESTS) Some results of glandular tests made according to the previous condition of the endocrine functions (Quelques résultats des épreuves glandulaires suivant l'état antérieur des fonctions endocriniennes). Claude (H.) & Bernard (Suzanne), Bull. et mem. Soc. med. d hôp. (Paris), 1919, 3.s., **43,** 1116-1120; Abst. Presse Méd. (Paris), **27,** 796.

The aim of this study was to obtain a method for the determination of the functional state of the endocrine glands in those cases in which the symptomatology is evasive or complex, by comparing the results of the effects of the administration of endocrine products in normal individuals and in those in whom obvious endocrine disturbance existed. The effect of the injection of extracts of the same gland may be quite different, however, depending upon the previous state of the functions of the endocrine gland stimulated to activity by the injection. In other words, the reacting tissue may have become sensitized. In acromegaly injections of hypophyseal extracts, even in large doses, is without effect. In subjects with typical exophthalmic goitre subcutaneous injections of hypophyseal extracts (posterior lobe) caused a notable but transitory slowing of the pulse and marked lowering of systolic pressure. In normal individuals, on the other hand, or in cases of tachycardia independent of thyroid conditions, the decrease of systolic pressure is slight and slowing of pulse does not occur. In thyroid insufficiency hypophyseal extracts gave rise to acceleration of the pulse, while systolic pressure was decreased as in normal subjects. The authors produced in 4 individuals presenting hypothyroid syndromes the reactions of hyperthyroidism by feeding desiccated thyroid in doses of .010 to .020 grams daily. Previous to the hyperthyroidization the patients responded to hypophyseal extract injections by accelerated pulse and the usual systolic pressure effects. After the administration of the thyroid preparations the same treatment with pituitary extract caused a lowering of the pulse rate. These facts are interpreted as indicating that a slowing of the pulse in a case of tachycardia after the injection of pituitary extract is evidence of a hyperactive thyroid. Adrenalin injections in the same subjects gave markedly abnormal increases in pulse rate. These reactions then are actually involved with increased thyroid activity; they have been repeatedly tested. It seems, then, that the presence in the organism of thyroid products in excess, either produced by the homologous gland or artificially introduced, favors the reactions to substances contained in hypophyseal extracts and adrenalin,

and induce phenomena sufficiently constant as to serve as a diagnostic measure for hyperthyroidism.—F. S. H.

(ENDOCRINE ORGANS) What fears and states of anxiety in a patient mean to the gynecologist. Bandler (S. W.), N. Y. Med. J. (N. Y.), 1920, **111**, 619-622.

Mental states and psychoses have a neurophysical basis and are not produced solely through psychic effects, but also by definite and specific endocrine activity. The adrenals and thyroid glands are the end-organs most closely related to fears, anxieties, and phobias. However, the corpus luteum is the primary factor which is responsible for these conditions, for the reason that a retained corpus luteum inhibits ovulation and excites disturbances in the thyroid and adrenal glands. Such a condition is combatable by the administration of ovarian extracts and suprarenal extract which contains the cortical material.—H. W.

(ENDOCRINE ORGANS) The instincts, the emotions and the endocrines in sterility. Bandler (S. W.), Med. Rec. (N. Y.), 1920, **97**, 383-391.

A lengthy article, containing much brilliant theorizing which is positively stated as proven, but most of it on very slender scientific basis. It is claimed that a large percentage of cases of sterility in women are not mechanical in origin and are unimproved by surgery, but can be cured by pluriglandular organotherapy. The author expects to publish a series of cases in which endocrine therapy was the only treatment given. [It is to be hoped that the cases will be reported in detail and the exact formulæ and dosage administered carefully recorded].—H. L.

(ENDOCRINE ORGANS) The balance between the endocrines and in each individual endocrine. Bandler (Samuel Wyllis), Med. Rec. (N. Y.), 1920, **97**, 638-647.

An elaborate consideration of the interrelationship of the ductless glands and their relation to the intellect, emotions, character, dreams, sleep, etc. The author goes so far as to believe that kidney diseases are due to endocrine abnormality, that fibroids and myomata of the uterus are the result of pituitary unbalance, that all tumors, benign and malignant, are due to endocrine action. "Many of the statements above made cannot as yet be substantiated by laboratory investigation; they have, however, stood the more convincing test of thera-

peutic application." [Those interested in such advanced and even startling ideas are referred to the original article, which does not readily lend itself to concise abstracting.]—H. L.

(ENDOCRINE ORGANS) The correlation of function; with special reference to the organs of internal secretion and the reproductive system. Bell (W. Blair), Brit. M. J. (London), 1920, **(i)**, 787-791.

The paper is a reproduction of a lecture delivered before the British Medical Association. The author is of the opinion that over-specialization on the part of the medical profession has led to the neglect of what he calls the "Correlation of Function" through the organs of internal secretion. Accordingly he advises the specialist, especially the gynecologist, to look beyond the confines of his particular anatomical territory for an explanation of the pathological conditions encountered.

The production of masculinity in woman by hyperplasia or neoplasia of the suprarenal cortex or anterior lobe of the pituitary is mentioned, as well as the fact that the pituitary body becomes permanently enlarged and changed in histological appearance in a woman after child-birth. This latter fact might be of use in medico-legal cases. The ovary is regarded as a means of maintaining the metabolism of the female at a higher level during the reproductive period, in order that she may nourish the child in utero and during lactation. Menstruation is regarded as "the monthly excretion of substances that would be concerned in the building up of a child were the woman pregnant." After the menopause the whole ductless gland system is involved. Atrophy of the thyroid coincident with atrophy of the ovaries has been demonstrated, and therefore thyroid extract is advocated in the treatment of mental conditions accompanying the menopause. Evidence is advanced to show that pituitary insufficiency is the cause of dystrophia adiposogenitalis. This is often produced by the pressure of a tumor on the stalk. Besides radiography, increased carbohydrate tolerance, subnormal temperature and low blood pressure may aid in diagnosis. The relation of the thyroid to the reproductive organs is also discussed.—L. G. K.

(ENDOCRINE ORGANS) Action of electrical currents on ductless glands and other tissues. De Kraft (F.), Med. Rec. (N. Y.), 1920, **97**, 136-138.

The author refers to the beneficial action of various forms of electricity in hyperthyroidism, obesity, amenorrhea, etc.

He believes that high frequency currents promote nutrition, check toxins, increase perspiration and elimination through the kidneys, restore luster, softness and moisture to the hair, improve the condition of the nails, increase metabolism, remove visceral congestion, etc. He mentions the uses of the diathermic, static wave and galvano-faradic-sinusoidal currents.—H. L.

(ENDOCRINE ORGANS) Results and active principles in organotherapy of abnormal menstruation (Über die Erfolge und das wirksame Prinzip der Organextrakttherapie bei Menstruationsstörungen). Esch (P.), Zentralbl. f. Gyn. (Leipzig), 1920, **44**, 561-568.

The influence of intramuscular organotherapy in abnormal menstruation is, according to the author, not due to a specific active principle, but may be observed after the injection of several kinds of proteins. Only the injection of hypophysis preparations may have a specific influence, as it causes contractions of the uterus.—J. K.

(ENDOCRINE ORGANS) Endocrinologist and internist. Herrick (W. W.), N. Y. M. J., 1920, **111**, 286-287.

The author sounds a note of conservatism relative to the present tendency to explain all things from an endocrine standpoint. Back of the endocrine organs and responsible for their disturbance lie other conditions, i. e., infections, metabolic disorders and psychic states.—H. W.

(ENDOCRINE ORGANS) Dietetic deficiency and endocrine activity, with special reference to deficiency œdemas. McCarrison (Robt.), Brit. M. J. (London), 1920, **(ii)**, 236-239.

Pigeons, guinea-pigs and monkeys were fed on diets deficient in the various vitamines. It was found that all endocrine organs, with the exception of the adrenals and the pituitary, undergo greater or lesser degrees of atrophy and depreciation in functional capacity in consequence of dietetic deficiencies. The adrenal glands and, in the male, the pituitary body, enlarge in consequence of dietetic defects, the former greatly, the latter slightly. The adrenals are the most susceptible of the endocrine structures to dietetic defects. The adrenin content of the enlarged adrenals varies with the character of the dietetic defect; it is in excess of normal when the food is deficient in vitamines, in proteins and disproportionally rich in starch; it is below normal when the diet is scorbutic, and also when concurrent infections are associated with diet-

etic defects. Oedema is invariably associated with massive enlargement of the adrenal glands in pigeons fed on autoclaved rice. But massive enlargement of the adrenals is not always associated with œdema. This association bears some intimate relationship to the adrenalin content of the enlarged organs, since when the content is high œdema occurs in 86 per cent of the cases and when the content is low œdema does not occur. Fresh butter contains some substance which tends to protect against œdema. This substance was not found in cocoanut oil. The hypothetical "anti-œdema" substance in butter has a pronounced influence over the adrenal glands. It appears to exert its protective action against œdema by maintaining their adrenalin content at a low level. Butter varies in its capacity to protect against œdema. This variation is dependent on the quality of the cow's food. Butter is richer in anti-œdema substance when the cows are fed on dry fodder. It is suggested that œdema is caused by the excess of adrenalin acting directly on the kidney to inhibit the flow of urine and to cause a retention of NaCl.—L. G. K.

(ENDOCRINE ORGANS) Grafts of glandular organs (Greffes d'organes glandulaires). Mauclaire (M.), Progrès Méd. (Paris), 1920, **35,** 345-349.

Mauclaire reviews the literature on organ grafting. Aside from the fact that citations of publication are lacking, the article is a valuable summary of available data. The topics treated are: thyroid grafts in animals and men; parathyroid grafts; thymus grafts; ovarian grafts in animals and in women; testicular grafts in animals and men; renal grafts in animals and men; adrenal grafts in animals and men, and, finally, in less detail, grafts of spleen, pancreas, salivary and mammary glands, hypophysis, prostate and liver. In each case the methods used, animals upon which the experiments were made and, to some extent, results are treated. The article, being itself a summary, can not be abstracted. It is concluded that although this type of work offers many difficulties, and more experience is necessary, the results already secured are very encouraging.—R. G. H.

(ENDOCRINE ORGANS AUTONOMIC N. S.) The patient's reaction: a neglected but important phase in the study of medicine. Pottenger (F. M.), Annals of Medicine (Haggerston, Md.), 1920, **1,** 52-54.

Pottenger points out the intimate relationship between the psychic factors and the symptomatology of disease and empha-

sizes the part played by the endocrine and autonomic systems in the evolution of disease pictures. The burden of the article is that these factors should receive relatively much greater attention at the hands of practical clinicians. [That they do not receive adequate attention is probably due to the paucity of definite diagnostic criteria in the fields of endocrinology and visceral neurology. It is the obvious duty of workers in these fields to establish such criteria.]—R. G. H.

(ENDOCRINE ORGANS) The skin as an index to health. Scholtz (M.), Med. Rec. (N. Y.), 1920, **97**, 824-828.

Scholtz calls attention to the relation between skin disorders and systemic diseases and mentions the syphilis syndrome, tuberculosis syndrome, diabetic syndrome, erythema multiforme group and focal infection, the leukemic syndrome, the precancerous syndrome and the endocrinous syndromes. A thick, dry, pasty skin, suppression of perspiration, lusterless brittle hair and alopecia suggest hypothyroidism; and many cases of chronic eczema, psoriasis, ichthyosis and scleroderma are improved by administration of thyroid. Hyperthyroidism produces thin, perspiring, easily flushed skin, urticarial attacks, pigmentation, dystrophies of the nails, keratinization and pruritis. The author mentions the bronze-like skin of Addison's disease and the successful treatment of some cases of vitiligo by extract of suprarenal. Fibromatous growths, warts, alopecia in men and hypertrichosis in women are sometimes due to hypophyseal disease. He also refers to the skin changes accompanying pregnancy and following castration, and to the angioneurotic dermatoses of Raynaud's disease, scleroderma, angioneurotic edema, etc.—H. L.

(ENDOCRINE ORGANS) Changes in the endocrine organs, especially the adrenal cortex, following occlusion of the pancreatic duct (Ueber die Veränderungen der endokriner Organe, besonders der Nebennieren-Rinde nach der Unterbindung des Ductus pancreaticus und ihre Bedeutung). Tokumitsu (Yoshitomi), Venhandl. d. japan. path. Gesellsch. (Tokyo), 1916, **6**, 21-23.

The first effect of tying the pancreatic duct in rabbits is a general atrophy of the pancreas. Subsequently the islands of Langerhans regenerate to, or above, the normal mass. In the adrenals the cortex becomes hypertrophic; the medullary cells become smaller and more thickly crowded and give a clearer chromophil reaction. The thyroid enlarges. In the hypophysis the eosinophil cells decrease and the "Hauptzellen"

increase. For a short time after the operation glycosuria can be produced with a smaller quantity of adrenin than in case of normal animals. Destruction of the adrenal cortex by knife or cautery causes, in itself, no glycosuria, but after tying the pancreatic duct such measures in the adrenals produce definite glycosuria. Normal rabbits die from the loss of ¾ of the adrenal cortex, but after occlusion of the pancreatic duct the loss of ¼ of the cortex is fatal. When thyroidectomy is combined with the above procedures glycosuria is prevented. On these data the author postulates a functional antagonism between the thyroid and the pancreas.—R. G. H.

ENDOCRINOPATHIES (Syphilis hereditaire tardive; endocrinopathies; hypophyse. Castex (M. R.) & Waldorp (C. P.), La Prensa Med. Argentina (Buenos Aires), 1920, **6**, 309.

A report of certain clinical observations and a critical study of the topic. The authors believe that hereditary syphilis is a factor in acromegaly and that the same factor is involved in most cases of gigantism. Similarly it may produce infantilism and the Fröhlich syndrome.—B. A. H.

(ENDOCRINOPATHIES) Hereditary syphilitic terrain and its relation to tuberculosis (El terrena heredo espicifics y sus relaciones con la tuberculosis. Mariño (E.) & Barilari (M. J.), Prensa med. argent. (Buenos Aires), 1920, **6**, 312.

Hereditary syphilis produces lymphatism, asthenic habitus and numerous endocrin dysfunctional states. Tuberculosis is often implanted in this soil. Amelioration is to be expected, in such cases, rather from tuberculin than mercury. —B. A. H.

Medical aspects of ENDOCRINOLOGY. Hertz (J. J.), Med. Rec. (N. Y.), 1920, **97**, 511-514.

A brief, fragmentary resume of some disturbances of the thyroid, parathyroids, adrenals, pituitary and pancreas with some suggestions regarding appropriate organotherapy; no new data.—H. L.

The position of ENDOCRINOLOGY in general medicine (Posicion dela endocrinologia en la medicina general). Marañón (G.), Real Acad. Nat. de Med. (Madrid), 1918, —, —.

Interesting general review of the glands of internal secretion in many diseases and syndromes the pathogeny of which is little known.—E. B.

GASTRIN Studies. V. Chemical studies on gastrin bodies. Koch (F. C.), Luckhardt (A. B.) & Keeton (R. W.), Am. J. Physiol. (Balt.), 1920, **52**, 508-520.

This is the fifth of a series of studies of gastrin bodies, the other papers of which have appeared in the Am. J. of Physiol., Vols. **37, 50** and **51.** This paper is a report of observations bearing more particularly on the chemical phase of the work. Various chemical procedures are described and the results noted. The conclusions drawn are as follows:

(1) A striking similarity exists between the effects of histamin and gastrin. (2) Gastrin appears to be more stable than secretin is reported to be, although they are similar in many respects. (3) Gastrin has not been precipitated by picric or picrolonic acid. (4) Gastrin appears to be a basic imidazol derivative which can be extracted as the free base by amyl alcohol. (5) Thus far histamin and pilocarpin are the only known imidazol derivatives which stimulate the gastric mechanism to secretion. (6) Choline acts with uncertainty and then only faintly as compared with histamin or gastrin.

—T. C. B.

(THYROID) Goiter. Cooke (A. B.), Calif. State. J. M. (San Francisco), 1920, **18**, 82-83.

No new data.—H. W.

(THYROID) Goiter. O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 503-505.

Goiter may be defined as a partial or complete enlargement of the thyroid gland. Any benefits derived from the ligation of the thyroid arteries is due merely to the rest subsequently imposed. Focal infections cannot be considered as causative factors in the production of goiter, for the Hawaiians, although extremely subject to focal infections, do not develop goiter.—H. W.

Modern treatment of STERILITY. Armitage (H. M.), N. Y. Med. J. (N. Y.), 1920, **111**, 360-363.

Defective implantation of the ovum is indicated in women who frequently miss a menstrual period and go over 10 to 14 days and then flood. Such cases should be treated with corpus luteum extracts inasmuch as the corpus luteum of the individual is not sufficient to bring about complete implantation of the ovum. Profuse menstruation is due to over-stimulation

of the endocrine organs and should be treated with preparations of thymus gland and mammary substance. Irregular menstruation often yields to the administration of thyroid, ovary and corpus luteum substances.—H. W.

(GONADS) A case of human bilateral hermaphroditism with bisexual glands (Un cas humain d'hermaphrodisme bilateral a glandes bisexuelles). Briau (E.), Lacassagne (A.) & Lagoutte (M.), Gynec. et Obst. (Paris), 1920, **1**, 155-179.

An extensive and detailed report of a case of bilateral hermaphrodism including the macroscopic and microscopic appearance of the abnormal genitalia. The individual possessed the efferent passages normal to both sexes, a uterus the dimensions of which would be admitted as those of a nullipara, two tubes of normal sizes and structure and spermatic cords each segment of which was normal. Moreover, there occurred bilaterally a mixed sex gland containing both ovarian and testicular tissue. The left gland was within the pelvis and presented the aspects of a functioning ovary together with spermatogonia producing testicular tissue, an ovotestis of predominantly ovarian function. The right gland was within the inguinal canal, possessed an epididymus and vas deferens, had produced spermatocytes and contained ovarian fragments. This the authors consider as an ovotestis predominantly testicular in function.—F. S. H.

Gonads, Histogenesis of the —— (Sobre la histogènesi de la glandula genital). Domingo (P.) & Vilaseca (S.), Treballs de la Societat de Biologia, Barcelona, 1918, **6**, 51-61, 11 pl.

The article is largely of technical histological interest. As regards the interstitial cells of Leydig, the authors remark that their origin has been much debated. They, themselves, believe the cells to be derived by successive differentiations from certain mesenchymatous cells in relation to the tunica albuginea and of the interlobular tissue and the walls of the tubules. In the testes of the human fetus the authors have recognized also certain interstitial cells which are voluminous, with clear protoplasm and irregular contour and transparent, spherical nuclei. Among them many mitoses are seen and multinucleate cells are observed. They seem to be analogous with the primordial ovules. The article is illustrated with eleven photomicrographs.—R. G. H.

(GONADS) The question of hermaphrodism in man and mammals (La question de l'hermaphrodisme chez l'homme et les

mammifères). Lacassagne (A.), Gyn. et Obst. (Paris), 1920, **1**, 273-296.

A bibliographic review.—F. S. H.

(GONADS) A case of pseudohermaphroditismus masculinus internus with tumor of testicle (Over een geval van pseudohermaphroditismus masculinus internus met gezwelvorming van den testikel). Lauwers (G. B.), Inaug. Dissertation (Amsterdam), 1920.

