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THE DEVELOPMENT OF THE RETICULATED BASEMENT MEMBRANES IN THE SUBMAXILLARY GLAND.

BY

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Professor of Anatomy in the University of California, Hearst Anatomical Laboratory of the University of California.

WITH 9 TEXT FIGURES.

Mall's¹ recent paper on the development of the connective tissue has done not a little to clarify our ideas concerning the origin of these perplexing products of the mesoderm. Their relation and ancestry he has traced back to a primitive syncytium from which they are all derived. To explain in his own words: "The network of fibrils which forms Wharton's tissue, to employ the best known example, is composed of a mass of anastomosing cells, a syncytium from which the connective tissues arise. In very early embryos the mesenchyme is composed of individual cells which increase rapidly in protoplasm and then unite to form a dense syncytium. The protoplasm of the syncytium grows more rapidly than the nuclei divide, so that in a short time we have an extensive syncytium with a relatively small number of nuclei. In its form the syncytium appears as large bands of protoplasm with spaces between them filled at times with cells and at other times with fluid. The second condition we have in the umbilical cord of young human embryos. About this time the protoplasm of the syncytium differentiates into a fibrillar part, which forms the main portion of the syncytium—the exoplasm—and a granular part, which surrounds the nucleus—the endoplasm. The fibrils of the exoplasm are very delicate and anastomose freely." From this period and these two differentiating products of the syncytium, Mall traces the development of cartilage, white fibrous tissue, reticulum, the cornea, and elastic tissue.

In describing the syncytium of the tadpole Malls says: "The point I wish to leave open is whether the mesenchyme was ever composed of individual cells. Was it not a syncytium throughout its development? At any rate, it is quite evident that the earlier syncytium if it exists

¹Am. Jour. of Anatomy, Vol. I, No. 3, 1902.

is a very incomplete one with very loose protoplasmic bridges, easily broken and easily united to allow the cells to wander in all directions during the earlier stages of development. So it may be that the syncytium as seen in the tadpole 3 mm. long has existed ever since the appearance of the mesenchyme." The apparent discrepancy between these two statements concerning the primitive condition of the mesenchyme may be explained from the fact that Mall's problem is not to solve that question but simply to trace the development of the connective tissues from the syncytial stage. The other problem is still unsettled, but, at the same time, not the least suggestive work is that of His which is quoted by Mall.

Now in tracing the development of the connective tissues Mall considered not only their simpler and more elemental relations, but also in a general way the manner in which they enter into the formation of certain organs, as, for example, the intestines and the framework of lymph glands. Reticulum he regards as distinct from white fibrous tissue, but concludes that it represents simply an embryonic form of that tissue. Together with reticulum, white fibrous tissue, the framework of the cornea, bone, and cartilage, must all be classed as collagenous. While it may be true that the framework of the lymph glands resembles a more embryonic type of white fibrous tissue, nevertheless, in other places reticulum shows peculiar, highly specialized adaptations to the needs of organs of which it forms the framework, suggesting the probability that morphologically, at least, it may represent the highest development of any of the fibrillated products of the syncytium. Such adaptations, for example, are beautifully shown in the framework of the submaxillary gland and many other organs.

It will be the province of a later paper to discuss the development of the exoplasmic fibrils in the submaxillary of the pig from the simple syncytial stage to the complex relations which they show in the adult, indicating at the same time some of the physical factors that may be involved in bringing these relations about. The specific point of the present communication, however, is to show how the reticulated basement membranes are formed from the primitive syncytial products. Throughout the literature and throughout the history of the development of the basement membrane idea, the question has been raised with considerable discussion whether or not these structures were homogeneous or fibrillar. Many investigators have maintained from the first that basement membranes in general were homogeneous, others showed with apparent conclusiveness by numerous digestive and precipitative methods that they were composed of reticulated fibrils. More

recently Mall² who has contributed extensively to the subject stated that a definite, homogeneous membrane surrounds some of the tubules of the kidney, which reacts, in many respects, not like reticulum or white fibrous tissue, but quite like yellow elastic tissue. These lie within the fibrillated basket-work he had previously found by digesting frozen sections of the kidney. This means that we must reclassify these structures and consider the entire group of basement membranes as consisting of two types, namely, the homogeneous and reticulated. For, while it is by no means certain that all the cell complexes of secreting glands are surrounded by homogeneous membranes, it is probable from the results of digestion experiments, that most secreting alveoli, acini, ducts and cell groups are embraced and supported by a membrane made up of a delicate interlacing meshwork of reticulum. We may find that many, if not most, of the glandular structures are embraced by homogeneous as well as the reticulated membranes, but the exact distribution of the homogeneous membranes can only be determined by a series of special investigations. Some method must be devised for the study of the origin of the homogeneous membranes, but the development of the reticulated fibrillar basket-work which embraces most glandular structures is readily followed in a series of embryos by Mallory's aniline blue fuchsin connective tissue stain,³ either used according to the original directions of Mallory or by the modifications more recently suggested by Dr. Sabin and quoted by Mall.

It may be well to call attention to the fact, however, that the stain has to be modified somewhat for each set of preparations. Owing, perhaps, to chemical differences in the cells or exoplasm at different ages, varying pictures are obtained, even when the stain is allowed to act under precisely the same conditions. Moreover, it is also true that the blue is very easily washed out of many of the finer fibrils, often giving rather unequal pictures unless the duration of the action of the stain is rigidly controlled.

In the preparations from which the following description of the development of the reticulated membranes is taken, the question of the origin and relations of the demilunes of Giannuzzi is clearly settled, but these facts will be discussed later in another place.

In a pig's embryo, then, 3 cm. in length, the submaxillary gland consists of a single tube with simple terminal arborizations lying below and medial to the ossifying mandible. At this time the gland is clearly defined from the adjacent structures because the dendritic branching

² Mall. Bulletin of the Johns Hopkins Hospital, Vol. XII, 1901.

³ Mallory. Journal of Experimental Medicine, Vol. V.

forming the organ, while probably not exceeding divisions of the first and second orders, consists of solid columns of cells lying in a rather dense syncytial connective tissue, from which they are sharply differentiated. The syncytium is not yet completely separated into exoplasm and endoplasm, to use Mall's terms for the fibrillar and cytoplasmic portions of the embryonic framework of the organ. Immediately surrounding the tubes is a dense blue staining line which has the same reaction as the exoplasm, while just outside of this, and, indeed, resting directly upon it, is a mass of branching and anastomosing syncytial cells which form, with the other cellular elements of the syncytium, a direct protoplasmic continuum.



FIG. 1. Terminal bud of Submaxillary arborescence showing the developing basement membrane and the adjacent syncytium. Exoplasm just differentiating from the embryonic connective tissue. Pig 3 cm. Fixed in Zenker's fluid. Magnified 900 diameters.

Still further external a somewhat clearer differentiation of the developing connective tissue into exoplasm and endoplasm is obtained. Short, branching anastomosing fibrils of varying caliber are seen scattered here and there in the syncytium; this exoplasm in many places appears as dots which represent often simply fibrils cut in cross-section. At a great many points exoplasmic fibrils extend from the surrounding tissues to the basement membrane and here and there one sees deeply-staining fibrils apparently in the endoplasm of the cells immediately surrounding the cell columns. Now, whether the basement membranes up to this point are formed solely by the deposition of fibrils or whether the syncytial protoplasm differentiates into exoplasmic structures just about the developing glandular cells, it is very difficult to say. but in all probability the basement mem-

branes in the early stages are formed in both ways, namely, by a primary deposition of exoplasm from the syncytium and later augmented by increments of millions of fibrils from the general syncytial exoplasm. Following the formation of the membranes beneath the epithelium of the buccal cavity or in the skin in these preparations does not throw definite light on this question for in a pig 3 cm. in length the membranes when viewed tangentially appear to be made up partly of exoplasmic fibrils and partly of a simple granular substance in the meshes. The problem is complicated by the fact that in the earlier embryos, the endoplasm is diffusely tinged by the blue element of the dye. This

much, however, is certain; the formation of the membranes about the growing apices of the cell columns which are increasing constantly in length and circumference is chiefly by successive deposits of fibrils so the layer of syncytium around the growing ducts and alveoli forms what may well be termed the deposition zone. In this region the nuclei in the earlier stages at least are very numerous. Somewhat further out there is a noticeable diminution in their number and in the exoplasm and endoplasm are many clear spaces which are apparently filled with fluid. The nuclei of the syncytial cells are oval or round, contain a very indistinct nucleolus and are in general about the same size as the nuclei in the developing cell columns. The membrane itself under the highest powers is more or less irregular and, while looking somewhat homogeneous, still bears in some places definite evidences of fibrillation. There, as in the buccal cavity, the staining of the endoplasm destroys to some extent the sharpness of the picture.

In the submaxillary gland of a pig 4 cm. in length there has been a radical change in the syncytium. While it has not entirely differentiated into endoplasm and exoplasm, the exoplasmic fibrils have become extensively anastomotic although somewhat short, irregular and ill-defined. Here and there they seem matted together by some interfibrillar substance which on coagulation has become slightly tinged with the stain and thus destroys to some extent the sharp contour of the fibrils. This happens often in the best preparations. Numerous granules are also found deposited on the fibrils or at their nodes. It is also possible that these may be displaced particles of endoplasm that have become detached from the cells and remained entangled in the exoplasmic network. The endoplasm is gathered as a small cellular mass about the nucleus forming bipolar or multipolar cells. In the area just around the apices of the growing gland, that is to say, in the deposition zone, the arrangement of the cells is such that, in general, the long axis of the nuclei is parallel with the basement membrane, while the cells in parts more distant have no such definite arrangement. This seems to indicate that the tension caused by the

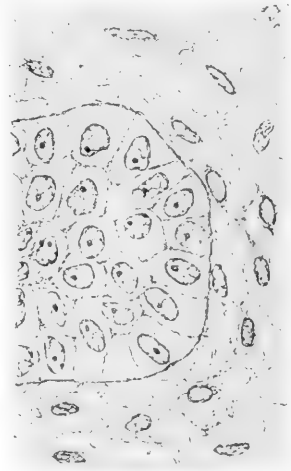


FIG. 2. Growing tips of submaxillary tree with the adjacent deposition zone from pig's embryo 4 cm. long. Exoplasm and endoplasm well differentiated. Fixed in Zenker's fluid. Stained by Mallory's method. Magnified 900 diameters.

tips of the growing tree is having a certain influence on the course and direction of the adjacent fibrils, and they, in turn, have influenced the position of the cells that lie either at their nodes or along their course. Relative to the entire syncytial mass, the growing tree forms a comparatively small proportion of the embryonic gland, so that either the force exerted by the growing columns is lost in the plastic mass or the exoplasm has not developed a sufficient strength to transmit it any distance from the foci where it is exerted. In the syncytium are numerous spaces which are quite clear and are probably filled with fluid. The basement membrane is more distinct at this period than in a pig 3 cm. in length, but the presence of so many syncytial cells immediately about the growing columns is no longer so frequently observed. Now an occasional nucleus with its endoplasm rests directly on the membrane and it is noteworthy that there is a marked diminution in the quantity of endoplasm about the nuclei. From this structure extending into the adjacent syncytium and forming with it a direct fibrillar continuum are

the exoplasmic fibrils which are so numerous in this region, that, as the columns grow out into the general syncytium, it is impossible that fibrils should not be laid down by thousands on the surface of the advancing columns.