The patient, who had normal sexual desires, was operated upon for hernia. Death by embolus followed. Post-mortem examination showed: Penis, bladder and rectum normal. On both sides the vasa deferentia were normal. Behind the bladder a mass of tissue was noted in which two Fallopian tubes were found and a uterus bicornuus. The right testicle contained a carcinoma. A very good bibliography on tumors of testicles and hermaphroditism is included.—J. K.

(GONADS) The production of artificial hermaphrodites in mammals. Moore (Carl R.), Science (N. Y.), n. s. **52**, 179-182.

A criticism of the works of Steinach and Sand (Endocrin., **4**, 266). "Steinach was unable to obtain either a growth or persistence of an implanted sex gland unless the gland of the host (gland of the opposite sex) was removed before the implantation was made."

Sand supports Steinach on the whole. "In explaining his failure to obtain growths of ovarian grafts in non-castrated infantile male animals he assumes a rather indefinite type of 'Immunity' on the part of the host towards the implanted tissue." Moore has been able to obtain growths of ovarian grafts, subcutaneously, intramuscularly and intraperitoneally in young male rats which had one sex gland intact and normal. The graft, eight and one-half months after implantation, presented all of the features of a normal ovary of similar age excepting corpus luteum tissue and the presence of a large number of atretic follicles. The behavior of the follicles of the grafts is similar to the corresponding structures of the young female sex gland before the age of sexual maturity. Mammalian testicular transplantation results in the loss of the germinal epithelium. "The grafts resemble a cryptorchid testis in that both retain the well-rounded seminiferous tubules, but all that remains of a cellular character are Sertoli cells. The testis graft does persist after transplantation in a female, with an

intact ovary, and it is as normal as autoplastic testicular grafts, either with or without previous castration. A male rat with one testis will function as a normal male during the time it is carrying two ovarian grafts as an integral part of its somatic structure."—F. A. H.

GYNECOMASTIA and the theory of a mammary internal secretion (Zur Kenntniss der Gynäkomastie und zur innersekretonischen Theorie der Brustdrüse). Novak (J.), Zentralbl. f. Gynäk. (Kiel), 1919, **43**, 253-258.

A report of 5 cases of gynecomastia and a discussion of the existing theories of mammary secretion. No new data. —F. S. H.

Experimental **HERMAPHRODITISM, historical remarks on—(Historische Beitrag zum experimentellen Hermaphroditismus).** Foges (A.), Wien. klin. Wchnschr., 1920, **33**, 224.

Data reported elsewhere. See Endocrin., **4**, 265. —J. K.

(HORMONES) Hormonal stimulation of the brain (Delas estimulaciones hormonales del encefalo). Mouchet (E.), Prensa med. argent. (Buenos Aires), 1920, **6**, 306.

Since the brain receives not only nerve stimulation but also blood, the author deduces that the mental state is dependent upon hormone as well as nervous influences.—B. A. H.

HYPERTHYROIDISM. Webster (A. B.), N. Y. Med. J. (N. Y.), 1920, **111**, 283-284.

After discussing the relation of focal infections to thyroid disturbances, the author bewails the fact that "surgery has gone mad in treating end results and not dealing with the primary cause," and then proceeds to justify surgical procedures on the abnormally functioning thyroid gland. However, he fails to state whether toxines or the thyroid itself is primarily at fault, or whether the condition in the thyroid is or is not the end result of altered functions in other parts of the body. —H. W.

(HYPOPHYSIS) The pathogenesis of diabetes insipidus. Bauer (J.) & Aschner (B.), Wiener. Arch. f. inn. Med., 1920, **1**, 297-334.

The authors give in tabular form an extensive series of metabolic findings in a typical case of diabetes insipidus in a

woman who had been under observation for ten years. They believe that diabetes insipidus may find its origin in the kidney or its innervation. This is often observed in the familiar constitutional form of the disease. A disease in the neighborhood of the nerve centres of the midbrain or fourth ventricle is the most ordinary cause. Nearly all cases in literature belong to this type. A primary change of the center for thirst perception in the cortex of the brain may combine itself with an irritation of the subcortical diuresis center. In this way psychical influences may act. It has never been definitely proved that the hypophysis itself may be the cause of diabetes insipidus. Even with loss of the diuresis regulating property of the hypophyseal secretion normal compensatory processes in the kidneys themselves may suffice to prevent diabetes insipidus.—J. K.

(HYPOPHYSIS) Radium therapy of tumors of the hypophysis, with syndrome of acromegaly (Radiumterapia nei tumori ipofisari a sindrome acromegalica). Bertolotti (M.), Radiol. med. (Milano), 1919, **6**, 315.

A number of cases have now been treated by radiation with some favorable results, and a notable improvement in several. As there is great variation in the symptoms according to the position of the tumor, this may account for variation in the results of treatment, and the negative results of X-ray therapy in some cases. In dystrophy from tumor of the hypophysis the author's own results have been unfavorable; similarly the clinical results of all tumors are varied, and the course of the disease may be from 2 to 59 years. In benign cases X-rays are advisable and useful. The detractors of X-rays assert that the improvement is a natural retrogression, but this is always of short duration, whereas the improvement after X-rays lasts much longer. The best results are obtained in early cases, and, as cystic degeneration follows in acromegaly, X-rays should be applied before this sets in. The author gives the history of a case treated by the gamma-rays of radium from the early days.

The first symptoms were seen in May, 1917, and by December the condition was already far advanced—vision nearly gone, impotency, asthenia, etc.—so that an adenoma or adenocarcinoma of the pituitary was suspected, most probably of the anterior lobe and of rapid and malignant development. A course of intensive radium treatment was begun, but by March, after two treatments, the patient was worse instead of better and the condition seemed desperate. Not till July was there

a slight improvement, when the vision of the left eye began to increase. Continuous though slow progress was made, and in September the radiograph showed surprising improvement in the profile of the sella turcica.

By December, 1918, the vision had so far recovered that the patient was able to resume his work as a designer, and all the symptoms had disappeared. This result was obtained solely by massive doses of radium applied bi-temporally, and neither the intrabuccal nor the intranasal method was employed. It follows that the rays are efficient at a distance of more than 10 cm. through tissues, and have probably an elective action on certain neoplastic cellular elements.—Med. Sc. Abst. & Rev., **2**, 204.

(HYPOPHYSIS) Permanent experimental polyuria (Polyurie expérimental permanente). Camus (J.) & Roussy (G.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 764-765.

A description of two cases of permanent experimental polyuria in dogs. Of endocrine interest is the statement that it is not the ablation of the hypophysis which determines the polyuria, but the superficial lesion of the base of the brain corresponding to the opto-peduncular space.—T. C. B.

(HYPOPHYSIS) A case of acromegaly (Sobre un caso de a.). del Cañizo (A.), Siglo Méd. (Madrid), 1917, ——, ——, (Nov. 17.)

A case is presented which manifested all the typical symptoms of acromegaly, but with certain other features worthy of comment. The condition developed at the unusually late age of 53 years. Especially interesting is the fact that the thymus was enlarged, as was demonstrated both by percussion and radioscopy; it was so pronounced as to give rise to frank symptoms of mediastinal pressure. The author discusses the possible relationship of the hypophysis and thymus to the development of the osseous tissues (citing the alleged production of experimental rickets through thymectomy by Klose, Vogt and Matti) and of the genital apparatus. Thymic hypertrophy in eunuchs is not unusual and in such a process as acromegaly, in which sexual activity is diminished, a similar enlargement of the thymus, as in this case, might be expected.—E. B.

(HYPOPHYSIS) A case of syphilitic diabetes insipidus (Ein Fall von Diabetes insipidus auf luetischer Basis). Chiari, Wiener klin. Wchnschr., 1920, **33**, 620.

A woman of 30 manifested cessation of menstruation, polyuria and polydipsia and multiple swellings of the bones. The quantity of urine reached 15 liters daily, with a specific gravity of 1001. The Wassermann reaction was positive. She was cured by antiluetic treatment. The author believes that a syphilitic change in the hypophysis or in the regio subthalamica was responsible for these symptoms. A skiagram showed no pathological changes.—J. K.

(HYPOPHYSIS) Study of a case of diabetes insipidus with special reference to the mechanism of diuresis and the action of pituitary extract upon it. Christie (C. D.) & Stewart (G. N.), Arch. Int. Med. (Chicago), 1917, **20,** 10-23.

A careful series of studies was made upon a female subject who excreted up to 20 liters of urine daily. She reacted well to pituitary extract but required doses of 2 cc. repeated three times in each 24 hours to maintain the effect. The relative hydration of the blood was investigated by determinations of electrical conductivity and by hematocrit readings of the blood. The relative volume of the serum was found to be slightly diminished and the conductivity slightly decreased, showing that the extract caused a slight dehydration of the blood. By Stewart's calorimetric method it was determined that the blood flow through the hands was increased during the period of reaction to the pituitary extract, hence the renal flow was probably decreased. Functional tests indicated that the diuresis was not in any way associated with pathological alterations in the kidneys.—R. G. H.

(HYPOPHYSIS, ADRENAL, THYROID) Hemostatic medication (Médication hémostatique). Dalché (P.), La Gyn. (Paris), 1920, **19,** 139-152.

A discussion of the various causes and treatments of genital hemorrhages in the female. Consideration is given to the use of the directly acting vaso-constrictor properties of hypophyseal and adrenal extracts and to the indirect activity of thyroid opotherapy in such conditions as the metrorrhagias of myxodema and obesity. Note is also made of the favorable coagulative action of the posterior lobe of the hypophysis.
—F. S. H.

HYPOPHYSIS opotherapy with favorable action in a case of obesity and diabetes insipidus (Action favorable de l'opothérapie hypophysaire dans un cas d'obésité et de diabète

insipide). Flandin (Ch.), Huber (J.) & Debray (M.), Bull. et. mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44,** 487-490.

A new example of the action of hypophyseal extracts on the polyuria of diabetes insipidus. In this case the urinary output of the woman, which was around 14 liters per 24 hours, was lowered to values of 10, 12 and even 6 liters as the result of the administration of the drug, although the effect was in general but transitory. No effect was observed as regards diminution of the obesity.—F. S. H.

(HYPOPHYSIS) Dystrophia adiposo-genitalis. Foerster, München. med. Wchnschr., 1920, **67,** 675.

Description of a case. The patient suffered from this disease for 20 years. There were headaches and some slight signs of acromegaly. The skiagram showed the sella turcica to be enlarged. The author diagnosed a benign tumor of the hypophysis.—J. K.

(HYPOPHYSIS) Dystrophia adiposo-genitalis. Hannema (L. S.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** 2434-2435.

The case is recorded of a boy of 13 years with polyuria, adiposity and extremely small genitals. There were no neurological nor any eye symptoms. Sugar tolerance was much increased. No enlarged sella turcica was detectable radioscopically.—J. K.

HYPOPHYSIS, A doubtful case of tumor of — (Een twijfelachtig geval van hypophysis gezwel). Hannema (L. S.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64, (I),** 2436-2438.

A woman of 34 for 4 years suffered much with headache. There was no vomiting, no eye symptoms and no polyuria. Recently her face has become broader and her feet have become larger and hairs have developed on breast and legs. Sugar tolerance is diminished. Radioscopically the sella turcica appears very large but of a perfectly normal form. There are certain hysterical symptoms and it is certain that the patient exaggerates her complaints. A tumor of the hypophysis is probable but not at all certain since a large sella with normal shape may be seen in healthy individuals.—J. K.

(HYPOPHYSIS) On the relation between the interstitial cells and the hypertrophy of the hypophysis. Hayami (T.), Verhandl. d. jap. path Gesellsch. Tokyo, 1919, pp. 43-44.

In order to determine which constituent of the testis is responsible for the hypertrophy of the hypophysis which usually follows castration, the author experimented with rabbits about three months old, which he divided into groups and treated as follows: (1) Double castration; (2) Castration on one side and vasectomy on the other; (3) Double vasectomy and treatment of the testicles with Röntgen rays. He studied only animals which lived for four months or more after the operation. Double castration produced the usual hypophyseal hypertrophy. Castration and vasectomy caused hypophyseal hypertrophy together with an almost complete cessation of spermatogenesis and an increase in the number of the interstitial cells in the remaining testes. Double vasectomy and treatment with Röntgen rays destroyed the epithelial and Sertoli cells and increased the interstitial cells, which must, therefore, in his opinion, be responsible for the resultant enlargement of the hypophysis.—E. V. C.

(HYPOPHYSIS) Occurrence of polyuria (diabetes insipidus?) in a case of epidemic encephalitis [Auftreten von Polyurie (Diabetes insipidus?) im Verlaufe eines Falles von Encephalitis epidemica]. Hoke (E.), Wiener klin. Wchnschr., 1920, **33**, 562.

During an attack of encephalitis lethargica polyuria (up to 10 liters daily) developed. When pituglandol was injected the quantity of urine was diminished to about 3 liters. The patient is still under treatment.—J. K.

HYPOPHYSIS extracts, Action of—on diuresis in the dog and rabbit (Accion de los extractos de hipófisis sobre la diuresis en el perro y el conejo). Houssay (B. A.), Galan (J. C.) & Negrete (J.), Soc. de Biol. de Buenos Aires, June 10, 1920.

The action of hypophyseal extracts upon diuresis is essentially different in case of different animals. In the rabbit one sees oliguria and anorexia, while in the dog there results an augmentation of diuresis except following profuse ingestion of water. It can not be determined, therefore, from the effects of such extracts in case of any one species of animal whether or not the hypophysis exercises a physiological influence upon diuresis—B. A. H.

HYPOPHYSIS Study of the carbohydrate tolerance in Eck fistula and hypophysectomized animals (posterior lobe removal). Liver function in the metabolism of sugars. Jacobson (Conrad), Am. J. Physiol. (Balt.), 1920, **52**, 233-247.

In animals deprived of the hypophysis there is a rise in sugar tolerance, and this rise can be lowered by administration of the extract of the posterior lobe. The lowering of the sugar tolerance is evidenced by hyperglycemia as well as glycosuria, and efforts have been made to determine the source of this glycogen. Good sized healthy dogs were used. A typical lateral anastomosis between the portal vein and inferior vena cava was made. The portal vein was ligatured in two places and cut between the ligatures, close to the liver hilus. The posterior lobe of the pituitary was removed by the intracranial method of Crowe, Cushing and Homans. The paper is largely concerned with sugar tolerance in Eck fistula animals, but the conclusion is reached that the glycogenic capacity of muscle is increased following posterior lobe removal in an Eck fistula animal as in an intact animal. The augmentation is, however, considerably slower. No augmentation of levulose tolerance is noted—T. C. B.

HYPOPHYSIS, Modern physiology and pathology of— (Der jetzige Stand der Physiologie und Pathologie der Hypophyse). Jacoby (M.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 742-743.

A general review without new facts. The author points out once more that it is necessary in diseases of one endocrine organ to consider the others as all these organs have a mutual influence on each other.—J. K.

Ossification of HYPOPHYSIS causing diabetes insipidus (Uber einen Fall von Verknocherung der Hypophysis, die Diabetes insipidus verursachte). Kawakita (S.), Verhandl. d. jap. path. Gesellsch., 1919, ——, 45-54.

Relates the case of a woman of 30 years in which diabetes insipidus was definitely associated with retarded development of the internal genitalia.—E. V. C.

(HYPOPHYSIS) Observations on two cases of diabetes insipidus, with account of the literature relating to association between pituitary gland and this disease. Kenneway (E. L.) & Mottram (J. C.), Quart. J. Med. (Lond.), 1919, **12**, 225-228.

The authors studied the composition and molecular concentration of the urine in comparison with that of the blood

serum in two cases of diabetes insipidus. When large amounts of sodium chlorid are given the urine output is so adjusted that the percentage of nitrogen plus that of the chlorin in the urine remains constant. The kidney, therefore, has not the power of concentration normally demonstrable after the ingestion of salt. The antidiuretic effect of pituitrin was demonstrated both in a normal subject and in a case of diabetes insipidus. It was found that hypodermatic administration but not administration by mouth, was effective. The writers could find no instance in the literature of diabetes insipidus in which hypophyseal abnormality was excluded definitely by autopsy observations, whereas, in a number of cases the posterior lobe of the hypophysis was definitely involved. Lesions of this structure are, however, not always accompanied by diabetes insipidus. The morphologic evidence is therefore not conclusive. Therapeutic evidence, however, is convincing that the hypophysis normally plays a part in the regulation of renal activity.—R. H. G.

(HYPOPHYSIS) Two cases of adiposo-genital syndrome of hypophyseal origin in the adult (Sur deux cas de syndrome adiposo-génital d'origine hypophysaire chez l'adulte). Lereboullet (P.) & Hutinel (J.), Bull. et mem. Soc. med. d. hôp. (Paris), 1919, 3. s., **43,** 745-754.

Case reports. No new data.—F. S. H.

HYPOPHYSIS, State of the—in encephalitis lethargica (État de l'hypophyse dans l'encéphalite léthargique). Marie (P.) & Tretiakoff, (C.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44,** 357-358.

Presentation of histological preparations of specimens of the hypophysis from two cases of encephalitis lethargica. The subjects were markedly somnolent during the progress of the disease. Macroscopically the glands were slightly congested without being notably swollen. On sectioning, a moderate diffuse congestion unaccompanied by leucocytic infiltration was evident. No appreciable alterations of the cells of either lobe could be seen. No gross lesions of the hypophysis were observed in these two cases, but in one case a small hemorrhagic area 2 to 3 mm. in diameter, accompanied by necrosis of glandular cells without leucocytic reaction, was found, while in the other case there appeared to be quite a number of blackish pigment granules disseminated among the cells or included in the protaplasm. Nevertheless, the au-

thors conclude that symptomatology of lethargic encephalitis cannot be explained by the condition of the hypophysis.
—F. S. H.

(HYPOPHYSIS) Diabetes insipidus in a baby. Narigawa (S.), Jikwa Zasshi (Japan), 1918, No. 213, 16-26.

There was no disturbance of renal function nor of blood pressure. Under treatment, which consisted of injections of 0.29 mil. of pituitary extract, there was improvement. The volume of urine decreased and the concentration of sodium chloride increased. (Abst. in China Med. J.)—L. G. K.

(HYPOPHYSIS) Two cases of hypophyseal adiposity with dwarfism (Zwei Fälle von hypophysärer Adipositas mit Zwergwuchs). Peritz (G.), Deutsche med. Wchnschr., (Berlin), 1920, **46**, 613.

Both cases are of syphilitic origin. The first subject is a girl of 14 with idiocy and a spastic paresis of the left side of the body. Her height is 123 cm. and weight 28.8 K. She shows typical adiposity. The second case is that of a boy of 3 years, with a weight of 12.8 K. and height of 82 cm. The skiagram shows an enlarged sella turcica. Intraspinal pressure is high. Probably there is here a hydrocephalus with resulting pressure on the hypophysis.—J. K.

(HYPOPSYSIS) Hypophyseal dwarfism (Hypophysärer Zwergwuchs). Priesel (A.), Deutsche med. Wchnschr., (Berlin), 1920, **46**, 704.

A short note on a case. The patient was 90 years old. There were pathological changes in the neurohypophysis and an abnormal sinus in the splenoid.