In a pig 8 cm. in length the cell columns show at their apices the beginning of a differentiation destined to mark the future alveoli. In the terminal buds a lumen has appeared and the cells are divided into two general, but more or less indefinite layers. Within the cells of the inner layer globules of mucus begin to appear making it a very simple matter to distinguish the alveoli from other portions of the gland by the presence of these characteristic mucous cells. The basement membrane is now somewhat thicker and more definite. Thousands of distinct fibrils run from the adjacent syncytium to lose themselves upon the growing membrane. In this, as in the earlier embryos, the deposition zone is quite as clearly marked out and consists now entirely of distinct, sharply-defined, exo-

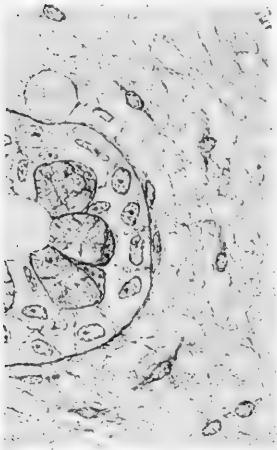


FIG. 3. Alveolus of growing submaxillary of pig 8 cm. long showing formation of mucous cells from the inner cellular layer of the alveolus. Basement membrane and syncytium of the deposition zone show the enormous numbers of fibrils that are being laid on the surface of the alveolus as it grows out into the glandular framework. Fixed in Zenker's fluid. Stained by Mallory's method. Magnified 900 diameters.

plasmic fibrils, containing a few nuclei lying immediately adjacent to the alveolus and surrounded by a little granular endoplasm. The nu-

clei of the syncytium are less numerous but still show the concentric arrangement about the growing buds, suggesting the continuance of the stress which, exerted in the younger stages, undoubtedly caused them to take this position. In the general syncytium the amount of exoplasm has markedly increased. The fibrils are branched and distinct, but of unequal size, the latter characteristic being most obvious in those bounding the little lacunae in the interstices of the syncytium.

In a pig $12\frac{1}{2}$ cm. in length the basement membranes are very sharply and deeply stained and show numerous fibrillar connections with the



FIG. 4.

FIG. 4. Alveolus from submaxillary gland of an embryo pig $12\frac{1}{2}$ cm. long, showing the gathering of the exoplasm into fasciculi and increase in the size and number of the lacunar spaces. The dots represent partly fibrils cut in cross-section and partly granules of endoplasm situated on the fibrils. Fixed in Zenker's fluid. Stained by Mallory's method. Magnified 900 diameters.

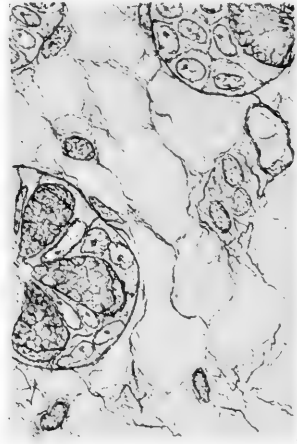


FIG. 5.

FIG. 5. Alveoli from submaxillary gland of pig's embryo 16 cm. long, showing the fasciculi and the irregular direction of the exoplasm and nuclei caused by the different forces exerted by the growing alveoli. Stained by Mallory's method, after Zenker's fluid. Magnified 900 diameters.

adjacent syncytium of the deposition zone. The anastomosing mass of fibrils now stands out with greater distinctness owing to the compact fascicular arrangement, a fact emphasized by interstitial lacunae which increase proportionally as the exoplasmic fibrils are gathered into bundles or fasciculi that bound these spaces. To this fact may be due the apparent diminution in the relative number of fibrils. The changes that occur between the ages represented in pigs $12\frac{1}{2}$ and 16 cm. in length are of some importance. Besides a general clarification and increase in the distinctness and definition of the fibrils, they may now be

observed running in very distinct fasciculi which bound still larger spaces. In some places there are groups of three or four nuclei surrounded by a common protoplasmic mass embedded in a dense fibrillar meshwork while at certain other nodal points of the fasciculi some nuclei have either little or no endoplasm at all. The basement membranes now have a much sharper outline and the fibrils of exoplasm that connect them with the general network do not appear so numerous because they are gathered into fasciculi. Many nuclei with a slight amount of endoplasm are observed flattened against the growing membranes with their long axis parallel to that structure. Now as the further development of the organ proceeds and as the alveoli grow closer together it must be obvious that the increments of exoplasm are in the form of fasciculi instead of individual fibrils. This, indeed, is in accordance with the appearances seen in digested specimens of the adult where a uniform network will be seen crossed by heavier strands of reticulum. In such cases, of course, this network represents the products of fibrillar deposits, while the strands, on the other hand, indicate fascicular deposition. As long as the alveoli are extending out into the general syncytium, sufficiently isolated to exert only the stress caused by their own growth, the nuclei and fibrils take the direction mentioned above, but, in the latter stages, where, owing to their great numerical increase, the alveoli begin to encroach on each other, we have the stress exerted by one alveolus transferred through the syncytium to another so that excepting those immediately touching the basement membranes, the nuclei and cells occupy no definite position. Of course, even while this is so, the exoplasm embracing larger units of the growing organ may show by its direction the lines of stress and strain exerted by the more differentiated structural complexes.

Pari passu with the changes that have been occurring in the developing organs, a constant relative diminution in the quantity of syncytium and gland substance has taken place. Whether this is absolute or simply a relative difference it is difficult to say, but the gathering of the fibrils into fasciculi during the later periods of embryonic life has, undoubtedly, much to do with this appearance. However, to a certain point the syncytium, particularly the exoplasm, seems to increase and from that time on there is a constant apparent diminution until it is, finally, all changed into basement membranes or interalveolar framework.

In a pig 19 cm. in length the developing alveoli are now rather closely pressed together so that between them there is quite a good deal of embryonic connective tissue. The basement membranes are

gradually becoming firmer and more definite and the exoplasmic fibrils



FIG. 6. Mucous alveoli of the submaxillary gland of pig's embryo 19 cm. long. Many of the basement membranes are now in apposition, although their identity is still distinct. Stained by Mallory's method, after Zenker's fluid. Magnified 900 diameters.

that run out into the adjacent syncytium are confined into smaller sharper bundles. These, with the progressing age of the embryo, have more definite and distinct characteristics. The fibrils are of unequal size and often run so that a definite cross hatch is seen along course of the fasciculi. In the syncytium there is very little granular debris, the dotted or granular appearance noted along fibril bundles or at their nodes being due to the intersecting strands of exoplasm cut in cross-section.

In a pig 22 cm. in length the alveoli are very closely approximated and the strands of exoplasm bridging the spaces between them are very sharp and take a deep clear blue stain. In places, the membranes which are now sharp and distinct are in close apposition with those of adjacent alveoli, although in some parts of the lobule, particularly the central region, there is still a considerable amount of general syncytium. Between the alveoli are bridges of exoplasm, in the mesh-work of which the connective tissue cells now lie. This portion of the syncytium becomes the interalveolar framework. These have differentiated and show several types, some round and some branched. At points where the alveoli are in apposition the nuclei are flattened out between them so that they now form in these situations elongated lanceolate-shaped nuclei which stain with the orange element of the dye and show an extremely granular structure. Those out in the looser syncytium still retain their spherical or ovoid contour and still show a poorly-marked nucleolus.

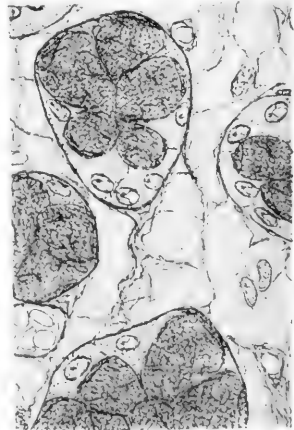


FIG. 7. Submaxillary gland of pig's embryo 22 cm. long. Stained by Mallory's method, Zenker's fluid. Magnified 900 diameters.

In the submaxillary of a pig two days old the alveoli are now almost entirely in apposition with each other. Here and there, one may find slight chinks or clefts where the basement membranes of

adjacent alveoli are not contiguous. The membranes stain an intense deep blue, like fine, delicate lines and are slightly thicker at the points where two adjacent membranes have fused than at the boundaries of the small interalveolar spaces. The fibrillar nature of the membrane is shown in places where the alveolus and its membrane are cut tangentially. Now the interalveolar syncytium has almost entirely fused with the basement membranes, but here and there oval or lanceolate nuclei rest in close approximation to the developing membrana propria. These nuclei, however, are provided with very little protoplasm. From now on it is a very simple matter to follow the changes that occur in the

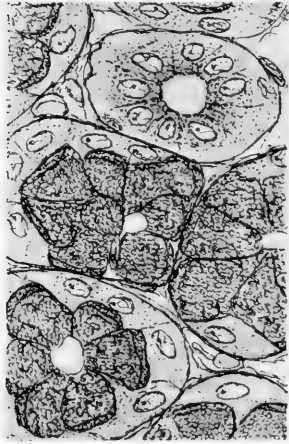


FIG. 8. Reticulated basement membranes about the mucous alveoli of the submaxillary gland of a pig two days old. Stained by Mallory's method, after Zenker's fluid. Magnified 900 diameters.

transformation of the organ as it appears at birth to the conditions of adult life. In the adult gland there is between the alveoli an almost complete disappearance even of the small interalveolar spaces and the basement membranes of adjacent alveoli now lie fused together by the fibrils so that they form a single sharp distinct blue line which is separated here and there by the elongated nuclei of the connective tissue cells. At many nodal points the blood-vessels can be distinctly seen. In some places there is still a considerable amount of framework left especially in the regions about the lobular ducts and those near the membrana limitans of the lobule. Even under the highest powers of the microscope these membranes appear as a homogeneous blue line except where the direction of the section

yields a tangential view, and thus betrays to a certain extent their fibrillar nature. This, of course, is shown absolutely by the digestion methods. To recapitulate, then, we see that the basement membranes are laid down almost simultaneously with the column of cells which springs from the buccal cavity and later forms by its dendronal branching the gl. submaxillaris. This membrane is deposited partly in the syncytium in which it lies and partly by increments derived from the exoplasmic fibrils of the embryonic connective tissue. As the ramification of the columns proceeds and the terminal buds of the growing gland come into closer approximation, the amount of syncytium between them greatly diminishes and gradually takes on a more definite fibrillated structure until finally the two fuse and form a single mem-

brane which is absolutely inseparable by any of the methods at our disposal.

The alveoli of the submaxillary of the adult pig have no elastic tissue either around them or in the interalveolar spaces. In studying, therefore, the development of the lobules through a series of embryos by means of elastic tissue methods, no reaction is obtained while the developing reticulated membranes are easily demonstrated by Mallory's method. Specimens of the embryonic glands that have been macerated for some time in a saturated solution of bicarbonates of soda and subsequently shaken to loosen and remove the cells show the fibrillated membranes but none of the homogeneous type. This is true of the ducts as well as the alveoli. If these preparations are treated with 0.5% HCl or 0.1% KOH the reticulated membranes swell and become clear and the individual fibrils can usually be seen with the immersion lens.

In this description there has been a somewhat loose use of the term syncytium, for even where the cells of the embryonic connective tissue have become separated and obtained their individuality, the word has in many cases been employed. It is very difficult, however, to draw a clear dividing line, because cellular independence is not, as a rule, granted to all of the elements in an organ at one time. Strictly speaking, of course, the syncytial stage ceases when the cells take up their individual existence, but to avoid confusion it is perhaps best to use the same term throughout, provided, it is understood that the tissue so designated is undergoing constant changes.

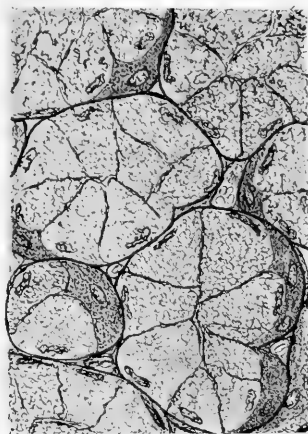


FIG. 9. Mucous alveoli of adult pig's submaxillary showing reticulating basement membranes. Stained by Mallory's method after Zenker's fluid. Attention should be directed to the fact that the scale of this drawing is just one-half that of the balance of the series. Magnified 450 diameters.

THE DEVELOPMENT OF THE PARAPHYSIS IN THE COMMON FOWL.

BY

FRANKLIN DEXTER, M. D.

Associate Professor of Anatomy, The Anatomical Laboratory, Harvard Medical School.

WITH 9 TEXT FIGURES.