(HYPOPHYSIS) Acromegalia y diabetes insipida. Pittaluga (G.), Siglo Med. (Madrid), 1920, **67**, 90-93.

Description of a case of acromegaly with intense diabetes insipidus. The author favors the hypopituitary theory of etiology of the diabetes, explaining such cases of acromegaly accompanied by polyuria as produced by the mechanism indicated by Falta, Marañón and others, namely, compression of the median and posterior lobes of the hypophysis by the hypertrophic anterior lobe. The condition may spontaneously be relieved as the compression subsides or the parts become anatomically or functionally adapted to the compression.
—G. M.

(HYPOPHYSIS) Extensive destruction of the sella turcica without clinical symptoms. Rosenheck (C.), N. Y. Med. J. (N. Y.), 1920, **111**, 554-555.

Case report of extensive destruction of the sella turcica in a man of 60 years without clinical manifestations.
—H. W.

Sarcoma of the HYPOPHYSIS with acromegaly extirpated by the frontal route (Sarcoma de la hipófisis con sindrome acromegalico. Extirpacion por via frontal, etc.). Sacco (A.) & Del Valle (D.), Asoc. Méd. Argentina, Sec. Chirujia, July, 1920.

The authors describe a case of acromegaly with grave visual disorders in which extirpation of the hypophysis was performed. The ablation was regarded as complete. The Frazier operation, i. e., ablation with aspiration, was performed. Thereafter a considerable improvement of the vision was noted, and this progressed, but marked glycosuria and other diabetic symptoms supervened.—B. A. H.

(HYPOPHYSIS) A case of diabetes insipidus. Schnabel (Truman G.), & Gerhard (Arthur H.), N. Y. Med. J. (N. Y.), 1920, **111**, 812-815.

Report of a case of diabetes insipidus with symptomatic arrest following the hypodermic use of pituitrin. Over three years have elapsed since the onset of the disease and over two years since the cessation of symptoms. The hypodermic use of pituitrin was followed by a very immediate antidiuretic effect. Sterile water, corpus luteum and adrenalin used hypodermatically were without effect. Extract of pituitary gland by mouth was ineffectual. The specific gravity of the urine, while still fixed at a low figure (1.012), was raised to a relatively higher one. Contradictions from the literature are cited to illustrate the uncertain status of renal output in relation to pituitary function.—Authors' Abstract.

(HYPOPHYSIS) Note on the presence of iodine in large quantities of sheep pituitary gland. Seamen (E. C.), J. Biol. Chem. (Balt.), 1920, **43**, 1-2.

No iodine was found in three lots of 30, 50 and 100 grams of sheep pituitaries.—F. S. H.

HYPOPHYSIS, Contribution to the study of the— (Contribución al estudio de la hipofisis). Silva (A.), Innaug. Dissertation, Santiago de Chili, 1917.

It was concluded from a series of experiments that in the normal subject hypophyseal extracts give a transient or prolonged vascular hypotension. Such extracts give, however, a unique reaction in the active form of tachycardia of Graves' disease. This is sufficiently characteristic as to serve as a diagnostic criterion. In this disorder the extracts give not only hypotension but also polyuria, transient glycosuria, pallor of the skin and contractions of the intestines and uterus. (Relative threshold values are not stated.—Ed.) The extracts appear to give rise also to phosphaturia.—J. R. P.

(HYPOPHYSIS) X-ray treatment of visual disorders or hypophyseal origin (Le traitment par les rayons X des troubles visuels d'origine hypophysaire). Terrien (F.), Arch. d'opth. (Paris), 1916, **5**, 257-286.

Terrien analyzes eight cases from the literature and adds two others,—one of his own and one of Prof. Lapersonne's. The article includes a valuable detailed discussion of technique. The rays can be sent either through the temples or through the mouth, but the latter is usually preferable. A one millimeter aluminum screen is used and 5 H. units administered. Experience has shown that no fear need be entertained of injury to the brain. The results obtained have been mostly satisfactory. The headaches have in most cases ceased at once and the visual acuity and visual fields improved. The somatic hyperplasia of the acromegalics has not diminished, however. Radiations should be administered only during the period in which the hypophyseal function is in an augmented state, since their action is to diminish the activity of the gland. When the process has reached a destructive stage the radiation can only hasten the appearance of symptoms of hypophyseal insufficiency. X-ray therapy has the outstanding advantage that, being harmless, it can be utilized early in cases in which indications for surgical intervention are lacking.—R. G. H.

HYPOPHYSIS extract, The action of—on peristalsis (Der Einfluss des Hypophysenextraktes auf die Peristaltik). Zondek (B.), Arch. f. d. ges. Physiol. (Bonn), 1920, **180**, 68.

Zondek has studied the action of the glandular extract by direct observation of the intestine through a permanent window of celluloid healed into the abdominal wall; the method

is that of Katsch and Borchers. By each injection of the drug there is a preliminary "psychic shock" which lasts two minutes, with complete interruption of peristalsis. The hypophysis extract stimulates peristalsis of the large intestine, but occasionally first causes slight inhibition. It also regulates peristalsis. Injections of the drug are recommended in postoperative intestinal atony.—Med. Sc. Abst. & Rev., **2**, 494.

INTERNAL SECRETIONS, Influence of—on blood pressure and the formation of bile. Downs (A. W.), Am. J. Physiol. (Balt.), 1920, **52**, 498-507.

In a previous paper (See Endocrin., 1919, **3**, 214), the author describes the effect of various internal secretions on the formation of bile. In the present paper the relation between blood pressure and bile is considered. The gland substances employed were mammary, orchic, ovarian, pancreatic, splenic, thymic, and thyroid. Adrenalin and secretin were also investigated.

There seems to be no constant relation between blood pressure and the amount of bile secreted. Adrenalin causes a rise of pressure and increased bile formation, while secretin, if it has any influence, lowers blood pressure and increases bile production. There was no constant relationship between blood pressure and bile production after the administration of thyroid. The experiments indicate that some at least of the endocrine organs exert a specific influence on the secretory activity of the hepatic cells leading to the production of bile.
—T. C. B.

INTERNAL SECRETIONS, Influence of—on the tumors of the dog (Influence des la sécrétion interne sur les tumeurs des chiens). Korentchevsky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 779-781.

The results of experiments on fifty-two dogs inoculated with sarcoma. In some the thyroid was removed, others were castrated; all were controlled. Castration and thyroidectomy clearly augmented the growth of sarcoma in the majority of cases. In all the animals, controls as well as operated, the tumors suffered retrogression and absorption as follows: Controls, 79 per cent; castrated, 56 per cent; thyroidectomized, 28.6 per cent. The introduction of a suspension of fresh testicle arrested the growth of the tumors, and accelerated their retogression.—T. C. B.

INTERNAL SECRETIONS, Influence of—on the tumors of mice (Influence des la sécrétion interne sur les tumeurs des souris). Korentchevsky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 783-785.

The influence of castration on the growth of carcinoma in mice was not clearly manifested. Extirpation of the spleen and the genital glands resulted in an increase in strength and rapidity of the growth of chondromata. This did not seem to be true for the extirpation of the spleen only. In general the same was true for carcinoma, but the results are not so clear cut. Thyroid alimentation diminished the percentage of successful inoculations and retarded the growth of carcinomata, and this was most marked with small doses. In thymus feeding also, the greatest percentage of unsuccessful inoculations and the smallest tumors, where successful, were furnished by the group receiving the smallest doses of thymus. The small doses probably stimulated the defensive oncolytic forces, retarding growth or preventing the tumor cells from implanting themselves in the organism. Pituitrin had no effect. The author concludes from his studies that the state of the glands of internal secretion may be one of the important conditions determining the non-receptivity towards tumors.—T. C. B.

INTERNAL SECRETIONS, Influence of—and of autolysate on the tumors of rats (Influence des la sécrétion interne et des l'autolysat sur les tumeurs des rats). Korentchevsky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 781-783.

Experiments were made on rats, the tumor being a fusiform sarcoma. Inoculation one and one-half months after castration gave 90 per cent of "takes" in the controls and 100 per cent in the castrated rats. The influence of castration was not very definite. Injection of a suspension of dogs' testicle, however, caused a retardation of the growth of the tumor. Injections of an autolysate of sarcoma in small amounts caused a retardation of growth, but larger doses were less energetic in their action. The same may be said for corpus luteum. Extirpation of the spleen seemed to augment the inoculability to sarcoma and favor its growth. Castration slightly attenuated the effect of splenectomy alone. Thyroid alimentation retarded the growth of tumors, and weak doses appeared to act better than strong. Pituitrin has shown no influence on the growth of tumors.—T. C. B.

INTERNAL SECRETIONS, Contributions to the pathology of—(Part II.) Nakamura (H.), Verhandl. d. jap. path. Gesellsch., 1919, ——, 41-43.

In the first part the author describes the effect of the ligation of both spermatic cords in rabbits killed 1, 2½, 4½ and 7½ months later, as follows: (1) A general increase in body fat which is most apparent after about 4½ months; (2) The interstitial fatty tissue of the thymus is reduced, the lymphatic cortical substance is increased, while the Hassal's corpuscles show no change in either size or number; (3) The thyroid is of the colloid type; (4) In the suprarenals there is a thickening of the cortical substance and an increase in the lipoid content of the cells, especially after 4½ months. The medullary substance is not increased, but after 7½ months shows a somewhat stronger chromaphil reaction; (5) There is also an increase in the chromophobe cells of the hypophysis.

In the second part he notes the following changes in the glands of internal secretion in persons of from 50 to 90 years of age: (1) Atrophy of the thymus and reduction in the size of the Hassal's corpuscles; (2) Variability in the follicular contents of the thyroid, deposition of lipoid and pigment in the follicular cells and increase in interstitial connective tissue; (3) Reduction in the suprarenal cortex and variability in its lipoid content; (4) The appearance of brown granular pigment in the posterior lobe of the hypophysis and the relative or absolute disappearance of eosinophile cells in the anterior lobe. In women the eosinophile cells are more numerous than in men.

The third and last part deals with death from suffocation in children in status thymicolymphaticus. It does not contain any new information.—E. V. C.

(INTERNAL SECRETIONS) Some remarks on the physiology of the ductless glands. Priestly (Henry), Med. J. Australia (Sydney), 1920 (i), 381-383.

A short review of the subject is given. No new data are included.—J. H. L.

(INTERNAL SECRETIONS) Mental deficiency and criminality. Schlapp (Max G.), Med. Rec. (N. Y.), 1920, **97**, 554-557.

The author divides mental defectives into three groups: (1) The traumatic type, in which there has been injury to the brain; (2) the formative type, in which the brain has not de-

veloped properly; (3) the functional type, "where there is a disturbance in the proportion of the different chemical factors in the surrounding medium from which the cells draw their necessary potential energy and activating substances, and therefore the cells do not react normally to stimulation." Schlapp believes a fair number of this latter group are caused by a disturbance of the internal secretions, and hopes that further study will permit more exact recognition of various types with consequent improvement under appropriate gland therapy. "In many of the cases examined at the Post-Graduate Hospital, chemical disturbance was found, and in more than half of these cases the cause was traced directly to certain of the internal secretory glands; and the encouraging part of it is that most of these people can be relieved if not cured." "Where the disturbance is of thyroid origin, methods have been fairly well worked out, and there has been some success with suprarenal unbalances, but the pituitary and other glands have not yet revealed their secrets."—H. L.

LIPODYSTROPHIA. Langmead (F.), Brit. J. Child. Dis. (Lond.), 1920, **17**, 33.

A case of a girl of seven years of age. The wasting was confined to the upper part of the body and ended at the level of the umbilicus. The face and neck were extremely wasted, the arms to a less extent, and the chest and trunk progressively less in a downward direction. The lower limbs were normal. The child was in general good health.—M. B. G.

(MAMMA) Homologous milk injection and mammary secretion during lactation (Eigenmilchinjection und Brustsekretion bei Wöchnerinnen). Lönne (Fr.), Zentralbl. f. Gyn. (Kiel), 1919, **43**, 908-915.

The injection under the nates of ½ cc. of milk from the breasts of the patient herself resulted in a marked increase in the secretory activity of the mammary glands in all of the six cases studied. Suggestion may play a rôle in the effect produced.—F. S. H.

(MONGOLISM) Two cases of Mongolian idiocy in the same family. Pardee (I. H.), J. Am. M. Ass. (Chicago), 1920, **74**, 94-95.

An interesting case report of two Mongolian idiots. The parents were Italians, the father 45 years of age, the mother 38 when the last child was born. These idiots were the young-

est in a family of eleven children. The other members of the family were normal. R. P., age 7 years, was born after prolonged labor, is undersized, has blepharitis; almond-shaped eyes: epicanthic folds; left external stabismus; thick lips; large protruding tongue with transverse fissures; broad, flat nose; soft, dry, hairless skin; hypotonic joints; oblique thumb and short little finger; undescended testicles, and no signs of the second dentition. His vocabulary is limited to single words. E. P., age 4 years, is very noisy, destructive and always busy. Physically he is the counterpart of his brother. The author discusses briefly the relation of the birth of Mongols to the period of the reproductive life of the mother. In this case the mother was of pronounced dyspituitary type, with nasal eyebrows, spacing of the incisors, obesity, frequent frontal headachés, and a history of diabetes in her mother. The children with their dry, smooth, hairless skin, small stature, prognathism, abnormal bony growths,, and undescended testicles show definite signs which could be classed as polyglandular. For these reasons the author favors a possible endocrine factor in the development of Mongolian idiots, despite the fact that endocrine therapy has hitherto been unavailing.—F. C. P.

Death following OBESITY (Muerta consecutiva a obesidad). Marañon (G.), Real Acad. Nat. de Med. (Madrid), April 20th, 1918.

The case is reported of a woman of 29 years, who was actually a monster. Her height was 160 cm.; weight, 157 K.; bust measure, 130 cm.; neck, 44 cm.; arm, 51 cm.; thigh, 96 cm., and abdomen at the level of the navel, 150 cm. She began to take on flésh after becoming affected with syphilis, menstruation becoming suspended at the same time. The subject died suddenly. Autopsy showed the ovaries to be larger than normal, weighing 17 to 20 gms., and very hard. The microscope revealed sclerotic ovarian degeneration. The thyroids were small and sclerotic, and there was persistence of the thymus.—E. B.

Clinical comments concerning opotherapeutic treatment in gynecology and obstetrics (Comentarios clinicos al tratamiento opoterápico en ginecologia y obstetricia). Botin (F.), Revista españ. de Obst. and Ginec., Madrid, 1918. ——, ——.

The author dwells upon the importance of opotherapy in many processes having relation to gynecology and the necessity for detailed study of the subjects. Frequently, besides

ovarian disturbances, there intervene other endocrine gland disturbances, these latter calling for the application of combined opotherapy.—E. B.

(ORGANOTHERAPY) Treatment and management of the neurasthenic individual. Neu (C. F.), Med. Rec. (N. Y.), 1920, **97,** 341-346.

The author devotes a paragraph to organotherapy in neurasthenia. He does not believe that much encouragement can be offered as yet for this type of therapeutics. "If it should be finally shown that certain disturbances of the functional interactivity of the internal glandular secretions are more or less responsible for producing the symptom-complex under consideration, and if it should be determined what brings about those disturbances of glandular activity, it may be possible that a therapy along these lines will be developed, but as yet very little is offered."—H. L.

OSTEOMALACIA: it is a rare or rather common disease. Dieffenbach (W. H.), Med. Rec. (N. Y.), 1920, **97,** 995-997.

"Nervous and mental depression during the climacteric frequently has, as a basis, calcium deficiency and osteomalacia is frequently associated with it. This points to gonad-ovarian deficiency." "As the parathyroid glands are now believed to preside over calcium metabolism as the thyroid presides over iodin metabolism, there is some reason to look for parathyroid abnormality in this disease. Adrenal deficiency is also believed to be a factor in many instances." The author advises trying organotherapy, particularly suprarenal, ovarian or testicular, and parathyroid, but presents no data demonstrating success by their use.—H. L.

OSTEOMALACIA, a study of the effects of certain organ extracts and oöphorectomy on the metabolism of calcium and magnesium. Freund (Hugo A.), & Lockwood (Bruce C.), Annals of Medicine (Hagerston, Md.), 1920, **1,** 67-76.

The authors record the valuable results of a study of a sort unfortunately relatively rare in the endocrine literature. A woman of 33 years, suffering from osteomalacia, was made the subject of a metabolic study under carefully controlled laboratory conditions. After a week's control period she was given successively desiccated thyroid gland in 5 grain doses, three times daily; pituitrin, 1 cc. hypodermatically, twice daily, and, finally, parathyroid extract in 1/10 grain doses—fre-

quency not stated. In each case the gland administration was continued for a week, with rest periods between experimental periods. Succeeding the parathyroid administration the ovaries were removed, both being found cystic. During each period of the study determinations were made of the calcium and magnesium intake and of the calcium and magnesium output in feces and urine. It was found that there was a marked calcium loss, as described by previous investigators in this disease. The magnesium showed a minute loss. In contrast with previously described cases, the greater amount of calcium was excreted in the urine. During the thyroid administration there was a negative calcium balance of 1.447 gms. as compared with a negative balance of 0.447 gms. during the control period. Similarly there was a negative balance of 0.327 gms. in case of magnesium during the thyroid period and of 0.027 gms. during the control period. During the pituitrin period the calcium balance was -2.604, and the magnesium balance -0.015. There was thus augmented calcium loss during both the thyroid and the pituitrin periods. The magnesium loss was more than ten times as great during the thyroid as during the normal period. During the pituitrin period there was little change in magnesium excretion. During the parathyroid period, on the other hand, there was a marked gain, both in calcium and magnesium, the balances being positive, 0.616 and 0.775 gms., respectively. After removal of the ovaries there was much greater loss of calcium and a slightly greater loss of magnesium than during any preceding period. The negative balance for calcium was 5.086 and for magnesium 0.291. The castration was not successful in arresting the disease, as is shown both by these figures and by the clinical condition of the patient a year later.—R. G. H.

(OVA) Grafts of the eggs of anura upon adults of the same species or upon adult urodeles (Greffes d'oeufs de batraciens anoures sur des adultes de mème espèces ou sur des batraciens urodelles adultes). Weber (A.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 891-892.

Not of endocrine interest.—T. C. B.

(OVARY) Effects of castration upon the automatic movements of the uterus in the guinea-pig (Effets de las castration sur les mouvements automatiques de l'utérus chez le cobaye). Athias (M.), J. Physiol. et de Path. Gén. (Paris), 1920, **18**, 731-743.

The uterus to be studied was removed from the body and preserved in a nutrient fluid. The automatic movements of

uteri from normal virgin guinea-pigs, before and after puberty, and of pregnant and non-pregnant uteri of normal animals that had had offspring were compared with the movements of uteri from similar animals which had had both ovaries removed at varying intervals before the experiment. Some of these latter were subcutaneously autografted with ovarian tissue a number of days after the preliminary operation. The observations of Fano, Bottazzi, etc., were confirmed, that the uterus possesses along with other muscular tissues a double contractile function, clonic and tonic. The clonic type is seen in the form of more or less marked automatic rhythmic contractions. The tonic function is revealed by oscillations of varying duration in the tone of the contracture. It was found that castration results in definite modifications of the motility of the uterus. These are evidenced by a gradual weakening and final disappearance of the involuntary contractions. The tonic function of the uterus, however, remains normal or is even increased. These modifications are attributed to the suppression of the internal secretion of the ovary. They are not seen in the animals that were grafted with ovarian tissue.

—L. G. K.

(OVARY) Deficiency of the internal sexual organs (Ontbreken der inwendige geslachtsorganen). Boshouwers (H.), Medisch Weekblad (Amsterdam), 1920, **27,** 109-110.

Description of a woman of 35 who never menstruated. She was of a male type (large hands and feet and weight of 174 cm.). The muscles were strongly developed. In the breasts no glandular tissue could be felt. The vagina was 3 cm. deep and ended blindly. Upon palpation by rectum no uterus or ovaries were felt. The author thinks of the possibility that the large hands and feet are caused by a hyperfunction of the hypophysis, the antagonist of which, the ovary, is lacking in this case.—J. K.

(OVARY) Hormones and menstruation. Burckhardt-Socin (O.) Corresp. Bl. f. Schweiz Ärtze (Basle), 1918, **48,** 1431-1435.

Ovarian extract is potent in so far as it contains substances derived from the corpus luteum. Two of these, "luteolipoid" and "lipamine," have been prepared in tabloid form: the first acts as a haemostatic, the other encourages the menstrual flow. The author claims valuable clinical results in their use in the relief of excessive bleeding, pain, and other menstrual disorders.—Physiol. Abst. **3,** 528.

(OVARY THYROID ADRENAL) Headache with mild endocrine disturbance. Garmendia (F. S.), Revista Médica del Uruguay (Montevideo), 1920, **23**, 57-61.

Garmendia reports two cases of headache for which thyroid insufficiency was evidently responsible, and which yielded to thyroid treatment. In another case, latent chronic suprarenal insufficiency was finally detected and under epinephrin treatment, supplemented by recalcification measures, the patient regained strength and the headaches disappeared. In his fourth case a young woman had violent headaches during the menstrual periods, with occasional milder headaches in the intervals, and menstruation was scanty and painful. Tachycardia, a soft pulse, and pains in the region of the ovaries confirmed the assumption of ovarian insufficiency, and under ovarian extract treatment there has been no return of the disturbances during the four months to date. The symptoms in the suprarenal case had been great weakness, frequent nausea, pains in the left hypochondrium, and intense and frequent headaches. Small patches of slight pigmentation were found in the axillae and at the waist. The headache in the thyroid cases was in the upper and front part of the head and lasted the whole day, the skin was dry, and the outer portion of the eyebrows was scant of hairs.—J. Am. M. Ass., **74**, 1357.

Influence of the OVARY on metabolism (Die Beeinflussung des Stoffwechsels durch das Ovarium). Guggisberg (H.), Zentrabl. f. Gyn. (Kiel), 1919, **43**, 561-564.

When 0.1 ccm. of a 1/1000 adrenalin solution is injected into normal women there occurs only a slight increase in the blood sugar. The injection of the same amount into women whose ovaries have been removed causes a marked rise of the blood sugar within half an hour. The same result was obtained in spayed rabbits. These results indicate to the author that the ovary plays a rôle in carbohydrate metabolism.—F. S. H.

(OVARY) Studies on the Graafian follicles (Estudio de la genesis y evolucion del foliculo de Graaf. I. Embryologia del foliculo de Graaf. II. Evolucion del foliculo de Graaf hasta su madurez). Guilera Molas (L. G.), Bol. de la Soc. Españ. de Biol. (Madrid), 1918, **8**, 246-286.

An interesting histological and physiological study impossible to abstract.—G. M.

OVARY, Clinical results of transplantation of— (Klinische Ergebnisse der Eierstocksüberpflangzung). Hartog, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 784.

Technical details. Autotransplantation is generally followed by reappearance of menstruation. Often two or three years after the operation menstruation becomes irregular and ceases.—J. K.

(OVARY) The involuntary nervous system in pregnancy and treatment of toxicosis with ovary (Das vegetative Nervensystem in des Gravidität und die Ovarialtherapie der Toxikosen). Hofbauer, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 758.

The sympathetic and parasympathetic nervous systems show during pregnancy an increased degree of irritability. This is caused, supposedly, by the increased function of hypophysis, thyroid and adrenals. In cases of hyperemesis during pregnancy the author saw good results of ovoglandol (doses, etc., are not given). During eclampsia ovoglandol may be tried to diminish blood pressure and to diminish the spasm of the blood vessels. The exudation diathesis and the inclination toward the formation of edema in pregnancy are also due to changes in the endocrine organ.—J. K.

(OVARY) Ovarian metrorrhagia and radiotherapy (Metrorragios ovariales y radioterapia). Macan (J.), Revista españ. de obst. y ginec. (Madrid), 1918, ——, ——.

In addition to metrorrhagia due to internal lesions there exists others which are exclusively due to disturbances of the ovarian functions. This gland possesses different hormones which mediate distinct functions. In the successive phases of the development of the corpus luteum, there are formed various lipoid substances which act in a characteristic manner. The young lutein cells contain "lipomins" or "lutamins" having properties stimulating congestive conditions and determining the modifications necessary to bring on menstruation. In the corpus luteum there are already developed "luteolipoid" substances possessing the property of inducing ischemia. To these is attributed the suppression of the menstrual flow during the period of gestation. When the corpus luteum is insufficient and fails of complete development, the "lipomins" persist but without forming the "ischemic" hormones, and therefore metrorrhagia occurs. The author recommends radiotherapy in these cases.—E. B.

(OVARY) Contribution to the clinical study of ovarian insufficiency (Contribución al estudio dela clinica de la insuficiencia ovárica). Marañón (G.), Revista españ. de obst. y ginec. (Madrid), 1917, ——, ——.

The ovary is a mixed gland having an exocrine function, ovulation, and another, the endocrine function. As regards the endocrine functions there exist three classes of hormones: (1) "Genital," elaborated by the corpus luteum, which actuates the genital life of the woman, affecting menstruation and conception; (2) "Sexual," which exert their influence upon the appearance and development of the primary and secondary sexual characters, probably engendered by the interstitial and folicular tissue, and (3) General, which act on the entire organism, affecting metabolism and the nervous system, principally the vegetative. Their origin is complex. The corpus luteum determines the structural changes necessary for menstruation, and equally for impregnation of the ovum, to the insufficiency of which it is possible to attribute inexplicable abortions, those not due to habitual causes, syphilis, etc. Other glands of internal secretion intervene in the physiology of the ovary, thyroid, hypophysis and suprarenal capsules. Considering these facts it becomes comprehensible how ovarian insufficiency may manifest itself in such different forms as: (1) Simple luteal insufficiency accompanied only by menstrual disturbances; (2) Total ovarian insufficiency in which in addition to the menstrual disturbances there is scant development of the primary and secondary sexual characters, tendency to obesity, local adiposity, trophoneuroses, headache, vasomotor disturbances, etc.; chlorosis and many cases of asthma have a hypovarian pathogeny; (3) Ovarian insufficiency accompanied by the reaction of other glands, thyroid-ovarian, suprarenal-ovarian, hypophyseal-ovarian and pluriglandular syndromes. In total ovarian insufficiency opotheapy ought almost always to be employed and in the combined syndromes ovarian with other glandular extracts. It is only when menstrual disturbances dominate that corpus luteum extract is employed. There exists ovarian hemorrhage due to the circumstance that the corpus luteum possesses different hormones according to the epoch of its development; some of these favor coagulation of the blood. This explains the paradox of the appearance of menorrhagia, which gives way to ovarian opotherapy.—E. B.

(OVARY THYROID) Two cases of catamenial angina (Sobre dos casos de angina catamenial). Martin Calderin (A.), Revista de med. y cirug. pract. (Madrid), 1918, ——, ——.

The author reports the history of two young women affected with thyroid-ovarian insufficiency. Coincident with the appearance of the menses, there appeared sudden attacks of streptococcic angina. This is a picture analagous to catamenial erysipelas, and undoubtedly is due to diminution of the organic defenses because of humoral disturbances which originate in endocrine insufficiency.—E. B.

(OVARY) The theory of ovulation and its relation to normal and pathological processes in the uterus with some remarks on hormone theory (Zur Lehre von der Ovulation und den mit ihr in Beziehungstehenden normalen und pathologischen Vorgängen am Uterus nebst Bemerkung zur Hormonlehre). Meyer (R.), Zentralbl. f. Gynak. (Leipzig), 1920, **44**, 473-479.

Complete data will be published in Archiv für Gynäkologie. This abstract of a larger article is of no immediate endocrine interest.—J. K.

Perturbations in the function of the OVARY and other endocrine glands and digestive disorders (Perturbaciones en el functionamiento del ovario y otras glándular endocrinas y alteraciones digestivas). Ygea Rodriguez (F.), Rev. españ. de obst. y ginec. (Madrid), 1917, ——, ——.

Observations of clinical cases frequently prove that digestive alterations are due to endocrine disorders. Among such cases was that of a young woman suffering from hyperthyroidism and gastric ulcer and, according to the physician who reported the case, ovarian disturbances, which brought on frequent and abundant menstruation. The hyperovarian syndrome of Dalché possesses very little clinical reality in those cases in which there is an absence of periodical menstrual disturbance and exaggerated flow. Modern knowledge of the physiology of the ovary and clinical observations lead more readily to the supposition that there exist in such cases an ovarian insufficiency and, more or less commonly associated therewith, hyperchlorhydria and gastric ulcer. Therefore the author with reason attributes the symptoms to vagatonia, inasmuch as the ovarian hormones tend to excite the tone of the vagus.—E. B.

(OVARY) The clinical signs of ovarian functional anomalies (Die klinischen Zeichen der Funktionsanomalien des Ovariums). Schröder (R.), Monatschr. f. Geburtsh. u. Gynaek. (Berlin), 1920, **51**, 217-232.

Constitutional factors may be responsible for excessive functioning of the ovaries, or the loss of inhibitory factors from other endocrine glands. Chronic metro-endometritis may develop as the consequence of long continued ovarian hyperfunctioning, but transient hyperfunction is usually a period of increased physical, mental and sexual vigor.

The etiology of ovarian insufficiency is remarkably many sided, yet such cases can be divided into two categories: those in which the cause of the insufficiency lies in the ovary itself,—primary insufficiency, and those due to an external harmful influence acting on the ovary,—secondary insufficiency. In the first group the author puts infantilism of all types, congenital and acquired. In the second group are put the various pathological growths affecting the ovary; the disturbances of internal secretion,—hyper-and hypo-thyroidism, adrenal and hypophyseal insufficiencies; cachexia of any type and acute and chronic intoxications arising from metabolic or nutritional disturbances; primary and secondary anemias; psychic disturbances and unknown causes arising at the climacteric; carbon dioxid intoxication from defective circulation; nervous or mental derangement; change of climate, and unknown causes.

If all these can be excluded, primary insufficiency of the ovaries may be assumed, and proper treatment instituted. Perverted ovarian functioning is manifested in irregular bleeding from the uterus from the persistence of ripe follicles without any corpus luteum stage. With cystic degeneration of the ovaries, the follicles do not ripen, but with this hemorrhagic metropathy the persistence of the follicles keeps the endometrium in a constant state of proliferation. Another anomaly for which perverted ovarian secretion is known to be responsible is the persisting corpus luteum. It may be so large as to simulate extra-uterine pregnancy.—F. S. H.

(OVARY) An ectopic ovarian cyst. Thompson (J. W.), Brit. M. J. (London), 1920 (i), 437.

Not of endocrine interest.—L. G. K.

A case of PSORIASIS with AMENORRHEA cured with ovarian therapy (Un caso di psoriasi generalizzata con amenorrea guarito con il trattamento opoterapico). Verrotti (G.), Riforma med. (Napoli), 1920, **36**, 321-322.

The patient whose case is reported had been ill of psoriasis and amenorrhea more than six years, and no treatment had given any lasting result. Finally, after a few months of

ovarian treatment the menstruation reappeared and the psoriasis was fully cured. Verrotti calls this psoriasis a toxidermia due to alterations of the utero-ovarian function and insists on autointoxication as one cause of the dermatoses.—G. V.

OVARY and symptoms of reduced function (Ovarium werking en de Z. G. uitvalsverschijnselen). Wesselink (D. G.), Neder. Maandschr v. Geneesk. (Leiden), 1920, **1**, 196-215.

In women suffering from menstrual disorders we must distinguish the complaint immediately before menstruation (which are due to hyperfunction of the ovaries) from the complaint during menstruation (which is due to a temporary cessation of the internal secretion of the ovary). These complaints are the same, but in lesser degree, as the complaints in the same person after castration. Therefore it is necessary in women with menstrual disorders who have to undergo gynaecological operations not to remove both ovaries if there is the slightest possibility of leaving at least one. Otherwise the menstrual complaints will return after castration in a permanent and more serious way.—J. K.

PANCREAS, Histogenesis of the islands of Langerhans in certain mammals (Sur l'histogénése des ilots des Langerhans chez certains mammiferes). Aron (M.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 631-634.

Of technical histological interest.

(PANCREAS) Life assurance and glycosuria. Cammidge (P. J.), Lancet (London), 1920, **i**, 836.

Advocates a determination of the blood sugar in cases of apparent glycosuria where there is doubt as to the nature of the reducing substance in the urine. Cases of pentosuria, levulosuria and pseudo-levulosuria show a normal blood sugar content, and after a test meal the percentage of sugar in the blood follows a normal curve indicating that the carbohydrate tolerance is not diminished in spite of the presence of "sugar" in the urine. The author places much more reliance on examinations of the blood than of the urine in the diagnosis and treatment of diabetes.—L. G. K.

(PANCREAS) Pancreatic dehydration in diabetic coma (La déshydration du pancréas dans le coma diabètique). Chauffard (A.) & Grigaut (A.), Bull. et mem. Soc. med. d. Hôp. (Paris), 1919, 3. s., **43**, 939-942.

It would appear from the results published by these authors that the water content of the pancreas of an individual dying in diabetic coma was less than normal; even the spinal fluid was thick and syrupy, and the coefficient of dehydration in the pancreas was 170 per thousand. Since, however, the values are apparently based on but one normal and one pathological case, the ultimate decision should be withheld.—F. S. H.

PANCREAS, The diagnosis of disease of the—. Feldman (W. M.), Brit. M. J. (London), 1920 (i), 553-554.

The author states that in individuals who are normally sympatheticotonic the Loewi adrenalin mydriasis test for pancreatic insufficiency is of no value since such persons give a positive reaction in the absence of any pancreatic derangement. Other tests are suggested (Aschner's oculo-cardiac reflex and the respiratory cardiac reflex) as of value in the diagnosis of disease of the pancreas by detecting signs of a hyperactive sympathetic nervous system. All three of these reactions are of use only when the patient is known to be normally a vagotonic.—L. G. K.

(PANCREAS) Life assurance and glycosuria. Fox (R. H.), Lancet (London), 1920, **i,** 836. Also May (O.), ibid, 836-837.

These authors dissent from Williamson's article (see abstract elsewhere in this number) in that they believe that an applicant for life assurance in whom glycosuria has been found should not be told the nature of his affection but should be merely advised to consult his own physician. Exception is also taken to the severity of treatment recommended for cases of temporary glycosuria. Many such cases are said to be "nothing more than a functional derangement," and consequently acceptance by the insurance companies at ordinary rates is advised.—L. G. K.

PANCREAS, The Schornstein Lecture on the diagnosis of diseases of the—. Garrod (A. E.), Brit. M. J. (London), 1920, **i,** 459-464.

A considerable portion of the paper deals entirely with the external secretory functions of the pancreas. Loewi's adrenalin mydriasis test as a sign of pancreatic insufficiency is recommended as an aid in diagnosis. The absence of glycosuria is said to afford no argument against the presence of disease of the pancreas. The same may be said of lowered sugar tolerance which may be present in disturbances of other ductless glands. Cammidge's reaction is advocated as

an aid in detecting pancreatic derangements. The author emphasizes the fact that "practically every sign, symptom or test may fail at times, and that in each individual case we need to balance the quantity and quality of the evidence for and against a lesion of the pancreas." It is still true, as Wardell stated in 1871, that "no symptoms are pathognomic of pancreatic disease; an assemblage of symptoms points to the probability of its lesion."—L. G. K.

(PANCREAS) Proof of nuclear digestion and the diagnosis of pancreatic insufficiency (L'épreuve de la digestion des noyaux et la liagnostic de l'insuffisance pancréatique). Labbé (M.), Bull. et mem. Soc. med. d. hôp. (Paris), 1919, 3. s., **43**, 794-785.

Of no endocrine interest.—F. S. H.

(PANCREAS) Anaesthetics and diabetes mellitus. Leyton (O.), Lancet (London), 1920, **i**, 736.

The author emphasizes the fact that a general anesthetic may lead to the transformation of a comparatively slight case of diabetes into one of great severity. A diabetic who has been able to take a diet supplying sufficient energy to allow the individual to maintain his weight and to do a certain amount of manual labor finds that after a general anesthetic he can no longer remain sugar free on a diet which will permit him to retain his weight. Therefore only absolutely essential operations should be performed upon diabetics, and spinal anesthesia and local anesthesia should be adopted when possible. Nitrous oxide with oxygen is less likely to damage the patient than ether, and ether is less harmful than chloroform.—L. G. K.

(PANCREAS) Incipient diabetes mellitus. Mason (E. H.) & Sutherland (C. G.), Can. M. Ass. J. (Toronto), 1920, **10**, 657-660.

Four cases are reported in which a transient glycosuria was discovered during life insurance or other examinations. In no instance did the blood sugar follow a normal curve after administration of 100 grams of glucose on a fasting stomach. In one case the sugar in the blood reached 0.348 per cent, a figure frequently not exceeded in many outspoken cases of diabetes mellitus after a similar proceeding. The blood sugar reached its maximum concentration on the average in 1.3 hours. The fasting blood sugar averaged 0.131 per cent. and

this figure was again reached 2.8 hours after the ingestion of the glucose. Three of the cases showed a slight glycosuria. The glucose threshold in the kidneys, as estimated on the fall of the curve, averaged 0.192 per cent, being remarkably raised in two cases, 0.2 per cent and 0.226 per cent. In none of the four cases could any abnormality in kidney function be determined.—L. G. K.

(PANCREAS) The glycogen in diabetes following pancreatectomy (Les glycogéne dans les diabéte par extirpatiòn du pancreas). Paulesco (N.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 562-565.

A recent hypothesis explains diabetes following pancreas extirpation by the fact that the liver and muscles have lost their power to fix glucose in the form of glycogen. It is desirable to know precisely whether the incapacity of the tissues to form glycogen is absolute or relative; whether it is the direct effect of pancreatic insufficiency or a phenomenon that is secondary and contingent. The experiments consisted of total ablation of the pancreas; at the same time a lobe of the liver was removed to determine the quantity of glycogen in the beginning of the experiment and finally the autopsies were performed. In one set of experiments the animal was starved; in the other it was fed on various sugars. The conclusion is that after total ablation of the pancreas the ability of the liver to retain glycogen is considerably reduced, but not annihilated. The same can be said for muscle. The power of the myocardium to fix glycogen remains normal and persists until death sixteen days after the operation. The glycogenic incapacity is relative,—a contingent phenomenon,—and not the cause of diabetes.—T. C. B.