The moment that one begins to examine the literature of this subject he cannot fail to be impressed with the difficulties which present themselves. The forebrain has been a favorite subject for study, consequently a great deal has been written on it, and so it is impossible to feel certain that all pertaining to it has been read. It has been considered from many points of view, by means of different methods, and has received many names, either when considered as a whole, or in its subdivisions. It does not seem to me to be necessary to mention each individual paper which I have read, so propose to include only those in my list of literature which have an actual bearing upon this special subject.

There is a difference of opinion in regard to the best subdivision of the forebrain, but all who have described it, as far as I know, take the velum transversum as its primary subdivider into an anterior division or prosencephalon, and a posterior division or diencephalon. The nomenclature lately proposed by Minot (9) although a trifle longer than that adopted by some writers, has the advantage of being more specific, and consequently I shall follow it, with the exception of the first subdivision. He subdivides the median line of the diencephalic roof into six divisions. First, the region of the post commissure. As he later points out in his paper, and I thoroughly agree with him, that this commissure is probably developed from the midbrain, and therefore should properly be considered as belonging to that region. Since this is probably the case, I see no reason for describing it as a portion of the diencephalic roof.

We will therefore omit this subdivision, and will consider the posterior commissure as a part of the midbrain, and will subdivide the median line of the diencephalic roof into five regions:

FIRST. The epiphysis. SECOND. The supra-commissure.

THIRD. The post velar arch. This extends from the supra-commissure to the velum.

FOURTH. The velum transversum. FIFTH. The paraphysal arch. This extends from the lamina terminalis in front, to the velum transversum behind. It is in this subdivision, close to the velum, that the paraphysis is found.

The history of the paraphysis in the lower vertebrates has been repeatedly studied and described. It is curious that so little attention has been paid to it in birds, especially since its presence has even been demonstrated in certain mammalian embryos. Selenka (12) was the first to identify the paraphysis in chicks. Burckhardt (1) mentions it in a 2.5 mm. embryo crow, and states (2), "In birds the paraphysis remains rudimentary and later cannot be identified." Minot (9) also refers to it in an embryo chick of about seven days. D'Erchia (5) identified the paraphysis in fish, and in mammalian embryos, and believes it to be a constant structure in all vertebrates, but reports no observations on birds. Francotte (7) identified it in a human embryo of twelve weeks, and believes it to exist in all vertebrate embryos. This is all the literature I have been fortunate enough to find relating to the paraphysis of birds.

Many of the preparations employed in this piece of research work belong to the Harvard Embryological Collection. Besides the sections here represented, intermediate stages of embryos were studied, as well as chickens varying from a few days to full-grown hens. The sections were invariably serial, and double stained with cochineal and orange G. Many specimens were hardened in Tellyesnick's fluid, which gave on the whole better results than Zenker's, and of course has the great advantage of being without corrosive sublimate. Thirty-six hours was perhaps the usual time the adult brains were allowed to remain in this fluid, and an equal amount of time in running water, and then they were treated by the progressive alcohol method. Great difficulty was experienced in making true longitudinal median sections of the adult brains. This was largely due to the depth of the longitudinal fissure and to the very thin inner wall of the lateral ventricle, which often in the process of hardening becomes more or less twisted. Much less difficulty was usually encountered in the earlier stages where the entire head was cut without removal of the brain. Nos. 1, 2, 3, 4, 5 and 7 of the following figures were drawn on the same scale, and all of the sections in this paper were drawn with the aid of a camera lucida.

Figure 1 is a sagittal section of the forebrain of a 6.7 mm. embryo.

The midbrain is somewhat obliquely cut, but the section in the region of the paraphysis is nearly median. One recognizes the large cavity of the embryonic forebrain, with its correspondingly thin walls.

At this stage the epiphysis (Ep) is simply an evagination of the roof, in front of which the posterior velar arch forms a gentle curve. Neither the posterior nor the superior commissure has made its appearance, nor as yet is there any indication of a choroid plexus. The velum (v) is plainly seen between the ventral portion of the posterior velar arch and the paraphysis. It appears as a somewhat triangular mass of mesenchymal tissue protruding into the cavity of the forebrain, but is actually separated from that cavity by the thin ectodermic wall. It extends transversely across the forebrain, and so divides it, as was previously mentioned, into the prosencephalon and diencephalon.

This is the earliest stage in which I have been able to identify the paraphysis. Embryos a trifle younger, present in sagittal section an appearance which closely resembles Fig. 1, with the paraphysis wanting. The paraphysis lies in the median line, immediately dorsad to the foramen of Munro, and anterior to the velum transversum. At this stage it is a simple evagination of the brain wall, and is identical with it in structure. It

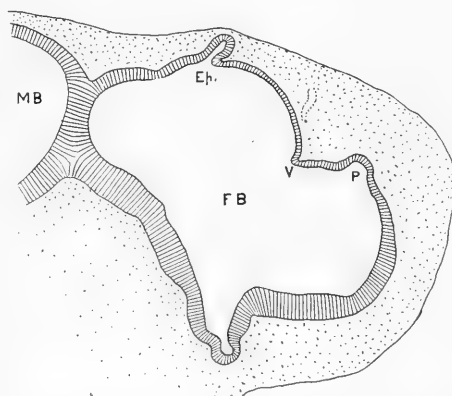


FIG. 1. Embryo of 6.7 mm. Harvard Embryological Collection. Sagittal series 477. Section 110. $\times 45.2$ diams.

contains a large cavity which communicates with that of the forebrain.

Fig. 2 is a most fortunate median sagittal section of a 19.5 mm. embryo in which the above-mentioned subdivisions of the forebrain may be readily identified. The posterior commissure is at this stage plainly visible. A well-developed epiphysis is present. This is the earliest stage at which I have been able to identify the superior commissure. It lies in its characteristic position, within the ectodermic brain wall, anterior to the opening of the cavity of the epiphysis. We will return again to this region, and will study it more closely with a higher power.

It is evident on comparing Figs. 1 and 2 that the posterior velar arch has now totally changed its shape. In Fig. 1, it forms a curve.

In Fig. 2, it consists of a horizontal and a perpendicular arm, which form together what is not far from a right angle. Moreover, it is perfectly apparent from this drawing, that the choroid plexus of the forebrain is developed only from the perpendicular arm, or anterior portion of the arch.

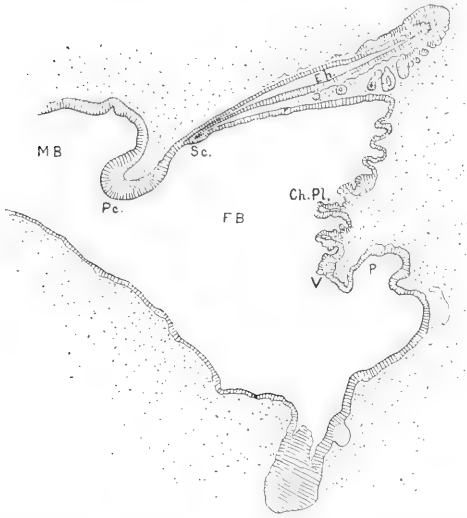


FIG. 2. Embryo of 19.5 mm. Harvard Embryological Collection. Sagittal series 473. Section 334. $\times 45.2$ diams.

This stage the paraphysis is much more developed and contains a large cavity communicating with that of the forebrain. Its wall is distinctly thicker than in the younger embryo.

Fig. 3 is not as fortunate a median sagittal section as the last. The paraphysis is shown exceedingly well, but the communication of the cavity of the epiphysis with the forebrain does not appear in this section. It is from an embryo of 43 mm., and is naturally much more developed than the previous one. The posterior commissure is very large. Portions of the tubules of the epiphysis are seen in the mesenchymal tissue above the roof of the third ventricle. The superior



FIG. 3. Embryo of 43 mm. Harvard Embryological Collection. Sagittal series 509. Section 362. $\times 45.2$ diams.

commissure has materially increased in size, and is found in its usual position. Anterior to this commissure a fold in the roof of the ventricle might easily be taken for the epiphysial opening, but such is not the case. The posterior velar arch has again changed its shape. What was formerly described as the horizontal arm is now distinctly ascending and forms with the perpendicular arm a fairly acute angle, with a direction of upwards and forwards. The perpendicular arm has not altered its position, but the choroid plexus springing from it is thoroughly well developed, lying in many folds, some of which have been cut transversely and therefore appear separated from the roof of the ventricle. The velum transversum is very much changed in appearance. The mesenchymal tissue has thinned, its choroid fold is very prominent, and but for its specific position it would be impossible to differentiate it from any other fold of the choroid plexus. (The breadth of this fold, as well as its position and relation to the paraphysis, are well shown in Fig. 4.)

The paraphysis presents a wonderfully regular outline, as well as cavity. It seems to be distinctly smaller than in the previous stage, which is particularly true of its cavity, but on the other hand, its walls are much thicker. A large vessel is seen in the mesenchymal tissue ventrad to the epiphysis. Its position is very characteristic. It gives off branches which supply the choroid plexus of the third ventricle, and the vessel then divides dorsad to the paraphysis, and each terminal branch supplies the choroid plexuses of the lateral ventricles posterior to the foramina of Munro.

Fig. 4 is a frontal section of an embryo's brain 45 mm. It is cut obliquely to the cavity of the paraphysis, as seen in Fig. 3. The two lateral ventricles, with portions of their choroid plexuses, the cavity of the forebrain with its choroid folds and optic thalami on each side, are all easily identified. The velum stretches transversely across the roof of the forebrain, between the paraphysis and the choroid plexus, and is continuous with the mesenchyma surrounding the optic thalamus. It is situated dorsad to the paraphysis. The paraphysis is seen lying in

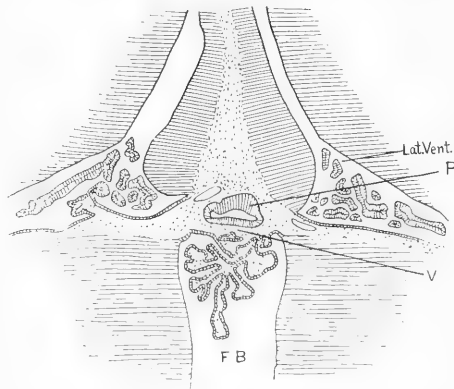


FIG. 4. Embryo of 45 mm. Harvard Embryological Collection. Frontal series 514. Section 772. $\times 45.2$ diams.

the mesenchymal tissue ventrad to the forebrain, and appears as an irregular ring of ectodermic tissue. Two of the above-mentioned vessels, which supply the choroid plexus, are met in this section.

Fig. 5 represents a sagittal section of a ten-days' chicken's brain. The section is not exactly in the median plane, consequently the choroid plexus has been separated from the roof of the third ventricle. It seemed to me to be unnecessary to draw in all the structures that have been previously represented. The epiphysis and both commissures are omitted. The picture, when taken as a whole, resembles very closely Fig. 3, an embryo of 43 mm. The dorsal wall of the posterior velar arch is even more perpendicular than in the above-mentioned figure. This tends to make the angle formed by the two limbs much more acute,

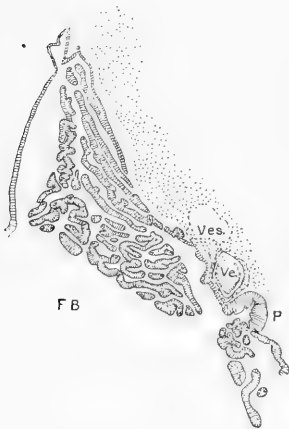


FIG. 5. Sagittal section of a 10 days' chicken's brain. $\times 45.2$ diams.

so that now both are quite perpendicular. The position of the anterior arm has changed very little, but the choroid plexus springing from it, is fully developed. Unfortunately, owing to the obliquity of the section, the velum has been separated from the roof of the ventricle, and consequently it does not appear in this section. Such a fold, were it present, would present no essentially different picture from that represented in Fig. 3. As we have already seen the velum is situated immediately behind the paraphysis. I believe that the first prominent fold of choroid plexus in an adult chicken, behind the paraphysis, represents morphologically the large, broad, well-developed velum transversum of the 6.7 mm.

embryo, as is represented in Fig. 1. There is almost no change in the appearance of the paraphysis. Its cavity is more constricted, but its walls are of about the same thickness, and of course its position in the two plates is identical. Above and to the left of the paraphysis there is a curious vesicle (Ve) which I am at a loss to explain, but will refer to again farther on.