(PANCREAS) Pancreatic infantilism. Sainz de los Terreros (C.), Siglo Med. (Madrid), 1920, **67,** 221-223; Abstr. J. Am. M. Ass. (Chicago), 1920, **75,** 138.

The author refers to backward growth from insufficiency of the pancreas. The literature records few instances of this, but he has encountered it in a number of children. The pancreatic insufficiency does not entail diabetes in children, although certain features of the metabolism resemble those of diabetes in adults and transient alimentary glycosuria is common in children. His experience has convinced him that the pancreas has three hormones in all probability, one serving for carbohydrate metabolism, one for the interglandular control of growth and development, and the third forming

the active element in the pancreatic juice. In children, insufficiency of the two last mentioned hormones will check normal digestion and also check normal growth, while the carbohydrate metabolism may proceed normally or with only minimal glycosuria and acetonuria. A child with pancreatic insufficiency begins to lose weight; acetone and preacetone bodies are thrown off in the urine and the thyroid, freed from the pancreatic hormone, functions to excess. There is usually a tendency to adenoids, pathologic tonsils, mononucleosis and often leucopenia; the resistance is low and the child contracts disease easily.—M. B. G.

(PANCREAS) The paranucleus of the pancreatic cell with reference to the work of Saguchi (Le paranucléus de la cellule pancréatique a propos d'un travail de Saguchi). Shaves (P. R.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 881-884.

Of histological interest.—T. C. B.

(PANCREAS) Life assurance and glycosuria. Williamson (R. T.), Lancet (London), 1920, **i,** 708-711; 934.

The author found a family history of diabetes in 22.4 per cent of 500 cases of diabetes while in a control series of 50 non-diabetic patients no family history of diabetes was obtained. He is of the opinion that a history of diabetes in one member of the family should not be regarded as requiring an extra charge for life insurance. However, a minimum extra charge is advised where two or more near relatives (brothers, sisters, parents) give a history of the disease.

If the urine of the applicant for insurance causes reduction of Fehling's solution and other symptoms of diabetes are present the case should be permanently rejected without further consideration. If there are no symptoms of diabetes, but Fehling's solution (or some modification) is reduced definitely, the case should be rejected, temporarily at least. Repeated examinations may be made to determine whether the reducing substance is sugar or some other substance. If the reduction of Fehling's solution is indefinite, before rejecting the case confirmatory tests for sugar should be made at once. If the reduction is not due to sugar the case may usually be accepted. The phenyl-hydrazin and fermentation tests are advised as confirmatory tests for glucose. If glycosuria is detected once only in several examinations of urine passed in the latter part of the day, and the sugar tolerance is not found to be lowered the case may be accepted with an

extra charge. However, if the sugar tolerance is diminished or if sugar is detected more than once rejection is advised. The author is also of the opinion that the examining physician should acquaint the proposer with the cause of his rejection and inform him of the exact significance of the glycosuria and of the importance of seeking treatment. It is essential that the patient be not alarmed as sometimes "a fear of diabetes," a neurosis similar to "sypilophobia" develops.

In a second paper the author defends his position that applicants for life assurance suffering from intermittent or temporary glycosuria should be informed by the examining physician of the nature of their ailment.—L. G. K.

PANCREATIC INSUFFICIENCY, Notes on a case of—. Symes (J. O.), Lancet (Lond.), 1920, (i), 494-495.

Not of endocrine interest.—L. G. K.

(PARATHYROID) The ammonia content of the blood and the neutrality regulation in epilepsy (Fortsatte Undersögelser over Neutraliteteregulation ved genuin Epilepsi). Bisgaard (A.) & Növig (P.), Hospitalstidende (Copenhagen), 1920, **63,** 49-62; Abst. Med. Sc. Abst. & Rev., **2,** 295.

The authors made about 2,000 blood examinations in 16 epilepties and a few normal controls. They found that blood ammonia varied in the epilepties from 0 to 1.42 mg. N. per 100 c.c., whereas the normal ranges is taken as 0.3 to 0.4 mg. The higher figures were obtained with regularity before an attack or a "psychic equivalent," while low values obtained after the attack. The urea content of the blood in epilepsy showed little deviation from the normal. The writers then compare the metabolism (calcium metabolism, as shown by the condition of the enamel, protein-metabolism, and NH_3 metabolism) characteristic of the three conditions, hypoparathyroidism in animals, tetany, and epilepsy, and they find striking uniformity in all. The most important difference is the absence in epilepsy of spasmophilic reactions which are common to hypoparathyroidism and tetany. The writers conclude that their investigations strengthen the view that genuine epilepsy is associated with hypo-function of the parathyroids. The recognition of a parathyroid epilepsy as a disease sui generis may also be followed by a subdivision of this disease according as the ordinary cases differ. Other details are given in the abstract cited.—R. G. H.

(PARATHYROIDS) Study of tetany in the adult incident to parathyroid apoplexy (Étude sur la tetanie de l'adulte par apoplexie paratyroidienne). Cordier (Mme. V.), Ann d. Méd. (Paris), 1920, **7,** 346-360.

A detailed report of a case of tetany in a man of 41 years with autopsy findings of a hematoma in the tracheo-thyroid region which had destroyed the right parathyroids, while the left parathyroids were hemorrhagic. The study of the progress of the disorder indicated that acidosis is an important symptom of tetany in the adult, although it was impossible to conclude that it is the basis. Opotherapy gave real relief in the earlier stages of the illness, but was ultimately unavailing. Tetany in the adult is briefly divided into five classes: (1) Surgical tetany; (2) Tetany in women attributable to an activity of the ovarian secretion on the parathyroids; (3) Tetanies of digestive origin in which possibly a particular kind of acidosis may play a part; (4) Tetany induced by infectious processes in the parathyroids; (5) Localized tetanies which are allocated to an endocrine insufficiency.—F. S. H.

(PARATHYROID) Tetany in the etiology of cataract (La tetania en la etiologia delas cataractas). Garrahan (J. P. & Belgeri (F.); Prensa med. argent. (Buenos Aires), 1920, **6,** 305.

The case is presented of a little girl four years of age who had suffered from convulsive attacks from her first to third years. She manifested hyperactive patellar reflexes, slight Chvostek's sign, hyperexcitability of the external popliteal nerve to mechanical stimulation and positive Erb's sign. She also had a zonular cataract. The authors believe that the cataract is probably to be ascribed to "latent tetany."
—B. A. H.

PARATHYROID transplantation, Data on the value of— (Erfahrungen über den Wert der Epithelkörperüberpflanzung bei postoperativer Tetanie). Jaeger (H.), Zentralbl. f. Chir. (Leipzig), 1920, **47,** 565-569.

Two cases were treated with transplantation with only very temporary success. In these cases administration of calcium gave no success, either. In some other cases some good effect was seen from calcium lactate.—J. K.

PARATHYROID immune bodies, On the Formation of—. Kishi (Isami), Tokyo Igakkwai, 1920, **34,** ——, (No. 9).

The author has attempted to make a serum for use in parathyroid tetany. He found that the serum of rabbits immunized against horse's parathyroid does contain a true parathyroid antibody which, however, lacks specificity, since it works equally well against the thyroid, pineal, hypophysis, suprarenal and lymph glands of the horse.—E. V. C.

(PARATHYROID) The importance of vagal and splanchnic afferent impulses on the onset and course of tetania parathyropriva. Palmer (W. L.), Am. J. Physiol. (Balt.), 1920, **52,** 581-590.

The great frequency with which tetany and gastro-intestinal disorders are associated clinically, led the author to think that afferent impulses reaching the central nervous system through the splanchnics and vagi might have some influence on the onset and course of parathyroid tetany. Two methods of procedure were followed. The first consisted in the determination of the effect of double vagotomy and splanchnectomy, and the second in the determination of the effect of gastro-intestinal irritation by means of croton oil. The technic of the operation and the results are given in detail. The conclusions drawn from the results obtained are, that neither double vagotomy and splanchnectomy, nor gastro-intestinal irritation have any influence on the onset and course of tetania parathyropriva.—T. C. B.

(PARATHYROID) Studies in the metabolic changes in experimental tetany. Togawa (Tokuji), (Tokyo), J. Lab. & Clin. M. (St. Louis), 1920, **5,** 299-306.

Togawa studied in eleven experimental young dogs and four controls the following: CO_2—combining power of the blood plasma, by the Van Slyke-Cullen method; the antitryptic power of the serum, by the Bergmann and Meyers methods; the non-protein nitrogen content of the serum, by Folin and Denis' methods. It was found that after parathyroidectomy (plus thyroidectomy) in dogs showing typical tetanic symptoms, a condition of acidosis always resulted, and the antitryptic power and the non-protein nitrogen content of the serum were usually increased. In cases, however, in which tetany did not occur, acidosis was not found. On the contrary a slight alkalosis was sometimes observed and the antitryptic power and the non-protein nitrogen remained practically unchanged.—R. G. H.

(PAROTID GLAND) Pellagra outbreak in Egypt. Enright (J. I.), Lancet (Lond.), 1920, (i), 998-1003.

From a study of pellagra among German prisoners of war, the conclusion is drawn that deficient diet or deficient digestion of the diet cannot be an important etiological factor. The food provided was abundant and varied. Parotitis was frequently an associated condition, and the suggestion is thrown out that the parotid gland forms an internal secretion which is required for protein utilization.—Physiol. Abst., **5**, 187.

(PINEAL) Comments on the function and clinical uses of the pineal gland. Berkeley (W. N.), Med. Rec. (N. Y.), 1920, **98**, 12-14.

There is now a recognized "pineal syndrome"—signs of cerebral tumor in the region of the corpora quadrigemina, concurrent with abnormal growth of the body, early appearance of axillary and pubic hair and remarkable sexual and mental precocity. The author in 1913 reported interesting experiments in feeding pineal gland to backward children with encouraging results in advancing the mental age. This work was confirmed and amplified by McCord. Horrax and Dandy obtained contradictory results from extirpation of the gland. The author inclines to doubt the reliability of surgical experiments because of the profound brain trauma incidental to the operation. Berkeley has continued his feeding of pineal glands to children (over long periods of time) with gratifying results. He calls attention to the advisability of combining pituitary, testis (or ovary) and thyroid with pineal gland when evidences of hypofunction of one or other of these glands is noticed. The gland preparation must be fresh and obtained from some well known and reliable source. Berkeley has also used pineal gland feeding in premature decay of the mental powers in old people and found that it quickens the slowed down mental processes, improves the memory and produces a remarkable cheerfulness and sense of well being. Finally, the author refers to Timmie's recent article in which he indicates a belief that progressive muscular dystrophy is of pineal origin.—H. L.

(PINEAL) On the nature of the epiphyseal cells (Sobre la naturaleza de las cellutas epifisarias). Hortega (Del R.). Bol. de la Soc. Españ. de Biol., Jan., 1917.

Histological study of the epiphyseal (pineal) gland which is considered a glio-epithelial organ, it not being possible to mark the limits between the epithelial and neurological elements.—G. M.

The PINEAL body; its structure, function and diseases. Jelliffe (S. E.), N. Y. Med. J. (N. Y.), 1920, **111**, 235-240; 269-275.

The pineal body may be considered as an independent organ certain parts of which have undergone a retrogressive evolution, while other parts have persisted and are undergoing progressive evolution. The lipoid material of the pineal body is related to visual purple of the photoreceptors of higher forms and is found in other forms in the pineal complex. This lipoid may be considered as an active transforming material for light energies. Alterations of the pineal structure can induce characteristic disease syndromes both as reactions due primarily to alterations of the gland itself or as syndromes due in part to the former, or to interference of functions of contiguous structures from pressure and extension of new growths. The article includes a general summary of the morphology, physiology and pathological physiology of the gland.—H. W.

(PINEAL) Pubertas praecox. Wiesenthal. Wiener klin. Wchnschr., 1920, **33**, 549.

Description of a boy of 20 months with development of penis as in a boy of 15 years, pigmentation of penis and erections. The voice is deep and the length of the body is as in a boy of 5 years. Upon radioscopy the ossification of the bones proved to be as in a boy of 12. There are no symptoms of brain tumor. The testicles are very small. The intelligence is normal. The cause of the condition has not been detected. — J. K.

(PLACENTA) Cytological studies on the human placenta and decidua with special reference to their internal secretory activity. Fujimura (G.), Tokyo Igakkwai, 1919, **33**, 15.

The author obtained material from 43 cases in many stages of pregnancy and studied it by means of the newer methods of technique designed to show the plastosomes (mitochondria). He draws a close analogy between the different cells of the placenta and those of other glands like the pancreas, suprarenal and so forth. He is of the opinion that the secretion is formed from the mitochondria, which change first into lipoid granules and then into droplets of more fluid nature which appear in the preparations in the form of uncolored vacuoles. He claims also to have determined the approximate time at which the different types of cells produce their various secretions: (1) The cells of the syncytium, from the

beginning of pregnancy to the end of the fourth month, being most apparent in the second and third months; (2) Langhans cells to the sixth or seventh month; (3) Zottenstroma cells from the end of the first month to the seventh month; (4) Small decidua cells from the end of the first month to the seventh month, and large decidua cells from the second to the sixth month. The paper is beautifully illustrated with lithographic plates and the extensive literature is carefully reviewed.—E. V. C.

(PLACENTA) Histogenetic and histophysiologic studies on the placenta (in the mouse). Ohashi (Y.), Tokyo Igakkwai, 1920, **34**, —— (No. 10).

This is a rather extensive contribution published in two numbers of the journal. The author divides his description into three stages, viz.: (1) Before placenta formation; (2) Placenta formation, and (3) After placenta formation. Special attention is paid to the origin and distribution of glycogen in the placenta, but comparatively little is said regarding the formation of internal secretions by the placental cells.

—E. V. C.

POLYURIA from cerebral piqure in dogs with denervated kidneys (Poliura por pinchazo cerebral en perros con riñones desnervados). Houssay (B. A.) & Carulla (J. E.), Soc. de Biol. de Buenos Aires, June 10, 1920.

Four cases were reported.—B. A. H.

POLYURIA from cerebral piqure in the dog (Poliura por pinchazo en el perro). Houssay (B. A.), Carrula (J. E.) & Romaña (L.), Soc. de Biol. de Buenos Aires, June 10, 1920.

The piqure was made by means of the cautery in a zone which was included between the optic chiasma and the protuberance. In some, but not all cases, this produced a marked polyuria. Similar polyuria was never observed in case the piqure fell outside the zone described. The polyuria so produced is primary; it is not due to polydipsia, vascular hypertension or glycosuria. The polyuria which follows hypophysectomy may be due, perhaps, to the cerebral piqure involved in the operation.—B. A. H.

PROSTATE, The internal secretion of the—and its relation to the testes (La sécrétion interne de la prostate et ses rapports avec les testicules). Bogoslovsky (G.) & Korentchev-

sky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 718-719.

Observations were made on eight dogs, two normal and six castrated. The normal equilibrium of exchange was established and the experiment divided into three periods. First, a period of three days for establishing the normal gaseous and nitrogen exchange. Second, a two or three-day period during which intravenous injections of emulsion of prostate, or of testicle, or both, were made. Third, a control period of one to three days. The results permit the following conclusions. Normal dogs show a slight increase of N exchange and diuresis under the influence of injections of prostate. In castrated dogs, the phenomenon is more accentuated—8 to 10 per cent. The simultaneous injection of prostate and testicle causes an augmentation of N up to 17 per cent, and of diuresis to 25 per cent. During the first four hours the N augmentation may be as much as 40 per cent and the diuresis 80 to 90 per cent. The prostate constitutes a powerful stimulant to the internal secretion of the testicles. The internal secretion of the testicles exercises a stimulating influence on the exchanges of protein substances especially.—T. C. B.

(PROSTATE) Loss of the specific secretion of cells cultivated in vitro (Perte de la sécrétion spécifique des cellules cultivées in vitro). Champy (Ch.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 842-843.

An attempt to ascertain if the properties of cultivated tissues are lost at the time of disappearance of the cytological characters. The prostate of the guinea pig was used, since the action of the ferment on the contents of the seminal vesicles can be clearly seen with small quantities of material. Fragments of the size used for culture give, when placed in vesicular fluid, a characteristic opaque appearance. Fragments placed in the ice chest for three or four days give the reaction unweakened; but if placed on plasma the reaction is lost by the fourth day. Histological controls show that the epithelium of the prostatic tubes survive, but give place to cicatrization at the surface as in other cultures; but it loses the particular characters of the normal prostate. The cells contain no characteristic secretion grains. There is, then, a correlation between the loss of differentiation and the disappearance of the characteristic secretion.

(SECRETIN) Action of acetone extracts of duodenal mucosa upon arterial pressure and upon the pancreas (Acció dels

extrets acetonics de mucosa duodenal sobre la pressió arterial i sobre del páncreas). Cervera (L.), Treballs de la Societat de Biologie, Barcelona, 1918, **6,** 19-21.

Extracts of duodenal mucosa made with acetone were compared with those made with acidulated saline solution as regards their effects upon blood pressure and pancreatic secretion. The acetone extracts were found to be somewhat less active but to produce a marked acceleration of pancreatic flow with no more than 10 mm. reduction of blood pressure. Hence secretin is not identical with Popielski's vasodilatin. Cervera suggests that the secretin acts on a "receptor substance" as postulated by Langley.—R. G. H.

(SECRETIN) Role of bile in the formation of secretin (Paper de la bilis en la formació de la secretina duodenal). Cervera (L.), Treballs de la Societat de Biologia, Barcelona, 1918, **6,** 22-23.

In view of the fact that secretin is supposedly elaborated normally in the duodenal mucosa in the presence of bile, Cervera investigated whether this latter substance plays any significant part in secretin formation. For a period of five days the bile was removed through a fistula, the loss of alkali being compensated for by the administration of sodium bicarbonate. At the end of the experimental period the duodenal mucosa was extracted in the classic manner and tested for its secretin content. The exclusion of bile from the duodenum had made no appreciable difference in the secretin formation.
—R. G. H.

Influence of SEX at different ages on the gravity of influenza (Influence du sexe aux différents ages sur la gravité de la grippe). Apert & Flipo, Bull. et mem. Soc. med. d. Hôp. (Paris), 1920, 3. s., **44,** 321-324.

A statistical presentation tending to show that grippe is of more severe effect when attacking females than the male.
—F. S. H.

SEX, Consideration of—in pediatrics (La considération du sexe en médicine infantile). Apert (E.), Bull. et mem. Soc. med. d. Hôp. (Paris), 1920, 3. s., **44,** 326-331.

From infancy on it is necessary to take into account in medical treatment the influence of sex. Disregard of the differences of the two sexes in planning hygienic and therapeutic measures is a grave error.—F. S. H.

Influence of SEX on the frequency of whooping cough (Influence du sexe sur la fréquence de la coqueluche). Apert (E.) & Cambessédès, Bull. et mem. soc. Med. d. Hôp. (Paris), 1920, 3. s., **44,** 324-326.

In France as in other countries, whooping cough is more frequent in females than in males.—F. S. H.

SPASMOPHILIA of older children (Die Spasmophille der älteren Kinder). Stneeman (H. A.), Jahrb. f. Kinderh. (Berlin), 1916, **86,** 43.

The author thinks that the glands of internal secretion may have a role in this disorder.—C. H. G.