Figs. 6 and 7 represent the same sections under different powers of magnification. It was desirable to draw this section with the same power as was employed for the others, but the field was not large enough to include the entire section and so it was thought advisable to first study its topography with a lower power, without which it does not seem to me that it would be intelligible. The figures represent frontal

sections which pass through the paraphysis of a three-days' chicken's brain. In Fig. 6 one is able to distinguish the narrow lateral ventricles, the slit-like cavity of the forebrain lying between the two optic thalami, a very minute paraphysis, and just above it a triangular cavity or vesicle. This seems to be the same structure which we saw in sagittal section (Fig. 5).

On examination of Fig. 7 the same regions are much more easily distinguished. Here the paraphysis is seen clearly to be a portion of the epithelial roof of the forebrain. Its cavity presents a very uniform appearance, but with a higher power, small fissures are observed running off from it, and piercing its wall for variable distances. A large transverse vessel separates it from the vesicle. The space between the

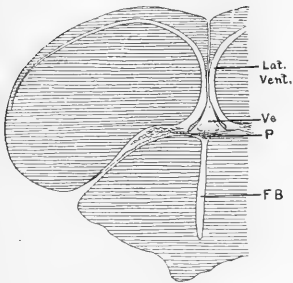


FIG. 6.

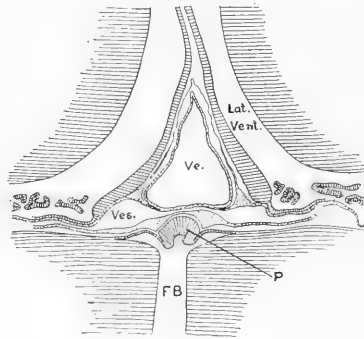


FIG. 7.

FIGS. 6 and 7. Frontal sections of a 10 days' chicken's brain. Fig. 6 \times 9.2 diams. Fig. 7 \times 45.2 diams.

paraphysis and the mesenchymal wall of the vessel, I imagine is due to shrinkage, but it must be said that it is peculiarly constant, and has been frequently observed as is here represented.

Fig. 8A represents a portion of the paraphysis as seen in Fig. 5 under a much higher power. Even with a comparatively low power, one can easily subdivide its wall into two regions. An inner, thinner layer, next to its cavity, and an outer, much thicker layer. The inner stratum stains more deeply than the outer, and is of about the same thickness as the ependymal layer of the brain. With a high power, the nuclei of this layer are seen to be somewhat oval in shape, and are crowded together in contradistinction to the outer layer where they are much more clearly defined, round in appearance, and more widely separated from each other. In a word, the outer layer seems to be a sort of modified ectodermic tissue. The above-mentioned clefts issuing from the

central cavity of the gland into its walls are in this section plainly visible.

It seems to me that Minot's (9) supposition regarding the paraphysis in amphibia and birds is a perfectly correct one. It is inconceivable that the paraphysis can for a moment be thought of as an organ of sense. It is much more probable that it is an appendix of the paraphysal arch, developed from the brain wall, and, as we have seen, its outermost layer in the adult is composed of a modified ectodermic tissue. In the younger stages its walls are thin and its cavity is large, but in the adult chicken or hen the reverse is true. A narrow, cleft-like cavity persists, surrounded by moderately thick walls. The gland is

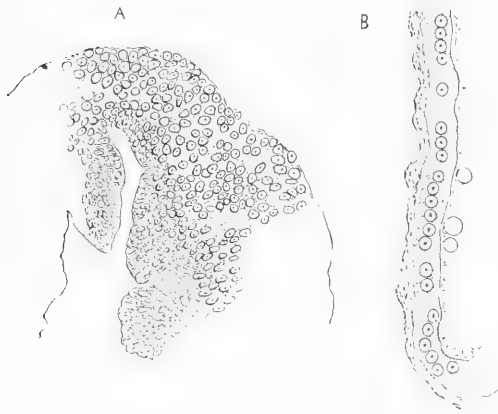


FIG. 8A. Paraphysis of a 10 days' chicken. Sagittal section. $\times 540$ diams.

FIG. 8B. Vesicle of a 3 days' chicken. Frontal section. $\times 540$ diams.

oval in shape and is not far from 150μ in its greatest diameter, which lies nearly parallel with the longitudinal axis of the cavity of the forebrain. It is an absolutely constant structure, and I have been able to identify it time and time again in the embryo, in the chicken, and finally in the full-grown fowl. Its position is very characteristic. The paraphysis is situated immediately dorsad to the foramen of Munro, and anterior to a prominent fold

of the choroid plexus which must morphologically correspond to the velum transversum.

Fig. 8B is a section of a portion of the peculiar vesicle above referred to shown under a high power. The preparation is from the same series as Fig. 7 but a different section, a little farther dorsad to it was chosen, as the cells seemed to show more distinctly than those in the previous section. The wall of the vesicle is granular in structure, with large round nuclei, which in each case contain a small, irregularly-shaped nucleolus. At times the nucleolus appears as a round dot, or presents a linear appearance. It may represent quite a regular cross, or even be star-like in shape. Externally there is a layer of mesenchymal tissue, and internally what presents the appearance of a distinct membrane. Within the cavity of the vesicle, there is almost invariably

an appreciable amount of coagululum. Frequently close to its wall, some spherical bodies are seen. These vary much in size, as well as in number. I have no notion whatever as to what they are. The triangular vesicle has been a very interesting puzzle to me, nor is it as yet solved. I call it a vesicle simply for the want of a better name. For a long time it did not seem possible that it was not a blood-vessel, or perhaps a lymph space, and to-day I am unable to explain it, so must leave the subject for future investigation. There are, however, a few curious facts in regard to it. It is an inconstant structure. I have seen it in embryos from 60 mm. in length, up to young chickens after birth, but I have never been fortunate enough to meet it in an earlier or in a later stage. At times it is present, but I am inclined to believe that it is more frequently absent. When present it seems to be situated in about the same spot, and may be identified in either a sagittal or a frontal section. In the former it is apt to be somewhat oval (Fig. 5); and in the latter triangular in section (Fig. 7).

In one series of the adult chicken, where the vesicle was absent, the blood-vessel (which appeared in Fig. 7 as a compressed vessel beneath it), was triangular in form, and presented precisely the same shape as this vesicle. As the vesicle begins to appear in serial sections the wall is first met, then one meets the cavity, and lastly a wall. Surely when one considers the structure of this object under the high power, it is difficult to conceive of its being either a lymph space or a blood-vessel, and after diligent search through many sections in several embryos, I have never been able to find a single blood corpuscle within its cavity, and as far as I know, its cavity does not communicate with that of the forebrain.

Dendy (4), in a most admirable and interesting paper on *Sphenodon*, refers to what he calls an accessory vesicle situated between the tubules of the paraphysis and the parietal stalk. He describes it as sacculated, irregular in shape, containing no blood corpuscles, unconnected with the forebrain, and as disappearing at a moderately late stage of development. He does not believe it to be either a vessel or a lymph space. Moreover, as pictured in his article, the lining epithelium seems to be of quite a different character from the vesicle in question. Burekhardt (1) mentions a vesicle in *lacerta vivipara*, which is close to the epiphysis, and could not, I should fancy, be confounded with this one. Under the head of "Nebenorgan" and "Nebenscheitelorgan," different kinds of vesicles have been described in different animals by various authors, but I fancy that they should all be associated with the epiphysis rather than with this vesicle, which certainly can have no connection with it.

Ritter (11) also speaks of a parapineal organ which does not seem to me to have any resemblance to the one in question. It is certainly a good subject for future investigation, and with my present amount of material one ought soon to be able to arrive at some definite conclusion in regard to it.

The presence of the supra-commissure in birds is denied by certain authors. Grönberg (8) states that it is not present in this class of animals, but admits its presence in all the mammalia. Dejerine (3) claims that it exists in all vertebrates. It has been described under various

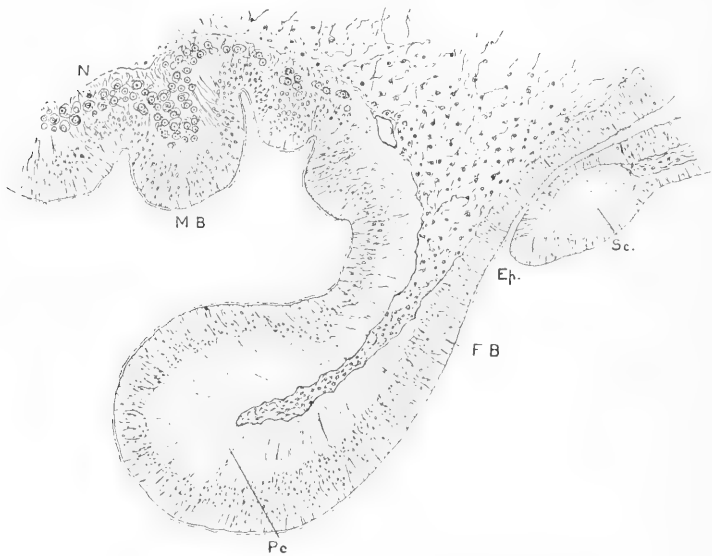


FIG. 9. Embryo of 25 mm. Harvard Embryological Collection. Sagittal series 516. Section 286. $\times 220$ diams.

names, but as far as I know, nothing has been said in regard to its development in birds, although Edinger (6) describes it in pigeons under the name of tractus habenulo-peduncularis. To Osborn (10) the simple name of supra-commissure is due.

In Fig. 2 an embryo of 19 mm. the supra-commissure is met for the first time, and after this date it must of course persist throughout life. The various descriptions of its fibers seem to vary in the number of words employed, rather than in any real difference of opinion in regard to the anatomy of the commissure itself. As far as I know all writers agree that its fibers arise from the ganglion of the habenula, and terminate in the ganglion interpedunculare of the midbrain.

Fig. 9 is a sagittal section of a 25 mm. embryo, and shows this region very clearly. The opening of the cavity of the epiphysis into the fore-brain is very apparent (Ep), and immediately anterior to it, within the ectodermic wall, the supra-commissure is first seen in a chick of about 19 mm. in length. Its position is very characteristic, for it is invariably described as being situated in this particular spot throughout all classes of vertebrates. The posterior commissure makes its appearance at an earlier date than the superior, and is consequently at this period very well developed. As was previously mentioned, it is properly considered to be a portion of the midbrain. This being the case I would call attention to the fact that its fibers terminate a very short distance from the epiphysial opening (Ep), or in other words, immediately posterior to it, consequently, it seems to me, that the opening of the epiphysis into the fore-brain is situated much nearer the line of division between the mid- and forebrains than it is commonly supposed to be, and that the portion of the roof of the midbrain which is formed by this commissure, extends a greater distance ventrad than we are apt to picture in our minds.

Some very curious, large nerve cells (N) may be observed situated in the wall of the midbrain. They contain a round nucleus, and an irregularly-shaped nucleolus. I call attention to them, since they are quite new to me.

To recapitulate:

1. The paraphysis appears as an evagination of the roof of the fore-brain, and first makes its appearance in a chick of about 6.7 mm. and is present throughout life. It is situated immediately dorsad to the foramen of Munro, is oval in shape, and contains a slit-like cavity which communicates with the cavity of the third ventricle.

2. The choroid plexus of the third ventricle arises only from the anterior half of the embryonic post-velar arch.

3. In the chicken, the first prominent fold of choroid plexus posterior to the paraphysis corresponds morphologically to the velum transversum of the embryo.

4. The supra-commissure may be first identified in an embryo chick of about 19.5 mm.

Finally, I should like to acknowledge my indebtedness to Prof. C. S. Minot, not only for his valuable suggestions, but also for the interest he has taken in this piece of work.

ABBREVIATIONS.

- Ch. Pl.*, Choroid Plexus.
Ep., Epiphysis.
F. B., Forebrain.
Lat. Vent., Lateral ventricle.
M. B., Midbrain.
P., Paraphysis.
Pc., Posterior commissure.
N., Nerve cells.
Sc., Superior commissure.
Ve., Vesicle.
Ves., Vessel.

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CONTRIBUTIONS TO THE ENCEPHALIC ANATOMY OF THE RACES.

First Paper:—THREE ESKIMO BRAINS, FROM SMITH'S SOUND.

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WITH 20 TEXT FIGURES

INTRODUCTION.

A problem of great importance in the field of somatic anthropology is the correlation of the intellect of races with brain-structure. There are certain ethnic traits with which education or civilization have had nothing to do, and which are properties inherent in the complex structure of the brain. In fact, the intellectual characters of the races exhibit remarkable differences; capacity and aptitude for learning are very variable; and since these are but the expressions of cerebral activity they naturally lead to attempts at explaining them in terms of correlated anatomical differences. One subdivision in encephalometry alone deserves especial study, that of the speech-centers,—receptive, emissive and associative,—a problem first essayed by Rüdinger in 1882. The profound differences in scope and complexity of the many languages, assiduously studied by linguists and philologists, assumedly depend upon differences in the architecture of those portions of the brain concerned in the mechanism of the faculty of language. Of course, it must be admitted that the proposition is a difficult one to establish, but to assume that in the brains of races typical differences of cerebral surface-morphology exist, is a belief which even the meager amount of material that has so far accumulated, renders justifiable. What is to be attained in this view is the establishment of a systematic anthropological encephalometry. The efforts of our predecessors in this direction may have seemed somewhat fruitless, but the more recent advances in this branch of science evoke increased exertion on the part of interested investigators, increased admiration for the organ pronounced by the great Reil “*die höchste Blüthe der Schöpfung.*”

In a search of the literature in anthropological and anatomical fields of work, descriptions of the brains of races are few in number and often of an unsatisfactory character. Not only is this to be deplored from the view-point of science generally, but it is particularly to be regretted in the case of those races which are rapidly becoming extinct and whose ethnological and anthropological relations would necessarily be incomplete without a well-grounded knowledge of their encephalic anatomy, both macroscopical and histological. The vital necessity of obtaining a large amount of available material to pursue the comparative study of cerebral development from the standpoint of somatic anthropology, is, of course, obvious. The difficulties to be overcome, though less serious than before, are still sufficient to render many of our efforts fruitless. Advances in the extent of our researches can not longer be postponed—if they are to be of value—for in the evolutionary progress of mankind many of the exotic races are rapidly becoming impure or even extinct. Instances of this are numerous. Of the race of Charruas Indians, now extinct, one brain has fortunately been preserved for us by Leuret and Gratiolet. How much longer will the North American Indian remain pure? The recent volcanic outbreak in the Antilles is said to have wiped out nearly every Carib in existence, a few individuals only remaining on St. Lucia and Dominica. The Australian natives, driven to the desiccated wastes of the interior; some African tribes, succumbing in the arid deserts, and the Eskimos, decimated by epidemics of small-pox, measles and pneumonia—all these and many others that might be mentioned, are dying out.

Strong pleas for an extended anthropological encephalometry were made as far back as the first half of the past century by such eminent anatomists as Tiedemann, Huschke, Gratiolet and Leuret. Tiedemann was the first to direct attention to this field of work. In his book, "*Das Hirn des Negers mit dem des Europäers und Orang-Outangs Verglichen*" (1837), he figured the brain of a negro and that of the famous "Hottentot Venus," comparing these with the European brain. Leuret and Gratiolet (1857) later presented the brain of a Charruas Indian from Uruguay, comparing it with a French brain.

Huschke, in default of available material, conceived the idea of studying intra-cranial casts made of wax and thereby arrived at a rough estimation of the general mass and conformation of the brain in a few races. This mode of study was, however, unsatisfactory as well as crude, as it lacked a description of the surface morphology and microscopical structure. Wagner (1860) made similar studies on intra-cranial casts, deploring at the time that every effort to obtain brains of rarer races was futile.

Perhaps the greatest interest in anthropological encephalometry was stimulated by the case of the classical "Hottentot Venus" (whose name was "Sartjee"), who died in Paris, and whose full-length portrait is now in the Museum of the Anthropological Society of that city. Observed during life by Cuvier, her skeleton and brain were preserved after death, to afford a valuable basis for the work of many investigators. Tiedemann figured the brain in 1837, Gratiolet again in 1854, Bischoff in 1868. Two additional brains of Bushwomen were described by Marshall (1864) and Koch (1867). The interest in the brains of the lower races soon increased and observations began to accumulate. The reader can judge of this from a review of the appended bibliography. In regarding the number of observations made, as well as the importance of the results attained in more recent years, especial mention may be made of the work of Retzius, Cunningham, Sernoff, Weinberg, Manouvrier, Rüdinger and A. J. Parker.

It cannot be hoped, by the few examples of racial brains here presented, to establish very significant facts concerning them, but the purpose of these Contributions is rather to add to those already described, with the hope of having still others added thereto. In time, a large number of specimens cannot fail to be amassed, and useful conclusions may then be derived.

The present paper upon this subject is the first of a series comprising the following:

1. Three Eskimo Brains, from Smith's Sound.
2. A Japanese Brain.
3. Two Brains of Natives of British New Guinea (Papuaans?).

All of these brains are in the collection of Professor George S. Huntington's Anatomical Laboratory, Columbia University.

THREE ESKIMO BRAINS, FROM SMITH'S SOUND.

GENERAL REMARKS.

Though widely distributed over Arctic America, and though subdivided into numerous tribes, the Eskimos differ but little in their dress, customs and utensils, and they form a remarkably homogeneous group of people. What is in the present instance of great consequence from the morphological view-point, so far as the surface-markings of the brain are concerned, is the almost complete isolation of the American Eskimo from all other races. Trading is carried on almost exclusively among their own tribes, and the intimate marriage-relation of

the members of this race must be considered as of vital importance in an investigation of this kind. In probably no other race is "in-breeding" so widely prevalent as among the Eskimos, and this it is which makes the conditions for the study of racial characteristics so nearly the ideal as can be.

Of the ethnic traits and the anthropological status of the Eskimo it is admissible to deal only in a general way, within the compass of this article. The Mongolian relation (or rather, the probable Mongolian origin) of this hyperborean race is generally conceded by the anthropologists. As to their mental capabilities, the information given us by the majority of travellers seems to indicate that the Eskimos are sharp-witted, exhibit remarkable aptitudes, and in general possess a considerable intellectual power. A remarkable aptitude in carving and drawing is a characteristic remarked by most travellers, particularly by Klutschak—himself an artist—and by Irving Rosse. Notwithstanding the crudeness of delineation and imperfection in detail, their ivory sculptures of birds, quadrupeds, marine animals and even the human form, display considerable individuality in conception and intelligent perception. Travellers needed merely to place the necessary materials in their hands, in order to profit by their ability to make drawings and maps which were practically as reliable as corresponding efforts of the civilized man unaided by instruments. The drawings, like those of the Chinese, have but one defect, being faulty in perspective.

As a mechanic, the Eskimo is, considering his poor opportunities and materials, very clever and painstaking. With an unbounded curiosity supplemented by intelligent observation he soon learns to imitate the white man in various kinds of handicraft.

Their ideas of property and commerce are distinctive from those exhibited by the lower races. Their sense of morality with reference to truthfulness, honesty and virtue are peculiar but natural and in accord with their traditions and environment. Their diversions and instincts, their social and domestic relations are interesting and distinctive of the race. When brought into civilized surroundings, and when fortunate enough to escape the scourges of tuberculosis and the other diseases to which they are so susceptible, they display an aptitude for learning and a capacity for intellectual development that is of no mean order.

FORMER DESCRIPTIONS OF ESKIMO BRAINS.—Only four Eskimo brains have hitherto been described; three by Chudzinski, and one by Hrdlicka (see Bibliography). Chudzinski's specimens were those of Eskimos who died of small-pox in the Hôpital de Saint-Louis, Paris. The brains had been placed in very weak alcohol for two weeks before

Chudzinski obtained them, and one of the brains, that of "Paulus Abraham," was in such an advanced state of decomposition that its weight could not be ascertained. Chudzinski made plaster-casts of the brains, and presented these to the Parisian Anthropological Society on May 5, 1881.

Two of the Eskimos were young men, the other was a girl. They were:

1. "Tobias Ignatius," male, age 23, died January 13. Brain-weight, 1398 grams.

2. "Paulus Abraham," male, age 35, died January 14. Brain-weight unknown.

3. "Ulrika Henocq," female, age 24, sister of "Paulus Abraham," died January 16. Brain-weight, 1256 grams.

Chudzinski nowhere states whence these Eskimos came. One must assume that they were from Greenland, and from an inferior tribe, differing in many respects from the inhabitants around Smith's Sound. Chudzinski states emphatically that with the considerable volume of the cerebrum of his Eskimos, there is a "notable simplicity in the fissural and gyral pattern"; not only are the gyres said to be quite broad and little marked by "tertiary fissures and divisions, but they are only slightly flexuous." This simplicity, he maintains, is especially marked in the frontal lobes, which are rather "flattened from above below." The general form was, according to Chudzinski, that of a dolichocephalic brain. The frontal lobe he describes as relatively small, while the parietal especially was considerably well developed. The frontal gyres were of "very simple configuration—especially in 'Tobias Ignatius.'"

Hrdlicka has commented upon this marked difference between the specimens described by Chudzinski and the one by himself, and says with good reason that this dissimilarity makes "a future acquisition of Eskimo brains very desirable."

BRIEF HISTORY OF THE BRAINS HERE DESCRIBED.—The three individuals whose brains are here presented, "Nooktah," his wife "Atana," and "Avia," belonged to a party of six Eskimos who were brought to New York in 1896 by Lieutenant Peary, from the neighborhood of Smith's Sound. The other three were "Kishu," chief of the tribe, his son "Menee," and a young man whose name is unknown. The last one was sent back to Smith's Sound. "Menee" is now about fourteen or fifteen years old, having recovered from an attack of incipient pulmonary tuberculosis. "Kishu" died in Bellevue Hospital, New York

City, in 1898, at the age of about forty-five years, and his brain has been carefully studied and described by Dr. Ales Hrdlicka.

The writer is indebted to Dr. Hrdlicka for the following measurements of the heads of these individuals during life:

No. 1.—“ATANA.”—*Stature*, 146.7 cm. *Head*: max. antero-posterior diam., 18.0 cm.; max. lateral diam., 14.5 cm.; cephalic index, 80.55 (sub-brachycephalic); horizontal circumference, 53.6 cm.

No. 2.—“НООКТАН.”—*Stature*, 155.0 cm. *Head*: max. antero-posterior diam., 18.8 cm.; max. lateral diam., 15.3 cm.; cephalic index, 81.38 (sub-brachycephalic); horizontal circumference, 56.2 cm.

No. 3.—“AVIA.”—*Stature*, 132.8 cm. *Head*: max. antero-posterior diam., 18.8 cm.; max. lateral diam., 13.7 cm.; cephalic index, 72.87 (very dolichocephalic); horizontal circumference, 53.3 cm.

The skulls measured as follows:

No. 1.—“ATANA.”—Max. antero-posterior diam. externally, 17.6 cm.; internally, 16.6 cm.; max. lateral diam. externally, 13.6 cm.; internally, 13.0 cm.; height, basion-bregma, (?); cranial index, 77.27; cerebral index, 78.31.

No. 2.—“НООКТАН.”—Max. antero-posterior diam. externally, 18.3 cm.; internally, 17.35 cm.; max. lateral diam. externally, 14.4 cm.; internally, 13.7 cm.; height, basion-bregma, 14.0 cm.; cranial index, 78.69; cerebral index, 78.96.