SPASMOPHILIA, Experimental studies on the pathogenesis of— (Experimentelle Beiträge zur Pathogenese der Spasmophilie). Resch (A.), Jahrb. f. Kinderh. (Berlin), 1917, **86,** 294.

Resch studied the effect of B-iminazolylethylamine, para-oxyphenylethylamine, ethylamine, tenosin, choline and hypophysin upon the galvanic excitability of the peripheral nerves in the rabbit. Para-oxyphenylethylamine in subcutaneous doses of 0.05 gm. daily for a period of ten days and hypophysin in quantities of 1 cc. over a like period, increased the galvanic excitability of the sciatic nerve. Tenosin was inactive, while the others increased the nervous threshold. In a long theoretical discussion the author considers the possible rôle of soluble toxic proteinogenic amines of either endocrine or alimentary origin in the spasmophilic syndrome.—C. H. G.

Familial SPLENOMEGALY (Über familiäre Splenomegalie). De Lange (C). & Schippers (J. C.), Jahrb. f. Kinderh. (Berlin), 1917, **86,** 459.

Also reported in Amer. J. Dis. Child., 1918, **15,** 249, and abstracted in Endocrin., 1918, **2,** 192.—C. H. G.

(SPLEEN) Action of splenic extracts on smooth muscle. Preparation and nature of the active principle (Action des extraits de rate sur les organes á fibres musculaires lisses. Préparation et nature du principe actif). Stern (L.) & Rothlin (E.), J. de physiol. et de path. gén. (Paris), 1920, **18,** 753-780.

Hot or cold water extracts of the spleens of various animals contain a substance, "liénine," capable of causing con-

sont-elles sous la dépendence des glandes génitales)? Mercier (L.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 470-471.

Mercier has observed that the secretion of the salivary glands of the male panorpa plays the role of an excitant to the female at the moment of copulation, and this gives rise to the idea that there may be a relation between these glands and the testes. The salivary glands attain a complete functional state at the moment when spermatogenic activity is finished, and it remains to see if the sexual dimorphism is not "en rapport" with the more or less precocious evolution of the genital glands.—T. C. B.

(TESTICLE) Treatment of eunuchoidism (Behandlung des Eunuchoidismus). Lichtenstern, München. med. Wchnschr., 1920, **67**, 620.

A young man of 20 was castrated for tuberculosis of both testicles. Eunuchoidism developed. It was cured by transplantation of a testicle of the father of the patient.—J. K.

TESTICLE transplantation, Influence of—on sexual life (Ueber die Beeinflussung des Geschlechtslebens durch freie Hodenüberpflauzung). Muhsam (R.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 823-825.

The author made testicular transplants in three patients. One of these had been castrated for tuberculosis of both testicles. One was suffering from bisexuality, while the third was homosexual. From the last patient one of the testicles was removed preceding the transplantation. In all cases the effect was splendid.—J. K.

(THYMUS) Report of a case of malignant thymoma with necropsy. Foot (N. C.), Am. J. Dis. Child. (Chicago), 1920, **20**, 1-14.

Report of a case in a child, male, aged 9 years, who gave a negative history until one month previously, at which time he began to complain of inspiratory dyspnea and inability to lie flat in bed because of marked orthopnea. Two weeks prior to admission to the hospital his mother noticed swollen veins at the base of the neck just above the clavicle. He had occasional fits of gagging and coughing, which would awaken him at night, but no cyanosis. Physical examination showed dullness on both sides of the sternum from the first to the fifth rib; breath sounds and voice sounds were increased. Radioscopy showed a large mediastinal tumor occupying the

traction of smooth muscle. This is said to be the active principle of the organ. Details of the method of preparation are given. Liénine is soluble in water and in alcohol, and insoluble in ether, chloroform, toluol, petroleum ether and benzol. It is thermostable and resists the action of acids and enzymes. It dialyses readily and does not give the biuret or Fehling's reaction. It is a nitrogenous substance, probably an amine. It acts directly on the smooth muscle fibre and not on the myoneural junction or nerve ending, thus resembling histamine in its site of action. (Seen also Endocrin., 1920, **4**, 260.)—L. G. K.

Splenomegaly and INFANTILISM (Esplenomegalia e infantilismo). Jiminez Adna (L.), Siglo med. (Madrid), 1917, ——, ——, (Sept.).

The author reports a case of infantilism with very marked splenomegaly due to Banti's disease. Other various cases are to be found in medical literature in which infantilism was accompanied by splenomegaly due to Banti's disease, hemolytic icterus, etc. These cases may properly be included in Pende's group of exo-endocrine syndromes.—G. M.

(TESTES) Experimental diabetes insipidus and genital atrophy (Diabétes insipide expérimental et atrophie genitale). Camus (J.) & Roussy (G.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 901-902.

Description of the genital organs of one of the dogs with permanent diabetes insipidus previously reported. The dog weighed 26 kgs., but had a small penis for its size, with small testicles badly descended, and poorly distinguishable scrotum. This may be due to injury of the hypophysis, but it is not impossible that the lesion of the opto-peduncular space of the brain may have caused the genital atrophy as well as the diabetes.—T. C. B.

(TESTES) The seasonal cycle of the testicle of the blind worm orvet (Les cycle saisonnier du testicule des l'orvet). Dalq (A.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 820-821.

A histological description of the male genital glands in the orvet, in different months of the year.—T. C. B.

(TESTES) Are the salivary glands of Panorpa dependent upon the genital glands (Les glandes salivaires des Panorpes

upper central part of the chest anterior to the great vessels. At the operation the patient took the ether well until partially anesthetized, but as anesthesia became more profound he grew markedly cyanotic. The ether was stopped and the usual restoratives administered with a resulting return of his color to the normal and his heart in apparently good condition. He, however, never regained consciousness and one-half hour after starting the ether he suddenly became very pale and respiration and heart stopped abruptly.

Necropsy showed a very hard lobulated tumor occupying chiefly the anterior mediastinum, lying just behind the sternum but not infiltrating the bone. It showed metastasis by direct lymphatic extension with three possible minor metastases at a distance. It did not penetrate the lung nor other neighboring organs much more deeply than their serous coverings or sacs. It was composed chiefly of small cells resembling microlymphocytes, but having vesicular nuclei, acidophil cytoplasm and tending very slightly to anastomose with one another by means of slender processes. This applied only to a decided minority of their number, the majority being discrete. The rest of the tumor was chiefly cartilagenous connective tissue. Neighboring lymph nodes, while they showed a few discrete tumor cells in their sinuses, were usually not incorporated in the tumor mass. The author feels that the tumor was of thymic origin and different from the lymphosarcomas that originate in lymphnodes. He gives a short review of the literature.—M. B. G.

(THYMUS) Primary malignant tumor of the anterior mediastinum. Lymphadenoma of thymic origin (Tumeur maligne primitive du médiastin antérieur. Lymphadénome d'origine thymique.) Dandy (Ch.) & Piédelièvre (R.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44,** 867-876.

The case is reported of a mediastinal tumor in a man of 40, which developed at the expense of the thymus. There were symptoms of obstruction of the superior vena cava. Under the microscope the tumor appeared as a lymphadenoma. In spite of the absence of corpuscles of Hassal, the authors insist that the tumor was of thymic origin.—R. G. H.

THYMUS, The normal weight of— (Ueber das normale Gewicht der Thymusdrüse). Ishibashi (Matsuzo), Verhandl. d. japan. path. Gesellsch. (Tokyo), 1916, **6,** 19-20.

The thymus glands from 421 autopsies in the Pathological Institute of the Imperial University at Tokyo were weighed

and the weights tabulated according to age from birth to 80 years. The smallest average weight was noted at 6 months (5.30 gms.). The highest weight fell at 14-15 years (16.28 gms.). From this age there was a gradual decline to about 10 gms. at 30 years and finally to 6.5 gms. at 70. The article affords valuable data for those interested in the anatomical constants of the thymus.—R. G. H.

THYMUS death in children (Contribucion casuistica al estudio dela muerte timica en los niños). Palancar (J.) & de Arcaute (L. R.), Archivos Españoles de Pediatria (Madrid), 1918, **2**, 208-241.

This article describes the sudden death of two children, one of 10 months and the other of 4. Autopsy revealed nothing abnormal except exceeding hypertrophy of the thymus, which weighed 30 and 28 gms., respectively. In the case of the younger child, histological study of the thymus showed extensive development and abundance of the corpuscles of Hassall, which indicates to the authors that in hypertrophy of the thymus there is glandular hyperfunction. The authors also take into account the different pathogenic theories of thymus death, hypertensive coagulative, and toxic action on the myocardium (Thymusherz of the Germans) and equally, the part which the suprarenals play (chromaffin aplasia in status thymicus). In these cases there was no alteration in the chromaphil system. The necropsy observations favor the view of Popper and Fishl, who attribute thmyus death to coagulation in the heart and vessels which impedes filling of the aorta.—E. B.

(THYMUS THYROID) Contribution to the physiology of the glands. 42. Studies of the function of the thymus and the thyroid as shown by the respiratory metabolism at normal and increased external temperatures (Beiträge zur Physiologie der Drüsen. 42 Mitteilung. Untersuchungen über die Funktion der Thymus und der Schilddrüse, geprüft am Verhalten des respiratorischen Stoffwechsels bei normaler und erhöhter Aussentemperatur). Ruchti (E.), Biochem. Ztschr. (Berlin), 1920, **105**, 1-42.

Working in Asher's laboratory with thyroidectomized and thymectomized rabbits, Ruchti found that these animals not only stand the removal of these glands but also are good subjects for studies of respiratory exchange. Thyroidectomy causes a marked decrease in the carbon-dioxide and water output, while thymectomy has but little effect, which, however, is

in the same direction. Simultaneous removal of both glands is followed by a great decrease in carbon-dioxide and water output and thyroidectomy after thymectomy has the same result, the lower values remaining constant. When thymectomy is done after thyroidectomy no lower results are obtained; but here, too, the values fail to rise at a later period as occurs when the thyroid alone is removed. These facts seem to be the first experimental proof that the thymus and thyroid stand in opposite functional roles. At higher external temperatures (33° C.) the operated animals show a lesser respiration rate than do the normals.—F. S. H.

THYMUS. Changes of the—in experimental infections of mice (Die Veränderunug der Thymus bei der experimentellen Infektion der Mäuse). Takeuchi (Kiyoshi), Verhandl. d. japan. path. Gesellsch. (Tokyo), 1916, **6**, 17.

Fifty-seven mice were infected with Bacillus coli communis. The ratio of the thymus weight to body weight was studied. This ratio increased at first, reaching its highest value in 50-70 hours. This "hyperplastic stage" was followed by an "atrophic stage." In the hyperplastic stage the gland appeared in the gross grayish-white, translucent and edematous. The microscopic findings were as follows:

Hyperplastic stage—	Atrophic stage—
Boundaries of cortex and medulla obscure	Boundaries still more obscure
Small cells in medulla markedly increased	Small cells almost lacking, leaving only reticular tissue and Hassal's corpuscles
Reticulated tissue, no notable change	Augmented growth; many multinuclear giant cells apparent
Eosinophile cells, not increased.	Not increased as in human subjects
Hassal's corpuscles, no noteworthy changes	No changes
Connective tissue increased	Increased.

—R. G. H.

(THYROID) Syphilis and Graves' disease. Editorial note, Med. Rec. (N. Y.), 1920, **97**, 698.

Levy-Franckel, Pierre Marie, Gaucher, Sainton and Schulman have called attention to the surprising frequency of syph-

ilitic Graves' disease. Iodides that are contraindicated in ordinary exophthalmic goitre are beneficial in the luetic variety.
—H. L.

Thyroid and heat regulation (Schilddrüse und Wärmeregulation). Adler (L.), Med. Klin. (Berlin), 1920, **16**, 108.

Data published elsewhere. See Endocrin., **4**, 160.

(THYROID) Goiter and "old tuberculin" (Struma und Alttuberkulin). Althen, München. med. Wchnschr., 1920, **67**, 651.

Goiter and Graves' disease are remarkably often combined with tuberculosis. Therefore the author tried to cure goiter with local application of Koch's "old tuberculin." Every three days he rubs the left arm, the left part of the thorax, the right part of the thorax, the right arm and the skin over goiter with one drop of tuberculin. Often after one treatment the goiter becomes smaller. If after one series no success is seen, a second one is tried, but at the same time twice daily 10 drops of "jodvason" are rubbed on the goiter.—J. K.

THYROID Hormone, Action of the— (Die Wirkungen des Schilddrüsenhormons). Asher (L.), Therapeutische Halbmonatshefte (Berlin), 1920, **34**, 221-224.

A general review. Iodothyrin is not able to replace the hormone of the thyroid. Oswald's thyreoglobin, however, can take the place of this hormone. It has not been settled as yet whether this is possible with Kendall's thyrotoxin.—J. K.

(THYROID) Problems relative to prophylaxis of rural endemics in Brazil (Algunos problemas relativos a profilaxia de endemias ruraes no Brazil). Aragao (H. deB.). **Cruz' and Chagas' disease (Molestia de Cruz e Chagas),** Vasconcellos (F.), Soc. de Med. e Cirugia de Rio Janeiro, July 15, 1919.

Chagas' disease was discussed in important papers by two disciples of Oswaldo Cruz. F. V. affirmed that the Trypanosoma cruzi was discovered personally by Oswaldo Cruz, and that for this reason the Brazilian trypanosomiasis should be called Cruz' and Chagas' disease rather than by the name merely of the latter. The two authors were in agreement that the pathogenic importance of the disease might seem to have been exaggerated were it not known that 29 well veri-

fied cases have occurred and these in acute form in young infants. It is true that diagnoses of the chronic form have often been made also by the finding of pulmonary cysts in guinea pigs into which blood of the patients had been injected, but it has been demonstrated that these pneumocysts may be found in guinea pigs not injected at all, and that they are due to another organism than the protozoon in question. Both authors maintain that it has not been proven that endemic goitre is due to the trypanosome, and they agree with Kraus, Maggio and Rosenbusch that there has been a confusion of two diseases existing in the same district. It is certain that these restrictions oblige a renewed study of the chronic form of the disease but do not detract at all from the interest in the masterly study which Chagas has made of the acute form.—B. A. H.

(THYROID-PARATHYROID) On the effects of thyro-parathyroidectomy in the castrated guinea pig (Sur les effets de le thyroparathyroïdectomy chez les cobaye chatré). Athias (M.) & Ferreira de Mira, Compt, rend. Soc. de biol (Paris), 1920, **83,** 876-877.

The aim of these experiments was to see if castration in the guinea pig had any effect on the results of thryoparathyroidectomy. Previous results by various workers have been conflicting. Eight males over 3 years of age that had been castrated at the age of one or two months, and three females castrated three and a half months previously were the material used, with one male and two females over 4 years old (normal) as controls. All the animals died after removal of the thyroparathyroid apparatus, the time of death varying between one and seventy-three days, the symptoms in the castrated animals being the same as in the uncastrated controls. The conclusion is reached that castration does not preserve the guinea pig from the fatal results of thyroparathyroidectomy.

The THYROID in infections. Barbara (M.), Annali di Clinica Medica (Palermo), 1919, **9,** 1-20.

Data reported elsewhere. See Endocrin., **4,** 93-94.

(THYROID) A preliminary report on the endocrine therapy of high blood pressure. Bandler (S. W.), N. Y. Med. J. (N. Y.), 1920, **111,** 972-974.

A brief report of seven cases of high blood pressure which responded favorably to thyroid extracts. No change of diet

was made in ambulatory cases. No teeth were pulled or tonsils removed.—H. W.

(THYROID) Goitre in an infant. Barnett (E. C.), N. Zealand M. J. (Wellington), 1917, **16,** 143.

In an infant five weeks of age the thyroid was enormously enlarged, threatening asphixia. At operation the isthumus was resected with a view particularly to forestalling asphixia. The results were excellent. The child's weight began at once to increase. The enlargement of the lobes of the thyroid gradually disappared and has not recurred. At the time of writing the child was perfectly well.—R. G. H.

(THYROID) Hereditary occurrence of hypothyroidism with dystrophies of the nails and hair. Barrett (A. M.), Arch. Neurol. & Psychiat. (Chicago), 1919, **2,** 628-637.

Barrett reports the case of a patient showing the disorder mentioned in the caption in whose family history for generations have occurred trophic disorders of the nails and hair together with various mental and nervous disorders. In case of the patient reported the skin felt somewhat thickened and there was puffiness under the eyes. The hands were pudgy and the fingers short and clubbed. The hands and feet showed cyanosis. The hair of both the head and body was scanty. The eyebrows consisted of but a few short stubby hairs. The nails of both fingers and toes were short, failing to reach by a quarter of an inch the ends of the digits. No lanula was present. The ends of the nails were thickened and broken, though the nail surface was smooth. The skin was dry and at the ends of the digits tended to exfoliate. The patient was subject to tics of the face and shoulder. Speech was thick and nasal. Bone conduction was lacking for the left ear. There was marked hyperopia. Thyroid medication resulted in marked improvement. Similar deficiencies had occurred in the family for at least six generations. Among 61 members both hair and nails were affected in 14 instances. The nail defect seemed to be about the same in all, but there was much variation in the degrees of loss of head hair. In the greater number there was an extreme scantiness as to the amount of hair. In no instance was there a total loss of all hair of the head, the most extreme cases showing a fine lanugo-like covering of the scalp. Aside from this particular abnormality there were other features that showed that in this family group there were conditions active in the production of a variety of disorders that are of much interest to neuropsychiatry. This is the high frequency of feeblemindedness and

neurologic disorders of a degenerate type among the family. The members of the third generation who had dystrophies of nails and hair, and all of their descendants, numbered 29 persons. Of these, 22 were definitely abnormal. Twelve of the latter had the characteristic family dystrophy, and 10 others, who lacked this, showed other constitutional and nervous disorders. These included one case of epilepsy, one of hysteria, one of severe tic, four instances of feeblemindedness, one of nocturnal enuresis and four died at an early age from marasmus. Even those who had the nail and hair dystrophy had other abnormalities. One of these was an epileptic; one had cancer; four were feebleminded, and one had nocturnal enuresis. The well known association of abnormalities of hair and of nails in hypothyroidism, and two fairly well defined cases of juvenile myxedema which led to this study, and the reaction of one patient to thyroid feeding, seems to warrant in Barrett's opinion the conclusion that the fundamental disorder in this family was of the thyroid gland.

A review of the literature discloses a number of other families with a similar history to that cited. A summary of these is included.—R. G. H.

(THYROID) Subtotal thyroidectomy. Bartlett (W.), Surg. Gynec. & Obst. (Chicago), 1917, **25,** 402-410.

The article is largely of technical interest, giving many details of operative procedure. The desirability of taking away most of both lobes of the thyroid (in exophthalmic goitre) is stressed. A small proportion of the gland, the amount depending upon the individual conditions, should be left. In twenty-six cases upon which the method was practiced the results were "practically ideal."—R. G. H.

(THYROID) Preliminary report on a new method for the clinical diagnosis of toxic thyroid states, with a note on serological technique. Berkeley (W. N.) & Koopman(J.), Med. Rec. (N. Y.), 1920, **97,** 1035-1037.