No. 3.—“AVIA.”—Max. antero-posterior diam. externally, 18.2 cm.; internally, 17.3 cm.; max. lateral diam. externally, 13.0 cm.; internally, 12.3 cm.; height, basion-bregma, 12.9 cm.; cranial index, 71.43; cerebral index, 71.09.

In addition to the three brains here described, and the brain of “Kishu,” there is a fifth Eskimo brain in Professor Huntington’s Laboratory; namely that of a girl named “Atmahok,” who died of tuberculosis in June, 1899, in the Walton Sanitarium, at Mt. Vernon, N. Y.

“Atmahok,” with her twin-sister “Zakesino,” had been brought to the United States, and exhibited in various cities in connection with lectures, by Capt. Miner Bruce, of Seattle, Wash., an Alaskan trader. The girls were eight years old. The body of “Atmahok” was received at the Anatomical Laboratory of the Medical Department of Columbia University, two days after death, and the autopsy was performed by Dr. Hrdlicka. The heat of the prevailing weather had already brought about an advanced state of decomposition of the bodily tissues, especially of the brain, and beyond its weight little could be ascertained. In its present state, nothing useful can be derived from the specimen. It is a great loss to anatomical science that this brain could not be preserved successfully, as it would have been of considerable interest to compare this Alaskan with the Eastern Eskimo brains; furthermore, in

the event of the twin-sister's brain being obtainable, the opportunity for seeking out evidences of hereditary similarity in the gyral pattern is irretrievably lost. "Zakesino," the twin-sister, is still in New York City, and is reported to be advancing rapidly in her school studies.

An interesting feature of the Eskimo brains so far reported is their weight. (See Table I.)

TABLE I.
ESKIMO BRAIN-WEIGHTS.

MALES.			
	Described by	Age.	Brain-weight.
"Tobias Ignatius."	Chudzinski.	23	1398 gms.
"Kishu."	Hrdlicka.	45?	1503 gms.
"Nooktah."	E. A. Spitzka.	55?	1470 gms.
Averages.....		41	1457 gms.
FEMALES.			
"Ulrika Henocq."	Chudzinski.	24	1256 gms.
"Avia."	E. A. Spitzka.	12	1227 gms.
"Atmahok."	(Weighed by Hrdlicka.)	8	1057 gms.
"Atana."	(Estimated.)	55?	about 1375 gms.

So far as one may venture to express an opinion concerning the weight of the Eskimo brain, it appears safe to say that it is rather above the average of the European brain. This is certainly true of the three male brains whose actual weight is recorded in the table, and the conclusion is further fortified by the results of the numerous cranial measurements of the Anthropologists.¹

Of the female specimens, the brain-weights of "Avia," "Ulrika," and "Atmahok" are actual figures; while the fourth, that of the old woman, "Atana," is estimated from the present weight. The other specimens, which had been immersed in a similar fluid for the same length of time, lost from 26 to 29 per cent of their original weight. "Atana's" brain may therefore be assumed to have originally weighed about 1375 grammes.

DESCRIPTION OF THE BRAINS.

The description of the fissures and gyres must necessarily be brief, emphasis being laid upon those features which most markedly differentiate these brains from each other as well as from those of other races, European brains in particular. Convinced that figures convey more information than words, and that they occupy less space, the writer

¹See Topinard's "Anthropologie."

presents a series of drawings showing all possible views, made directly from the specimens by himself, with the incidental aid of a stereograph.

The nomenclature here employed is that proposed largely by Wilder, and accepted by the Association of American Anatomists and the American Neurological Association; a nomenclature unquestionably superior to that of the B N A in consistency, clearness and conciseness. The writer prefers the angloparonym "gyre" (plural "gyres") to the Latin "gyrus" and "gyri." All anfractuositities of the surface are designated "fissures," the term "sulcus" being abandoned entirely.

The fissures and gyres have been uniformly designated in the figures by abbreviations (see list at the end of this article). Where the length of fissures is given, the measurements were made by a moistened string laid along the course of the fissure.

The comparative dimensions of the cerebral parts, as well as the conformation of the cerebellum, pons and oblongata will be discussed in the sequel of this series.

1. BRAIN OF "ATANA."

(See *Figures 1 to 6.*)

Our first specimen is that of an adult female, "Atana," the wife of "Nooktah." Her age is in the neighborhood of fifty-five years, and she is described as having been unusually intelligent, as may be judged from the fact that she was the "medicine-woman" of her tribe. She died of tuberculosis on March 15, 1898, at 2 p. m., and her viscera were removed at 4.30 p. m. of the same day. Unfortunately, the brain was not weighed while fresh. It was placed in a mixture of formal and alcohol. Its weight on May 25, 1901 (i. e. after over three years), was as follows:

Left hemisphere, 446 grammes; right hemisphere, 439 grammes; cerebellum, pons and oblongata, 163 grammes. Total, 1048 grammes.

It may be assumed that the original weight was in the neighborhood of 1375 grammes.

THE CEREBRUM.

The cerebrum is quite firm in the deeper parts, but the cortex is exceedingly soft and does not admit of much handling without damage to the surface.

In general, the cerebrum is very well developed. Fissuration is, if anything, rather superior in complexity to that shown by average European brains. This complexity is a trifle more marked upon the left

hemisphere and the trend of minor fissures and ramifications is in a transverse direction, so that many of the principal longitudinal fissures anastomose with each other. This is so marked in Eskimo brains that brachycephaly alone hardly seems to account for it, if we may be guided by past experience. The fissures are of good depth, and contain, in many instances, several interdigitating subgyres. A notable feature of all the fissures is the close apposition of the gyres, making all examinations of the depths of the fissures exceedingly difficult.

The gyres exhibit marked tortuosity, and are of intricate yet delicate contour. The maximum width of any gyre is 14 mm.; the average being about 8 mm.

Both insulae are exposed to view; more so on the left than on the right side.

Viewed dorsally or ventrally, the general outline is that of an elongated hexagon, with its maximum width at the junction of the marginal and supertemporal gyres. This region is particularly prominent on the left side. Viewed laterally, the notable features are a pronounced fullness and rotundity of the frontal lobe, while the parieto-occipital boundary is only moderately convex; this with the nearly straight ventrolateral boundary gives the caudal portion of the hemisphere a more slender contour than is usually encountered. In all respects the development of the frontal lobe preponderates over that of the remainder of the cerebrum, the parietal area being particularly under the average extent found to prevail in European cerebra.

The callosum is well formed, of average thickness in the genu and splenium, but rather slender in its middle portion or body. Its length is 44.7 per cent of the total cerebral length.

One feature in the shape and position of the cuneus deserves particular mention. In this cerebrum, as in nearly all the others of Eskimos, the calcarine and postcalcarine, whether separate or confluent, do not describe the well-marked curve (convexity dorsad) toward the ventromesial border as seems fairly characteristic of Caucasian brains. In this brain, for example, the calcarine complex passes directly caudad and in a nearly straight line, and reaching the hemispherical border at a point much further dorsad. This naturally renders the ventral border of the cuneus straight instead of curved, as usual.

LEFT HEMICEREBRUM.

THE INTERLOBAR FISSURES.—*The Sylvian Fissure and its Rami.*—The sylvian fissure proper is 4.5 cm. in length. It is quite shallow cephalad, as the following measurements of the depth will show: Presylvian depth, 10 mm.; medi-sylvian depth, 18 mm.; post-sylvian depth, 25 mm.

Its course approaches the horizontal very nearly, and it is a little more tortuous than is common.

The basisylvian, measured from the temporal pole, is 20 mm. in depth. The presylvian is simple, and 14 mm. in length. The subsylvian is also 14 mm. long and ends in a bifurcated manner. The episylvian is 25 mm. in length and anastomoses with the intermedial. The hyposylvian is distinct and 14 mm. in length.

The Central Fissure.—The central fissure, 10.5 cm. in length, presents the usual five alternating curves. It does not anastomose with any other fissure. Its dorsal end crosses the dorsi-mesal margin to appear for about 1 cm. on the mesial surface of the paracentral gyre. The dorsal third of the fissure, as will be noted in Figure 3, approaches the intercerebral cleft in a perpendicular manner, not, as is usual, at a distinctly acute angle. From the fissure spring two short caudal and two cephalic rami.

Occipital Fissure.—The occipital fissure has a mesial length of 3.4 cm., and a dorsal length of 2.2 cm. On the mesial surface the fissure describes a compound curve, and anastomoses deeply, cephalad, with what possibly corresponds with Wilder's adoccipital. A superficial anastomosis is effected with the cuneal fissure. Dorsally the fissure ends in a simple manner, limited by a well-developed paroccipital gyre.

Calcarine Fissure.—The calcarine fissure is 3 cm. in length, and is limited dorsally by a slightly depressed transcalcarine isthmus. The postcalcarine passes well upon the occipital polar surface, attaining a length of 4 cm., and bifurcating laterally.

The occipito-calcarine stem is 3.2 cm. in length and joins both the occipital and calcarine fissures at considerable depth.

FISSURES OF THE FRONTAL LOBE (LATERAL SURFACE).—*Precentral Fissural Complex.*—The three integral parts of this complex, namely the supercentral, precentral and transprecentral, anastomose to form a continuous fissure springing out of the sylvian and passing without interruption to the dorsal margin. The supercentral is of irregular zygal shape, and is confluent with the superfrontal and precentral. The precentral is tortuous and ramified, and anastomoses with the sylvian by means of the transprecentral, and also with the subfrontal, the diagonal, and a medi-frontal segment. The diagonal fissure is situated between, and runs parallel with the presylvian and the conjoined precentral-transprecentral. The diagonal does not dip into the sylvian cleft as deeply as is common.

The superfrontal fissure springs from the supercentral, is quite long, and is notable for its zig-zag course and transverse ramification.

The marked tendency to transverse anastomosis, particularly in the prefrontal region, renders the interpretation of certain fissures a matter of great difficulty. So far as the representation of the medifrontal is concerned, there exist a few segments in the medifrontal gyre which de-

serve mention. One of these has been described as anastomosing with the precentral. Another springs from the orbitofrontal and joins the superfrontal.

The subfrontal fissure is of unusual form. Arising from the neighborhood of the cortical islet at its junction with the diagonal and an anastomosing ramus of the precentral, the fissure sweeps rather far dorsad, to end in a hook-like manner about 2.5 cm. cephalad of its caudal origin. Dorsad the fissure anastomoses with the superfrontal.

The orbitofrontal is distinct, about 3 cm. in length and is joined by a medifrontal segment.

The radiate fissure is simple, 2.3 cm. in length and anastomoses with a tri-radiate (intra-subfrontal) fissure dorsad. One other fissural element curves around the cephalic hook of the subfrontal (Figure 1).

MESIAL SURFACE.—The supercallosal is 8.5 cm. in length, and freely confluent with the paracentral. Numerous rami springing from it traverse the mesial surface of the superfrontal gyre.

The paracentral fissure is very irregular, sends off several rami, and is confluent with a transparietal fissure as well. The cephalic limb is short. The caudal limb just reaches the dorsi-mesal margin. One intraparental ramus is particularly long.

The inflected fissure is distinct and independent. Its dorsal length is 15 mm.; mesial length, 13 mm. Its direction is practically perpendicular to the dorsi-mesal border on both surfaces. Its lateral end is embraced within the dorsal fork of the supercentral. Mesially, its relations are, as usual, caudad of the cephalic paracentral limb.

The rostral fissure is well-marked, 4.5 cm. in length, and bifurcated cephalad. There is no subrostral. The fronto-marginal is represented by but one segment.

ORBITAL SURFACE.—The orbital fissure resembles a reversed letter K (X) in shape, with numerous ramifications (see Figure 4).

The olfactory fissure is 5 cm. in length, and of simple form.

GYRES OF THE FRONTAL LOBE (LATERAL SURFACE).—The postcentral gyre is of bold contour throughout, and generally wider than the precentral. Its connection with the subfrontal gyre is interrupted, as before described, by the confluence of the precentral and transprecentral fissures.

The superfrontal gyre is quite large and richly fissured. There is some uncertainty as to its lateral limits in the prefrontal region, owing to the tendency to transverse communications amongst the various frontal fissures.

The medifrontal gyre is of greater width caudad than cephalad, and contains three small independent fissural segments. There is, however, not a very marked tendency toward a longitudinal subdivision of the gyre into two tiers.

The subfrontal gyre is of unusual width, owing to the high sweep of its limiting fissure—the subfrontal. Its configuration is rendered exceedingly complex by numerous more or less transversely directed fissures and ramifications (Figure 1).

MESIAL SURFACE.—The mesial surface of the superfrontal gyre is wide, richly fissured by transverse pieces. The callosal gyre is more simple, and is marked by several rami of the precuneal, supercallosal and paracentral.

The paracentral gyre is about 4 cm. in length, its dorsal margin is indented by the central, the inflected, and by an intraparacentral piece which joins the paracentral over a vadium.

The orbital surface is very much fissured, rather more so than on the right side; the mesorbital gyre is narrow, the postorbital quite distinct.

FISSURES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—(For the sake of convenience and clearness, the features of the parietal and occipital lobes are described together.)

The Postcentral Fissural Complex.—The postcentral fissural complex, comprised of the postcentral and subcentral segments in this instance, is a continuous fissure, and anastomoses with the sylvian fissure ventrally, and with the parietal fissure caudally. The main portion of the postcentral describes an angular course more or less parallel with the central, its dorsal end bifurcating to embrace the caudal limb of the paracentral. The whole course of the fissure so much resembles a duplication² of the central fissure, that only a careful study of its relations to the other fissures in its neighborhood can settle all doubts.

The transpostcentral is independent.

The parietal fissure springs from the postcentral over a deep vadium, passes caudad in an angular course, anastomosing with the intermedial, a transparietal and the paroccipital. The transparietal is a long fissure which crosses the dorsi-mesal margin to anastomose with what possibly represents Wilder's adoccipital.

The paroccipital presents the usual zygial shape, with the stem curved laterad. Its cephalic ramus joins the parietal over a deep vadium. The caudal ramus is unusually long (27 mm.).

The intermedial fissure is of zygial type, and joins both the episylvian and the parietal. By these anastomoses there exists a confluent series of fissures by means of which one may trace a course from the sylvian to the paroccipital in two ways: one by way of the subcentral-parietal anastomosis, the other by the episylvian-intermedial-parietal.

The complex of fissures in the angular and post-parietal gyres is difficult to describe. One prominent fissure (called by Schäfer (in Quain's Anatomy) the "ascending second temporal," but whose origin is probably traceable to the primitive exoccipital) is confluent cephalad with the super-temporal just where the latter changes its course in the dorsal direction. Its situation is not unlike that in the other Eskimo brains, particularly that of "Nooktah," and the right half of "Kishu." A tri-radiate fissure, doubtless an exoccipital segment (Figure 1, EOP) curves around the caudal ramus of the paroccipital, and is separated from the postcalcarine by a narrow gyre.

MESIAL SURFACE.—The precuneal fissure is a zygon, not confluent with any other fissure. Further dorsad there is a fissure joining the occipital, which traverses the dorsi-mesal margin, previously alluded to as a possible adoccipital.

²A similar condition misled Sperino in his description of the brain of the Anatomist Giacomini. See the author's paper, Phila. Med. Jour., August 24, 1901.

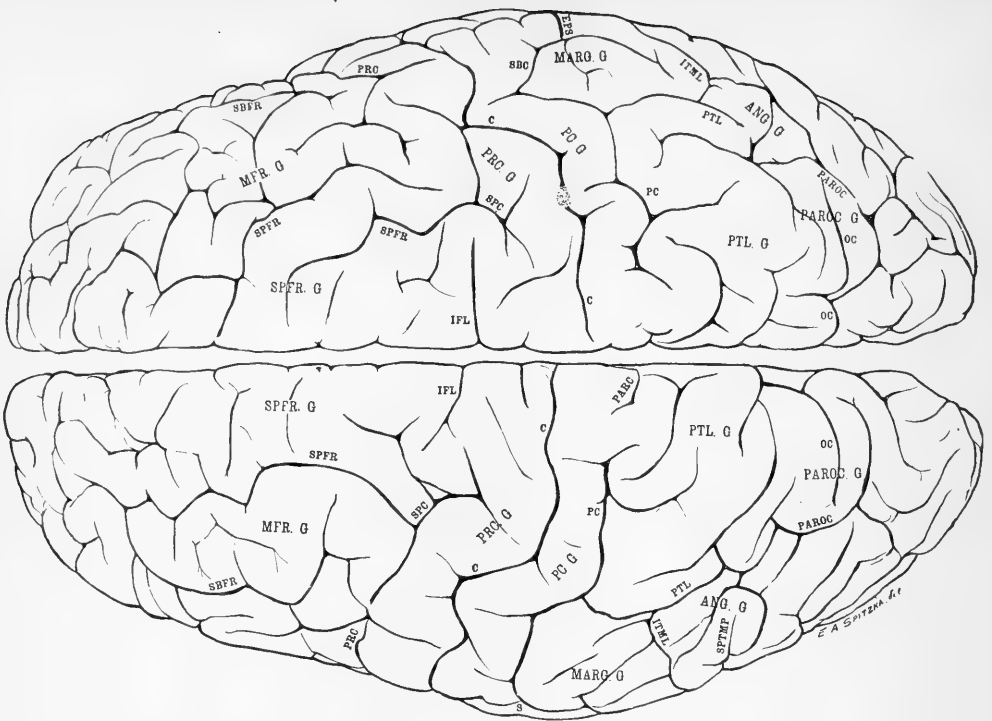


FIG. 3. Brain of "Atana;" dorsal view.

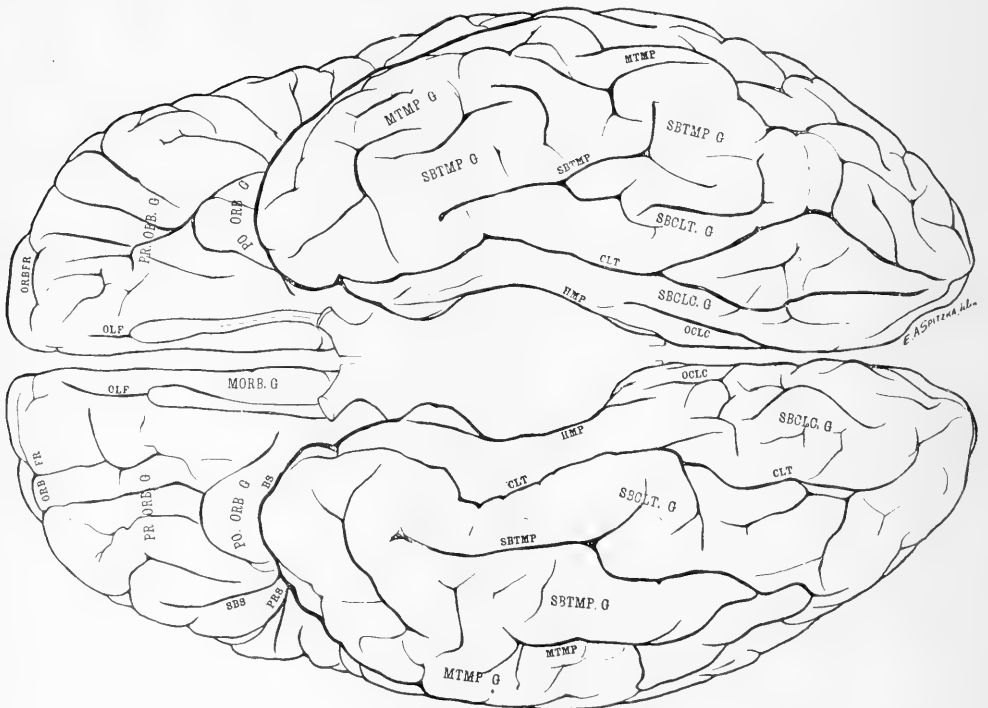


FIG. 4. Brain of "Atana;" ventral view.

The cuneus is marked by several fissures, the more distinct being a cuneal fissure joining the occipital over a slight vadium, and a much-ramified segment near the dorsal border—an irregular postcuneal.

GYRES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—The postcentral gyre is narrower than the precentral, especially in its dorsal portion, and is distinctly demarcated from the adjacent gyres.

The parietal gyre is of fair size and well-fissured, but shorter than common.

The paroccipital gyre is of good size, U-shaped, curving around the simple-ending occipital fissure.

The marginal gyre is of good size, and is traversed by the episylvian, by rami of the intermedial, and by an independent fissure.

The angular and post-parietal gyres are exceedingly complex. Numerous fissures and ramifications often anastomosing in an intricate manner as well as deep vessel-grooves render a description of this region difficult.

The precuneus and callosal gyre present nothing unusual.

The cuneus is of moderate size. Its ventral border, as before stated is rectilinear. Its surface is richly fissured.

FISSURES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The supertemporal describes a very tortuous course. Its length is 13 cm., extending from near the temporal tip well into the angular gyre. Just opposite the ventral end of the central fissure, the supertemporal communicates with the sylvian by means of a fairly deep vadium, and there are other numerous anastomoses.

There are at least four meditemporal segments of irregular ramified shapes. The subtemporal is represented by two pieces separated from each other by a very narrow isthmus.

The collateral fissure attains a length of 12.5 cm., and describes a marked zig-zag course. In the post-temporal region, the fissure divides into two equally long rami, which, diverging at first, again approach each other very closely. The lateral ramus, by comparison with the opposite hemiserebrum seems to represent the usual course of the main stem.

A deep groove, representing the post-rhinal (amygdaline) fissure, arises from the basisylvian cleft, and joins the collateral over a slight vadium.

The transtemporal fissures and gyres are well marked and present nothing unusual.

GYRES OF THE TEMPORAL LOBE.—The supertemporal gyre is very tortuous, due to the tortuous course of the supertemporal fissure, as well as to the numerous indentures of other fissures. In some places the gyre is quite narrow, in others, fairly broad. The meditemporal gyre is of quite as tortuous a contour. The subtemporal is the most massive of all. The subcollateral and subcalcarine gyres are of the usual form.

INSULA.—The insula is rather long and narrow. A portion of the pre-insula, as stated before, is not fully covered by the opercula, so that an area of about 1 sq. cm. remains visible on the lateral aspect. The pole of the insula is prominent. The transinsular fissure is long and distinct. The insular gyres are simple; the post-insular gyre is quite narrow; the preinsular gyres are four in number.

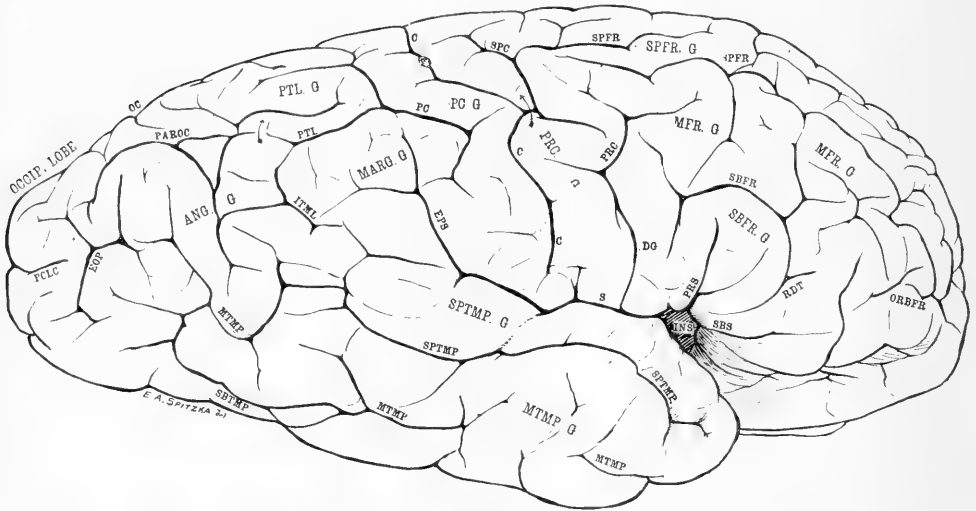


FIG. 5. Brain of "Atana;" lateral view of the right hemisphere.