Using normal dog thyroid as antigen, Berkeley tested 175 human sera of which 40 were from patients with suspected thyroid diseases; 18 of the 40 were undoubted instances of Graves' disease and gave positive complement fixation response. Control serums in 135 cases gave negative results in all except one. Furthermore, as the positive Graves' disease patients improved under treatment the test changed from four plus to two plus, etc. The test has been repeated hundreds of times and has been checked carefully with controls. The author hopes it will prove of value in differentiating per-

plexing cases from true hyperthyroidism and will aid in judging the effects of treatment. Dog thyroid would seem to contain a substance native in the dog but toxic in man. This substance Berkeley calls cynothyrotoxin and presumes that it is formed in the human thyroid under the abnormal chemical conditions which appear when exophthalmic goitre develops. The antigen is an extract of the mixed thyroids of five or six dogs. It slowly deteriorates and a fresh supply must be obtained in three weeks. Details of preparing the antigen are given.—H. L.

Carcinoma of the THYROID. Blaxland (A. J.), Brit. M. J. (London), 1920, (i), 454.

In the writer's experience adeno-carcinoma of the thyroid is rare, and a correct diagnosis is not usually made until the growth has spread through the capsule of the thyroid and the chance of cure by operation is remote. He cites a case occurring in a woman of 25. The lobe in which the tumor was situated was removed without difficulty and the diagnosis was made on microscopical examination. This patient had had the other lobe of the thyroid removed six years previously for parenchymatous enlargement.—L. G. K.

(THYROID) A case of goitre with nearly total external ophthalmoplegia (Een geval van struma met ophthalmoplegia quasi totalis externa). den Boer (M.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64** (I), 2284-2286.

A woman of 34 with Graves' disease was operated upon. Ten years later she developed recrudescence of goiter with ptosis of both eyelids and paresis of the eye muscles, paresis of the levator palatina dextra and hemiplegia laryngis sinistra. The pulse was 70; there were no tremors and no hyperhydrosis, i. e., there were no symptoms now of Graves' disease. A combination of simple goitre and paralysis of the muscles mentioned above has never previously been described.—J. K.

THYROID, Hemorrhagic syndrome cured by thyroidin (Syndrome hemorragique guéri par la thyroïdine). Bottaro (L. P.) & Mussio Fournier (J. C.), Anales de la Fac. de Med. (Montevideo), 1920, **5**, 191-194.

See Endocrin., 1920, **4**, 366-368.

(THYROIDS PARYTHYROIDS) The effect of thyro-parathyroidectomy on the heart and circulation. Part II. Ac-

tion of guanidin on the heart of the frog. Burns (D.) & Watson (A.), J. Physiol. (Lond.), 1920, **53,** 386-390.

This work was undertaken to determine whether the nicotine-like action of guanidin afforded sufficient explanation for the circulatory disturbances following parathyroidectomy. Heart tracings taken after administration of guanidin compared with those taken before almost invariably showed cardiac retardation, whether the guanidin was injected into the dorsal sac, or painted on the heart, or the heart bathed in solution. Two causes for the retardation have been adduced: (a) Stimulation of the vago-cardiac nerves, and (b) pronounced vaso-constriction with reflex inhibition. There was a primary acceleration probably due to stimulation of the accelerator nerves of the heart. By the use of atropine and nicotine the point of action of guanidin has been localized. It has a nicotine-like action on the sympathetic neurons.—T. C. B.

(THYROID) Maladies and medicines. Campbell (Arthur), Practitioner (Lond.), 1920, **104,** 305-312.

The article consists of brief notes about sundry diseases and drugs. The author describes the first case of myxedema he saw, which was in 1883, a few days before the disease was first described. He mentions a case of Charcot's latent exophthalmic goitre.—H. L.

(THYROID) Basedow's disease accompanied by hypertrophy of the eyelids and cheeks (Maladie de Basedow avec hypertrophie des paupières et des joues). Chauffard (A.) & Monnot (P.), Bull. et mem. Soc. med. d. hôp. (Paris), 1917, 3. s., **41,** 421-423; 482-484.

Report of an interesting coincidence of Basedow's disease and hypertrophy of the eyelids and lips not oedematous in character.—F. S. H.

(THYROID) Goitre in pregnancy. Crotti (A.), Am. J. Obst. (N. Y.), 1917, **75,** 450-455.

Data published elsewhere. See Endocrin., **3,** 105.

(THYROID) The somatic causes of psychoneuroses. Dana (Charles L.), J. Am. M. Ass. (Chicago), 1920, **74,** 1139-1143.

The case is reported of a boy, aged 19, with a well marked psychoneurosis. He was subject to "seizures" of a peculiar sort. He would suddenly feel as if there were a burning, torturing fluid in his head and pouring through his body. After

a short time this feeling was superseded by nervousness, restlessness and apprehension. He finally had to give up all attempts at educational work. He succeeded no better at farm work. When seen by Dana he had been for four years nervous, hysterical and entirely lacking in courage or capacity to carry on any sort of work. His habits were good, as were his intelligence, affection and desire for recovery. There were no objective signs of nervous disease nor stigmata of schizophrenia. The physical description given does not point to any definite endocrine anomaly unless a dry skin and subnormal temperature be taken to indicate such. He was put on thyroid treatment, ten, and later, four grains a day. "Within two weeks after treatment was begun the boy was rather magically changed. He lost his fears and restlessness, and nervousness and insomnia. He was able to go out alone. He went back to his work and became practically well and continued so for nearly three years." He takes thyroid intermittently when he notes a tendency of the nervous symptoms to return and gets entire relief. The author refrains from endocrine theorizing on the case.—R. G. H.

A case of INFANTILISM. Elmslie (R. C.), Brit. J. Child. Dis. (Lond.), 1920, **17**, 39.

Report of a case occurring in a girl aged 15 years and 10 months, whose height was 3 feet. Skiagrams of the wrists showed cupping of the ends of the diaphyses with widening of the epiphyseal cartilages as in rickets, while the hips showed coxa vara of the rachitic type. Sexual development was absent, breasts undeveloped, pubic hair absent and menstruation not yet begun. Albuminuria and chronic intestinal trouble were present. No studies were made of the general metabolism. From the description it appears as if the condition were due to a combined dysfunction of the thyroid, pituitary and sexual glands.—M. B. G.

(THYROID OVARY) Polyglandular syndrome with late epilepsy (Un nouveau cas de syndrome polyglandulaire avec épilepsie tardive). Etienne (G). & Richard (G.), Bull. et mem. Soc. méd. d. hôp. (Paris), 1920, 3. s., **44**, 154-158.

The authors report the case of a woman of 32 who had for the past three years suffered with generalized convulsions which appeared on the second or third day of each menstrual period. The periods were much reduced. The seizures stopped at once under combined thyroid-ovarian therapy, but for a time there were epileptic equivalents. The patient was clearly

sympathicotonic. The seizures were explained as due to spasms of the cerebral blood vessels which were regarded as due to thyroid-ovarian insufficiency. (The reviewer noted several years ago that ovarian extirpation in experimental animals leads to augmented irritability of the sympathetic nervous system.) (See also Tracy, Endocrin., **4**, 221.)—R. G. H.

(THYROID) A case of acute senile hyperthyroidism (Un caso de hipertiroidismo). Fernandez Sanz (E.), Anales de la Real Acad. de med. de Madrid, May, 1917.

A female subject of 82 suddenly exhibited a most acute Basedow syndrome. At this age hyperthyroidism always has a menacing prognosis, but this subject was entirely cured by medical treatment.—G. M.

(THYROID) The treatment of goiter. Foss (H. L.), N. Y. Med. J. (N. Y.), 1920, **111**, 285-286.

A defense of surgical procedure in the treatment of goiters, especially the exophthalmic forms.—H. W.

(THYROID) The principles underlying the treatment of toxic goitre. Frazier (Charles H.), Penn. M. J. (Athens, Pa.), 1920, **23**, 437-444.

Frazier emphasizes our ignorance of the etiology of toxic goitre. In stressing the importance of the thyroid gland he alludes to: (1) the disturbances related to its influence on the vegetative or sympathetic nervous system; (2) the visceral disturbances as represented by the vagotonic and sympathecotonic types; (3) the symptoms related to disorders of the central nervous system; (4) the disturbances of growth as in cretins, the alterations in the skin, etc., and (5) the disturbances arising from the relationship of the thyroid to the other glands of internal secretion. The author classifies toxic goitre patients into five groups. (1) The mildly toxic of the adolescent group rarely require surgery. (2) In the mildly toxic of the adenoma group operation is usually a matter of choice and not of necessity. (3) In the grave toxicosis of the adenomata, not the true exophthalmic type, but often with as grave an outlook, operation is inevitable, according to Frazier. (4) In the initial hyperplastic goitre without a pre-existing adenoma, the author is a very positive advocate of operation,—the earlier the better. (5) In the degenerative or atrophic or terminal stage of a more or less prolonged hyperthyroidism, there is manifestly no justification for surgery. In determining the

toxicity of a given case, basal-metabolism and blood sugar tests are valuable but should never be the sole criteria on which to depend; other objective and subjective signs must be taken equally into consideration, weighed and balanced. Frazier is an enthusiastic advocate of nitrous oxide anesthesia in toxic goitre operations. If ligation is done it should include the superior pole and not merely the superior thyroid artery. The author's mortality has been 3.5 per cent.

(Frazier's article and Goetsch's article abstracted in this issue were read before the Pennsylvania State Medical Society and an interesting discussion by several clinicians, including Plummer, is also published at the close of Frazier's paper.)

—H. L.

(THYROID) "Epinephrin hypersensitiveness test" in the diagnosis of hyperthyroidism. Goetsch (Emil), Penn. M. J. (Athens, Pa.), 1920, **23**, 431-437.

The author prefaces his article by reference to the work of Eppinger, Falta, Rudinger, Hess, Oswald, Cannon, etc., in demonstrating that excessive thyroid secretion renders the sympathetic nervous system sensitive to the action of epinephrin. He then describes in detail the technique of his "Epinephrin hypersensitiveness test." The test may result in considerable exacerbation of the objective signs and symptoms with but moderate increase of subjective phenomenon, or vice versa. Either combination would be considered positive. His conclusions are based on a clinical study of approximately 300 cases of thyroid disease. Goetsch finds the test definitely positive in cases of exophthalmic goitre; negative in colloid goitre cases without symptoms of hyperthyroidism and mildly or moderately positive when increased thyroid secretion prevails. In toxic adenoma the test is positive, in non-toxic adenomata negative. The test is helpful in differentiating incipient tuberculosis from mild hyperthyroidism in which, clinically, the diagnosis may be difficult; in the former there is no response to epinephrin, while in the latter the reaction is positive. The author attaches considerable importance to this phenomenon. He recommends the use of the test also in differentiating other conditions simulating hyperthyroidism such as psychasthenia, psychoneurosis, hysteria, neurasthenia, dementia precox, alcoholism, tabagism, acromegaly, arteriosclerosis and several other diseases. Furthermore, he believes the test of value in estimating the degree of toxicity in a given case of hyperthyroidism, and also finds that improvement in the response to epinephrin

(that is, a less positive reaction) runs parallel with decreased toxicity. The test also has the advantages of simplicity in apparatus and technique and is inexpensive.

THYROID, Metastatic abscesses of the—associated with hyperthyroidism; report of a case following repeated attacks of sore throat. Greenburg (David), J. Am. M. Ass. (Chicago), 1920, **74**, 165.

A report of a case of exophthalmic goitre, preceded by repeated peritonsillar abscesses and streptococcus sore throat. The author believes that bacteria may be a factor in the causation of exophthalmic goitre, if not directly, at least by effecting such changes in the physiology of the gland as to make its appearance likely.—F. C. P.

(THYROID) Sporadic cretinism (Ueber sporadischem Kretinismus). Guleke. München. med. Wchnschr., 1920, **67**, 734.

Two cases. A deaf mute boy of 13 showed some spontaneous improvement without treatment. Perhaps there was some spontaneous new formation of thyroid. In a second case, a girl of 16, three pieces of fresh thyroid were implanted without marked success.—J. K.

(THYROID) Morphologically demonstrable fat substances and the oxidase reaction in the human thyroid. Haeberli (E.), Arch. f. path. Anat., etc. (Berl.), 1916, **221**, 333-351.

In young individuals the fat content of the thyroid consists largely of neutral fats, i. e., fatty acid esters of glycerol. Thyroids of older individuals contain mainly neutral fats; cholesterol esters are seldom found, free cholesterol never. Microchemical staining reactions may lead to errors in the chemical differentiation of lipins. The granules in the epithelial cells of the thyroid, as those in other epithelial cells, consist of a variety of substances, among which are fat and pigment. The fat in the epithelial cells is permanent fat and increases with age. Fresh thyroids constantly contain oxidase granules within the epithelial cells. These granules are closely associated with the stored fat. Chem. Abst. **14**, 2023.

Investigations on the THYROID gland (Part II). Horisawa (H.), Verhandl. d. jap. path. Gesellsch, 1919, pp. 54-57.

The author has made a study of the size and weight of the fresh thyroid gland in 529 individuals of different ages and of

the formalin fixed gland in 401 more. In males between 26 and 42 years old it weighs on an average 17.47 gms. and in females between 20 and 33 years of age, 15.30 gms. In 223 cases he gives also the percentage of thyroid to body weight. If detailed observations were made regarding the cause of death, anatomical variations in the gland, incidence of goitre in the vicinity, etc., this contribution should be one of considerable value.—E. V. C.

THYROID extirpation in the horse (La tiroidectomia en los caballos). Houssay (B. A.), & Hug (E.), Soc. de Biol. de Buenos Aires, May 6, 1920.

The experimental series included eight animals. These were observed for a period of five years. Thyroidectomy resulted in death with cachexia in three cases, retardation of growth in case of young animals, with synovial edema, retardation of sexual development, hypothermia, etc.—B. A. H.

(THYROID) Experimental goitre produced by water from Cerrillos (Bocio experimental provocado por el agua de Cerrillos). Houssay (B. A.), Soc. de Biol. de Buenos Aires, May 6, 1920.

Goitre was observed in rats that had drunk of this water. This is the first instance of experimental goitre reported from South America.—Author's Abst.

THYROID GLAND, Papilliferous carcinoma of the—. Hughes (B.), Brit. M. J. (Lond.), 1920 **(i)**, 362-363.

The patient was a girl of 13 years. The papilliferous carcinoma which was removed at operation was of 10 months' duration and involved the right lobe of the thyroid gland and some of the lymphatic glands on the right side of the neck and was also adherent to the trachea and to the carotid sheath. At the time the paper was written, three months after the operaion, there was no sign of recurrence. The condition is extremely rare, especially in children. The papilliferous form is far less malignant than the ordinary carcinomata, the history often extending over years. These tumors show little tendency to infiltrate; the metastases are local and situated in the glands of the neck, and they may appear years after the removal of the original growth. The affected glands remain movable and discrete and their removal is easily accomplished. The original tumor, if removed before infiltration has occurred, shows little tendency to recur.—L. G. K.

Carcinoma of the THYROID. Hughes (B.), Brit. M. J. (London), 1920, **(i)**, 586.

The author states that he has never seen a case of adenocarcinoma of the thyroid gland in which operation could be definitely said to have effected a cure. The early involvement of the trachea and surrounding structures as the growth becomes extracapsular makes operation extremely difficult. The earliest symptom may be cough and blood stained expectoration caused by ulceration of the growth into the trachea.

—L. G. K.

(THYROID) Nerve block anesthesia in superior thyroid pole ligation. Hunt (J.), Northwest Med. (Seattle), 1920, **19**, 49-50.

The author describes a method of nerve block sufficient to permit superior pole ligation and recommends it for the reasons that time is saved by blocking before starting the operation, since infiltration does not produce sufficient anaesthesia under twenty to thirty minutes; that shock is lessened, and that better skin repair results when infiltration along the line of incision is not resorted to.—H. L.

(THYROID) Research on the artificial provocation of metamorphosis in batrachians, notably in axolotl. Biological measure of the efficacy of thyroid preparations (Recherches sur la provocation artificielle de la métamophose chez les batrachiens, et notamment chez l'axolotl. Mesure biologique de l'efficacité des préparations thyroïdes). Jensen (C. O.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 315-317.

The author has previously shown that intra-abdominal injections of iodothyrin determine metamorphosis in axolotl. Since then he has elaborated a method for measuring the action of iodothyrin and other thyroid preparations by determining the minimum dose necessary to provoke metamorphosis.

—T. C. B.

THYROID gland and anomalies of metamorphosis in the anura (La glande thyroïde et les anomalies de métamorphose chez les anoures). Jensen (C. O.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 948-949.

The author has studied the thyroid in specimens of Rana esculenta, R. arvalis and Bufo vulgaris that presented various anomalies with regard to metamorphosis. In a lot of Bufo

larvae three individuals metamorphosed very early. In these the thyroid was not hypertrophied, but the follices were filled with masses of colloid with a stronger affinity than normal for eosin. In the larvae of R. arvalis, of which the development was notably more advanced than that of the controls, the thyroid attained dimensions much greater than that of the control; the follicles were large and filled with colloid, but not proliferated. It is possible that the secretory activity of the thyroid had been more intense in these individuals than in the controls. In the larvae of R. esculenta that had passed the winter at a temperature of 6-10° the thyroid was found at the end of March very large on account of swelling; the follicles were filled with colloid having little affinity for eosin; the epithelium was very flat. Larvae of the same size and state of development, collected from the same pond, but killed in October, served as controls. Giant larvae of R. esculenta were also studied, and a histological description of the thyroid is given.

—T. C. B.

(THYROID) Endocrine tropisms: thyrotropism. Kaplan (D. M.), N. Y. Med. J. (N. Y.), 1920, **111**, 275-280.

This is one of a series of articles in which the author is attempting to show that every individual is dominated by the makeup of his endocrine system. According to the author, a thyrotrop may show his tropism in four different ways: an over action, an under action, a perversion of the secretion, or the first two may be present at the same time. The various findings under each condition establish the character of the individual possessing them. All thyroidal conditions cannot be ascribed to primary disturbances in the thyroid for the pathology of other endocrine organs results in a condition in which the thyroid attempting to compensate brings destruction upon itself. Hence the thyroid, as such, should not be held responsible until the functions of the other endocrine glands have been completely established, nor removed until organotherapy and modern medical procedures have been thoroughly applied. Many cases improve on ovarian extract, 5 grains a day, and hand in hand with their improvement goes a dermal condition analogous to acnea rosacea.

In some respects this "dominance of the endocrines" reminds one of the old theory of phrenology and especially of physiogomony dressed up in modern or "new thought." The manner of the author in "initiating" the reader into the secrets of endocrinology presupposes that the reader has scarcely heard of the wonders of the ductless glands.—H. W.

(THYMUS THYROID) Internal secretory organs in morbus Basedowii. Kato (M.), Verhandl. d. jap. path. Gesellsch, 1919, ——, 59.

On the basis of the study of ten cases of Graves' disease the author concludes that this condition is closely related to the so-called status thymicolymphaticus.—E. V. C.

Deficient THYROID secretion as an etiologic factor in gastric and duodenal ulcers and in hyperacid conditions. Katz (Joseph), Med. Rec. (N. Y.), 1920, **97**, 916.

Brief report of four cases, three of hyperacidity and one of gastric ulcer, which were strikingly improved by thyroid extract.—H. L.

(THYROID) Determination of iodine in connection with studies in thyroid activity. Third paper. Kendall (E. C.), J. Biol. Chem. (Balt.), 1920, **43**, 149-159.

A detailed description of the procedure to be followed for the accurate determination of iodine in amounts found in thyroid tissue.—F. S. H.

(THYROID) DIABETES and exopthalmic goiter (Diabéte et goitre exopthalmique). Labbé (M.), Ann. de méd. (Paris), 1920, **7**, 95-103.

After nothing that he has observed a coincidence of diabetes and Basedow's disease in five cases, but has never found myxedema associated with the former, the author gives brief protocols of the patients presenting the associated pancreatic and thyroidal disorders. The susceptibility of such patients to acidosis is partially attributable to the increased nitrogen metabolism induced by the hyperthyroidism.

Medication with hemato-ethyroidine and valerian and bromides gave little if any relief. Better results were obtained with quinine and sodium salicylate. Treatment with iodine preparations gave most favorable results both in lowering the glucosuria and in general amelioration.—F. S. H.

(THYROID) Loss of both eyes from the exopthalmos of hyperthyroidism. Lahey (F. H.), Boston M. & S. J., 1920, **182**, 427-428.

X-ray treatments resulted in a reduction of the pulse rate, a gain in weight and improvement of the general condition.

However, the exopthalmos continued to progress and ulcers of the right eye led to its enucleation. Later the left eye was removed for the same reasons after severance of the sympathetic cervical ganglion had failed to arrest the condition.
—H. W.

(THYROID) Metabolism as an aid in diagnosis, prognosis and treatment of hyperthyroidism. McGuire (Stuart), South Carolina M. Ass. J. (Greenville), 1920, **16**, 107-119.

McGuire believes that the determination of basal metabolism, although a very promising method, has not yet been sufficiently long in use to permit a final evaluation of its significance in the diagnosis of "hyperthyroidism."

A patient with hyperthyroidism may have a high metabolic rate and not be as seriously ill as another with a lower rate but who has structural changes in the heart, liver or kidneys. The onset of hyperthyroidism is insidious and difficult to recognize in its early stages in which the metabolic rate will clearly differentiate it from hysteria, neurasthenia, tuberculosis, and other conditions with which it may be confused. Again, in the later stages there develop symptoms due to degeneration of the heart, liver or kidneys, and it is difficult to say how much the patient suffers from hyperthyroidism and how much from damage to the vital organs. Here also a determination of the basal metabolism will be of value, not only for diagnosis but for prognosis as well. Usually, a patient's clinical symptoms coincide with his metabolic rate; but sometimes they do not. Patients with high metabolism and moderate tachycardia are more seriously ill than those with moderate metabolic increase and a very rapid heart action. In treating a patient for hyperthyroidism, the estimation of the metabolic rate is of value first to determine the safety of the measure to be employed, and second to ascertain its efficiency.—R. G. H.

(THYROID) Zur Lehre der STRUMA INTRATHORICA. Mayer (Karl), Zentralbl f. Chir. (Leipzig), 1919, **46**, 536.

Mayer found that X-ray photographs enabled a diagnosis to be made of intrathoracic goitre and enlarged thymus, although a dermoid cyst cannot be distinguished from the above. The retrosternal goitre may be a continuation of the goitre in the neck, but an intrathoracic goitre may exist without any enlargement of the gland in the neck. Moreover, accessory thyroids may be met with at any point in the line from the base of the tongue as far down as the front of the arch of the aorta

and pericardium, or even in the posterior mediastinum.—Med. Sc. Abst. & Rev., **1**, 173.

(THYROID) The treatment of early hyperthyroidism. Meredith (Florence L.), N. Y. Med. J. (N. Y.), 1920, **111**, 289-291.

The state of being generally below par leads to the acquiring of infections and to metabolic and secretory disturbances. In young women nonhygienic modes of living often result in thyroidal disturbances, hence the normalizing of the life of the individuals so affected is a logical procedure in the care of early hyperthyroidism. In thirty young women suffering from early hyperthyroidism marked improvement followed the establishment of a normal mode of living.—H. W.

(THYROID) Functional PANCREAS insufficiency. Moyer (A.), Ztschr. f. exp. Path. u. Therap., 1919, **20**, 273-297.

Disturbances of pancreatic function are a part of the aftermath of the war. The disorders are evidenced by fecal examinations after test meals, studies of individual specimens of pancreatic juice, etc. Gastric achylia and thyroid disturbance frequently accompany this functional perversion of secretion. There is apparently a gastrogenic, neurogenic, and thyreogenic complex bound up with the pancreas disturbance, which is fundamentally possibly connected with the type of nourishment ingested during the war.—F. S. H., Chem. Abst., **14**, 2027.

THYROID extract, The life history of the first case of myxoedema treated by—. Murray (G. R.), Brit. M. J. (Lond.), 1920, **(i)**, 359-360.

For data seen Editorial (p. 600) in this issue.

(THYROID) X-ray treatment of Graves' disease (Om Behandlingen af Mb. Basedowii). Nordentoft (S.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 1169-1175.

In 1918 Nordentoft published fifty cases of Graves' disease treated with X-rays in the period July, 1915 to December, 1917. His present paper deals with a new series of fifty cases, only three of which were males. At the Aalborg Kommune Hospital the practice has been adopted of exposing only the region of the thymus to the X-rays. He gives a few illustrative cases, but does not attempt to tabulate or classify his results, confining his estimate to general terms. He is greatly impressed by the efficacy of this treatment, with which better results can be

achieved than with any other. He urges its adoption at an early stage before the disease has got well established, and he advocates large and few doses in preference to small and frequent doses. With the adoption of this principle, and the inclusion of the thymus in the area exposed, he anticipates that severe and fatal cases of Graves' disease will become so rare that many medical men will never see them. Discussing X-ray fatalities in connection with Graves' disease, he suggests that timid dosage may partly be responsible, and he quotes Forsell in support of his hypothesis that the small dose merely stimulates, whereas the large dose inhibits the activities of the thyroid. He also notes that in certain fatal cases of Graves' disease death probably occurred in spite of, not because of, the X-ray treatment.—Med. Sc. Abst. & Rev., **2**, 202.

(THYROID) Toxic goitre. O'Day (J. C.), N. Y. Med J. (N. Y.), 1920, **111**, 287-289.

The removal of each lobe of the thyroid gland in five cases did not give the slightest relief, hence something more than the hyperthyroidism is involved in toxic goitre. The injection of toxic goitres with mucin is of no avail as treatment, although mucin is supposed to be the material which infiltrates the body tissues in cases of myxedema. The cause of toxic goitre is not known.—H. W.

Bone tumors of THYROID origin. O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 374-375.

The author believes that normal detached thyroid epithelial cells are self-asserting within two environments, namely, the bony tissue and the parent structure itself.—H. W.

(THYROID) Is endemic goiter a water disease? O'Day, (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 634.

Areas of the United States where goiter is endemic in character without exception are supplied with water deficient in mineral content. Hence endemic goiter, which is always retentive goiter, is the result of the deleterious effects that mineral free water has on the consistency of the thyroid's secretion. This view is the direct opposite of the one previously held. The relation of water to goiter, if there is one, apparently remains to be solved.—H. W.

(THYROID) What is the cause of goiter? O'Day (J. C.), N Y. Med. J. (N. Y.), 1920, **111**, 556.

Diffuse and nodular goiters may be assumed to arise because of obstruction of one or more of the few lymphatic trunks which drain the thyroid. Such an obstruction would mean the accumulation of secretion within the follicles until, one after the other, they would burst and fuse to form a large cavity with the cuboidal epithelial cells of each flung back to be compressed into the wall of the cyst. The cause of this interference in drainage may be either mechanical or physiological. The latter is due to some defect which permits the production of an over-thickened product too heavy and thick for easy egress. Hence, persons of nervous temperament readily fall victims to goiterous conditions. On the other hand, "lymphoid temperaments," Hawaiians, Polynesians, etc., do not demonstrate retentive goiters.—H. W.

(THYROID) Diabetes in association with toxic goiter. O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 815-816.

Two cases of toxic goiter associated with diabetes had their carbohydrate tolerance restored following subtotal thyroidectomy. In one case the thyroid was injected with boiling water, a definite reduction of the sugar content keeping pace with the piecemeal cooking of the gland.—H. W.

(THYROID) Emotive exophthalmic goiter and hypertrophy of the parotids (Basedowisme post-émotionnel et hypertrophie des parotides). Railliet (G.), Bull. mem. Soc. med. hôp. (Paris), 1918, 3. s., **42**, 1151-1154.

A report of a case of a soldier who suffered contusions as the result of which Basedowian symptoms developed; these were accompanied by marked enlargements of the parotids.

—F. S. H.

(THYROID) Intestinal hemorrhages in a hemophilic Basedowian treated with serum from a rabbit in a state of anaphylaxis (Hémorragies intestinales chez un Basedowien hémophile. Traitement par le serum de lapin en état d' anaphylaxie). Raymond & Rouquier (A.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 485-487.

A report of a case of Basedow's disease in which intestinal hemorrhages occurred and were stopped by two injections of 10 cc. of rabbit serum from an animal in the anaphylactic state from horse serum injections.—F. S. H.

THYROID and PANCREAS, Giant cell sarcoma of—. van Rijssel (E. C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63,** (ii), 2014-2024.

Correction of citation, Endocrin., **4,** 345.

(THYROID) Toxic goiter following epidemic influenza. Roeder (C. A.), Surg., Gyn. & Obstet. (Chicago), 1920, **30,** 357-358.

Our knowledge of the etiology of goiter has not kept pace with our methods of treatment, an empiricism accounting for the prevalence of various types of enlarged thyroids. All non-malignant goiters can be divided into (1) colloid, (2) adenomatous, and (3) hyperplastic, and are either toxic or non-toxic. This simplification of the classification we owe to Plummer and it has greatly cleared our vision of a previously hopelessly described pathological condition. The etiology concerns us more than the treatment, and every goiter indicates a lack of some form of prophylaxis. The thyroid may have very little connection with the other glands of internal secretion, as to date it is extremely rare to find a goiter, hypo- or hyper-plastic, with various abnormalities of other glands. The infectious theory has lately gained popularity, and rarely do we find any type of goiter without a suspicious pair of tonsils or alveolitis and no goiter has been properly treated without the eradication of such foci. The author reports eight cases of toxic goiter (three adenomata and five hyperplastic) following immediately on the attack of epidemic influenza; the toxemia from the goiter succeeded the attack of influenza so closely that recovery from the latter was not complete before the symptoms of thyrotoxicosis began. There had been no toxic signs or symptoms from the thyroid previously. The close relationship between the two conditions is so marked that it can be accepted as a most convincing proof of the etiological factor being bacterial. At the time this abstract is being written the same author has observed fifteen cases all following epidemic influenza.—Author's Abst.

THYROID, Myxedema in total aplasia of the— (Ueber myxödem bei totaler Thyreoaplasie). Rössle, München. med. Wchnschr., 1920, **67,** 735.

Report of a post-mortem of a dwarf of 28. No trace of thyroid could be detected. The skeleton was formed as in a child of 4; there was a diminished endochondrial and periosteal ossification. Arteriosclerosis, especially of the aorta was seen.

The hair was poorly developed; the skin showed typical myxedema. The uterus and ovaries were as in a normal woman of 28. Only one parathyroid was found. The hypophysis was large (725 milligrams). The thymus consisted only of fat. The pineal, pancreas and spleen were normal. The zona glomerulosa of the adrenals showed a marked sclerosis.—J. K.

(THYROID ADRENAL) Fluctuations of thyrosuprarenal activity in general diseases. Sajous (C. E. de M.), N. Y. Med J. (N. Y.), 1920, **111,** 265-269.

Such diseases as pneumonia of the aged, dementia precox, influenza and the like represent failures of metabolism the result of toxins which affect the endocrine or defensive organs. Such diseases, therefore, should be treated along the lines of organotherapy, especially with adrenal and thyroid preparations.—H. W.

(THYROID) Urinary incontinence of hypothyroid origin (La incontinencia de orina en el hipotiroidisma). Salgado (A. A.), Innaug. Dissertation, Santiago de Chili, 1918.

Urinary incontinence of hypothyroid origin is definitely recognized by many authors; in such cases thyroid preparations constantly give favorable results. Salgado reports seven cases of this sort. In his experience those cases of enuresis that are accompanied by fecal incontinence are always due to chronic benign hypothyroidism.

[The problem of the relation of endocrine conditions to the physiology of the sphincters could profitably receive careful and extensive experimental investigation.—Ed.]—J. R. P.

(THYROID) The selection of operation for exophthalmic goiter. Sistrunk (W. E.), J. Am. M. Ass. (Chicago), 1920, **74,** 306-308.

Of technical surgical interest.—F. C. P.

(THYROID) Goiter in skiagrams (Der kropf in Röntgenbild). Sommer. Deutsche med. Wchnschr. (Berlin), 1920, **46,** 616.

Of no endocrine interest.—J. K.

THYROIDAL constipation. Strauss (S. G.), N. Y. Med. J. (N. Y.), 1920, **111,** 281-283.

The establishment of thyroid deficiency with constipation is an indication for thyroid therapy. Doses of from 1/10

to 2 grains may be used without other catharties until recovery is complete.—H. W.

(THYROID) Comparative investigations on the changes in the thyroid in different diseases. Takeuchi (K.), Verhandl. d. jap. path. Gesellsch., 1919, p. 58.

The author advances the following conclusions on the basis of his study of the thyroid in 325 cases: (1) The "thyroiditis simplex" of de Quervein, which consists chiefly of abundant desquamation of the epithelial cells and reduction in the amount of colloid substance, is not, as he supposed, specific for infectious diseases, for these appearances are less apparent in typhus abdominalis and spirochaetosis icterohemorrhagica than in non-infectious diseases. (2) Since these changes are more apparent in heart failure, diseases of the larger blood vessels, nephritis and cirrhosis and cancer of the liver, he is of the opinion that there is some connection between changes in the thyroid and alterations in the circulatory system. (3) In tuberculosis, malignant tumors, etc., the thyroid is more affected when the chief lesions are present in the thorax, which indicates a further connection between changes in the thyroid and the organs of the chest.—E. V. C.

(THYROID) On the influence of complete thyroidectomy during pregnancy upon the development of the fetus and on the duration of gestation. Ukita (T.), Acta Scholae Med. Univ. Imp. in Kioto, 1919, **3**, 287-297.

This report is based upon a study of the effect of thyroidectomy in six pregnant rabbits. Unfortunately no narcosis was used. Assuming that the thyroid gland begins to function in the fetus after the middle of gestation, the operations were performed between the seventh and tenth days after conception, in order to obtain the maximum effect. Maternal thyroidectomy immediately disturbs the development of the fetus in utero. The duration of pregnancy is nearly doubled and the young at birth are small and weak with hypertrophied thyroids and show retardation in development of their centers of ossification. The author believes, with Halsted, that the increase in the size of the thyroids is compensatory to the maternal thyroidectomy. The article is in English.—E. V. C.

(THYROID HYPOPHYSIS) The interpretation of headache. Wilson (W.), Practitioner, 1919, **103**, 274-296.

Among other causes of headache, the author mentions menstrual and climacteric headaches the mechanism of which he finds difficult to explain. He refers also to headache associated with hypothyroidism and relieved by thyroid extract; headache due to pituitary affections and usually occurring early in the disease before any obvious change in skeletal structures. The pain is situated deep in the head behind the root of the nostrils at the site of the sphenoidal sinus. These pituitary headaches are intermittent and the patient is quite prostrated. Relief from the attack is quite sudden. He considers these patients suffer from diminished pituitary activity and relief is obtained by administration of whole gland pituitary extract provided there is no malignant growth or spreading cyst.—H. L.

(THYROID) A comparison of methods for determining thyrotoxicosis. Woodbury (M. S.), J. Am. Ass. (Chicago), 1920, **74**, 997-999.

A report of the observation of a selected group of eleven cases of thyrotoxicosis by clinical study, by histological examination of the thyroids removed at operation, and by postoperative progress. The clinical observations included a careful history, the response to Goetsch's epinephrin chloride test and a study of the basal metabolic rate as determined by oxygen consumption (Benedict portable apparatus). Woodbury states that while the epinephrin chloride test is generally conceded to be essentially an indicater of hypersensitiveness of the sympathetic system, it appears to be a fact that positive responses to the test are more common in cases in which there is thyrotoxicosis. The test should be used especially in doubtful cases since it stimulates closer study and offers additional aid in formulating a diagnosis. Observations of the level of basal metabolism alone, as now estimated, should not be regarded as sufficient criteria in determining the presence or absence of toxic states associated with the thyroid. The author concludes that while functional tests are of great value in the compilation of evidence, especially in relation to the degree of toxicity, reliance should not be placed on any one of these. The diagnosis should be based on the results of a complete examination, with special attention to the possibilities of errors in psychoneurotic patients.—F. C. P.

Endocrinogenic VISCEROPTOSIS (Les ptosis hormónicas). Quaristi (V.), Prog. de la Clinica (Madrid), 1918, ——, ——.

In addition to visceral ptoses due to mechanical disturbances, such as genital prolapse in women who have borne

many children and suffered from lacerations and relaxations, the author believes there are others manifested in young persons which are due to endocrine alterations. Among such are: (1) Visceral dislocation due to spasms or ptosis; (2) Vascular disturbance, varix, etc.; (3) Neuroses. These three symptoms are exhibited most clearly in varicocele and rectal prolapse. There exist, moreover, genital prolapse, nephroptosis and gastroventeroptosis, in addition, and in all these cases we speak of consecutive neuroses. It is the author's opinion that these disturbances ought to be regarded as coexistent, and that they are due to lack of muscular and vascular tone. This being determined the cause is to be sought in the endocrine and vegetative systems, especially in suprarenal and hypophyseal insufficiency. The rational treatment of these conditions is opotherapy.—E. B.

(VAGOTONIA SYMPATHICOTONIA) Experiments on the influence of the involuntary nervous system on the blood (Untersuchungen zum Einflusz des vegetativen Nervensystems auf das Blutbild). Friedbery, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 480.

Drug injections were made in children. It is not enough to examine the blood-picture of clinical cases of vagotonia or sympathicotonia, but the involuntary nervous system must be stimulated artificially and the blood-picture must be examined after this stimulation. It was observed that after stimulating the vagus with pilocarpin, depressing it with atropine or stimulating the sympathic with adrenalin the blood-pictures were practially identical. This is a strong argument against Falta's theory of the existence of a vagotonic and a sympathotonic blood-picture. The action of pilocarpin and adrenalin on the blood has probably nothing to do with the nervous system but is due to an influence on the hematopoietic organs.

—J. K.

Acute and chronic VAGOTONIA (Ueber aktute und chronische Vagotonie). Feilchenfeld (Leopold), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 627-629.

The author makes the following classification:

I. Acute vagotonia with spasms of vagal origin; in these cases patients are women and usually hysterical. They suffer from fits beginning with shivering, headache, giddiness, nausea and vomiting. Often loss of consciousness is observed; the patients are pale; the pulse is slow.

II. Chronic vagotonia: In these cases physical stimuli may cause the attacks as described under I.

III. Paroxysmal tachycardia.

IV. Acute vagotonia in asthenocardia.

[It is a very old fact that a hysterical woman may have attacks and that diseases of the heart may give symptoms resembling those under I, but the evidence that they are due to vagotonia is by no means convincing.]—J. K.

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