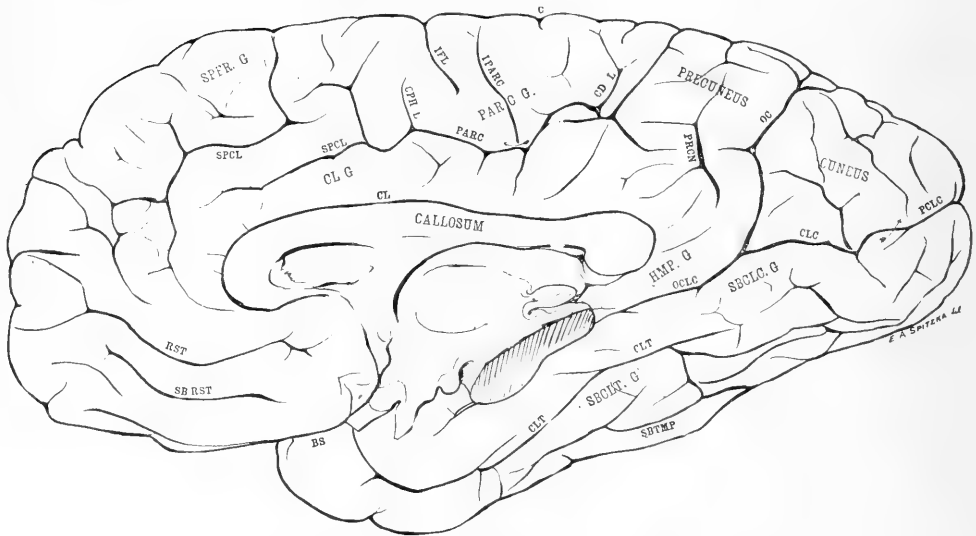


FIG. 6. Brain of "Atana;" mesial view of the right hemisphere.

RIGHT HEMICEREBRUM.

THE INTERLOBAR FISSURES.—*The Sylvian Fissure and its Rami.*—The sylvian fissure is 4.3 cm. in length and is deeper cephalad than on the left side: Presylvian depth, 14 mm.; medisylian depth, 19 mm.; postsylvian depth, 23 mm.

Its course is angular but generally approaches the horizontal. The basisylvian, measuring from the temporal tip, is 20 mm. in depth. The presylvian is bifurcated, the longer limb attaining a length of 15 mm. The subsylvian is simple and 20 mm. long. The episylvian is unusually long (32 mm.) and sends a caudal ramus into the marginal gyre. The hyposylvian is merely indicated by a slight notch.

The Central Fissure.—The central fissure is 10 cm. in length. As on the left half, the dorsal third of the fissure is quite straight and perpendicular to the intercerebral cleft. At 3 cm. from the dorsi-mesal margin, the fissure is interrupted by a hard, probably tubercular growth, adherent to the adjacent walls of the central gyres, indicated in Figures 5 and 3 by a dotted area. Cephalad the fissure anastomoses with the long limb of the supercentral over a vadium. The dorsal end is barely visible on the meson. The ventral end is separated from the sylvian by a slightly depressed isthmus.

Occipital Fissure.—The occipital fissure attains a mesial length of 3.5 cm., a dorsal length of 2.5 cm. The fissure is of fairly uniform depth, and while exhibiting several interdigitating subgyres, shows no definite cuneo-quadrate subisthmuses. On the meson the fissure sends a ramus into the precuneus. Dorsally, just at the dorsi-mesal border, there is an appearance of trifurcation, owing to the presence of two adjacent fissural elements which run into the occipital cleft cephalad and caudad (Figure 3). Closer investigation shows the deep occipital to continue laterad between these two pieces, and end in a simple manner in the paroccipital gyre.

The Calcarine Fissure.—The main stem of the calcarine is 2.1 cm. in length, and bifurcates caudad, the dorsal limb joining the postcalcarine over a slight vadium ("transcalcarine isthmus"). The postcalcarine is 4 cm. long and extends well upon the lateral surface. The straight course of the combined calcarine and postcalcarine fissures, noted in other Eskimo hemispheres, is quite marked in this case.

The occipito-calcarine fissural stem is 3.5 cm. in length, and is deeply confluent with both the occipital and calcarine. Its cephalic end approaches the hippocampal fissure very closely.

FISSURES OF THE FRONTAL LOBE (LATERAL SURFACE).—*The Precentral Fissural Complex.*—The supercentral is of zygal shape, and is confluent with the superfrontal. Its ventral limb is long and anastomoses with the central, but is separated from the precentral by an isthmus (Figure 5). The precentral is also of zygal type; its ventro-cephalic ramus is confluent with the sylvian by means of the well-marked diagonal. The transprecentral is an independent fissure.

The superfrontal and medifrontal fissures are difficult to trace in definite courses, particularly in the prefrontal region. The marked tendency

of these fissures to anastomose transversely divides the corresponding gyres into several transverse rather than the usual longitudinal gyral portions.

The subfrontal fissure is fundamentally of zygial shape, with its stem curving round the presylvian, and its cephalic limbs anastomosing ventrad with the radiate, dorsad with a medifrontal.

The orbito-frontal is represented by two segments; the mesial one anastomosing with a medifrontal.

MESIAL SURFACE.—The supercallosal is divided into two segments by an oblique isthmus. The caudal segment is confluent with the paracentral at considerable depth, and extends as far cephalad as the splenium. The cephalic segment is the larger piece, and is very much ramified. The two segments for a part of their course run parallel with each other, giving an appearance of duplication.

The paracentral is very flexuous, 3.8 cm. in length, terminating at each end by the usual cephalic and caudal limbs, and anastomosing caudad with an intraprecuneal fissure.

The inflected fissure is deep, well-defined, and both its dorsal and mesial lengths are 15 mm. Its lateral end lies cephalad of the supercentral; its ventral end lies caudad of the cephalic paracentral limb.

The frontomarginal is barely represented. The rostral and subrostral fissures are both well marked.

ORBITAL SURFACE.—The main orbital fissure (Figure 4) is of zygial shape, and distinctly demarcates a post-orbital gyre, with several sagittal pre-orbital gyres. An independent sagittal orbital fissure lies mesad in the preorbital region.

The olfactory fissure is simple, and 5 cm. in length.

GYRES OF THE FRONTAL LOBE (LATERAL SURFACE).—The precentral gyre is fairly flexuous, and is quite narrow at the site of its interruption by the anastomosis between the central and supercentral fissures.

The remaining frontal gyres, especially the superfrontal and medifrontal are of an exceedingly complex configuration owing to the zig-zag courses and transverse anastomoses of the much-ramified frontal fissures.

The subfrontal gyre in comparison with its fellow of the left side is small.

MESIAL SURFACE.—The mesial surface of the superfrontal gyre is broad, and marked by numerous rami of the supercallosal, as well as smaller fissural segments.

The paracentral gyre is about 4 cm. in length. Its dorsal border is indented by the well-marked inflected, and only slightly by the central. There is a vertical intraprecuneal which joins the paracentral over a slight vadium.

ORBITAL SURFACE.—Compared with the left half, the gyres are simpler, and in the preorbital region present fairly regular, sagittally directed gyral tiers.

FISSURES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—*The Postcentral Fissural Complex.*—The confluent post- and subcentral together measure 7 cm. in length, running parallel with the central. Sev-

eral rami spring from the combined fissure, and it anastomoses with a segment of the parietal. There is no transpostcentral.

The parietal is interrupted by a narrow isthmus not far from the paroccipital. In the parietal gyre are several fissures, the most cephalic one (see Figure 3) corresponding with Brissaud's transparietal.

The paroccipital is of very unusual form, owing to the overlapping of the cephalic portion of the paroccipital gyre by a parietal gyral operculum.³ The overlapping is considerable in extent, hiding from view both the cephalic ramus and stipe of the paroccipital. An independent preparoccipital fissure dips under this operculum, as does a segment which runs parallel with the parietal. The entire arrangement is very unusual indeed, and seems not without significance in its bearing upon the development of the paroccipital from the primate exoccipital. The caudal ramus is short; the caudal stipe long and tortuous and anastomosing with the occipital fissure.

The intermedial fissure joins the supertemporal parietal and an unnamed fissure in the angular gyre, confluent with the paroccipital.

The exoccipital complex is intricate. There is a zygal, much-ramified exoccipital segment whose caudal limbs embrace the lateral extremity of the postcalcarine; a cephalic limb anastomoses with a meditemporal segment.

MESIAL SURFACE.—The precuneal fissure is of zygal shape, but the course of the stem is in an unusual direction, namely, dorso-ventrad instead of caudo-cephalad.

There is a tri-radiate intraprecuneal fissure which anastomoses with the paracentral.

The cuneus is richly fissured.

GYRES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—The postcentral gyre is of more uniform width than the precentral, and is rendered quite flexuous by the indenting rami of the adjacent fissures.

The parietal gyre, aside from the peculiar opercular formation by which it partially overlaps the paroccipital gyre, and while shorter than its fellow on the left side, is intricately convoluted.

The paroccipital gyre is of a peculiar form. In the overlapped portion, as described before, there is a preparoccipital fissure, while two other fissures arise from the occipital cleft.

The marginal gyre, curving round the bifurcated episylvian, is very broad. The angular and postparietal gyres present a very complex configuration, being broken up into several areas by numerous confluences of fissures. An imaginary line passing from the occipital, via the exoccipital stem to the distinct postcalcarine, seems to demarcate quite clearly the conventional lateral bounds of the occipital lobe.

MESIAL SURFACE.—The precuneus is rather smaller than usual, and peculiarly fissured. The cuneus is of fair size, and well supplied with fissures. The callosal gyre presents nothing unusual.

³ This peculiar configuration will be described and discussed in more detailed form in a special contribution upon the paroccipital fissure generally.

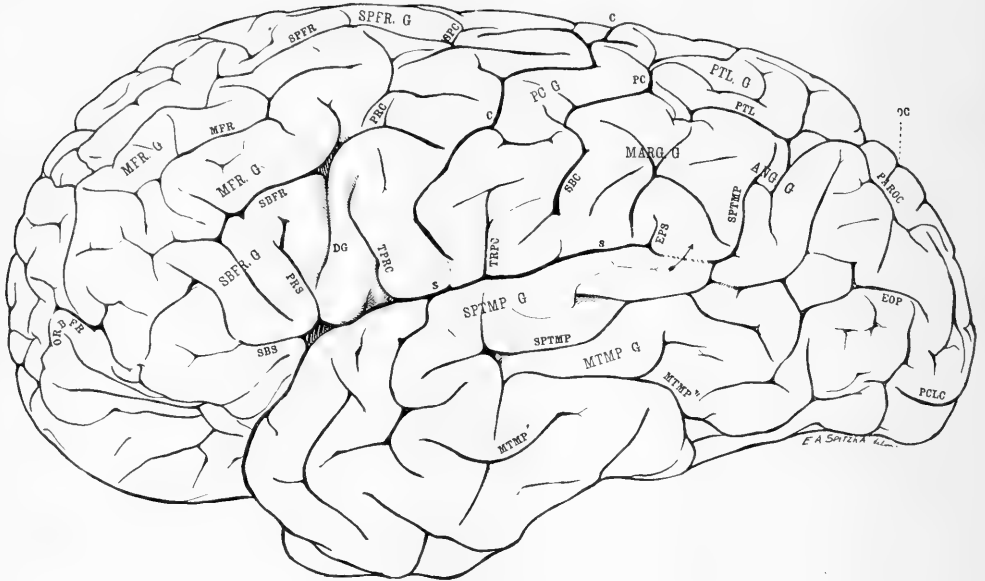


FIG. 7. Brain of "Nooktah;" lateral view of the left hemisphere.

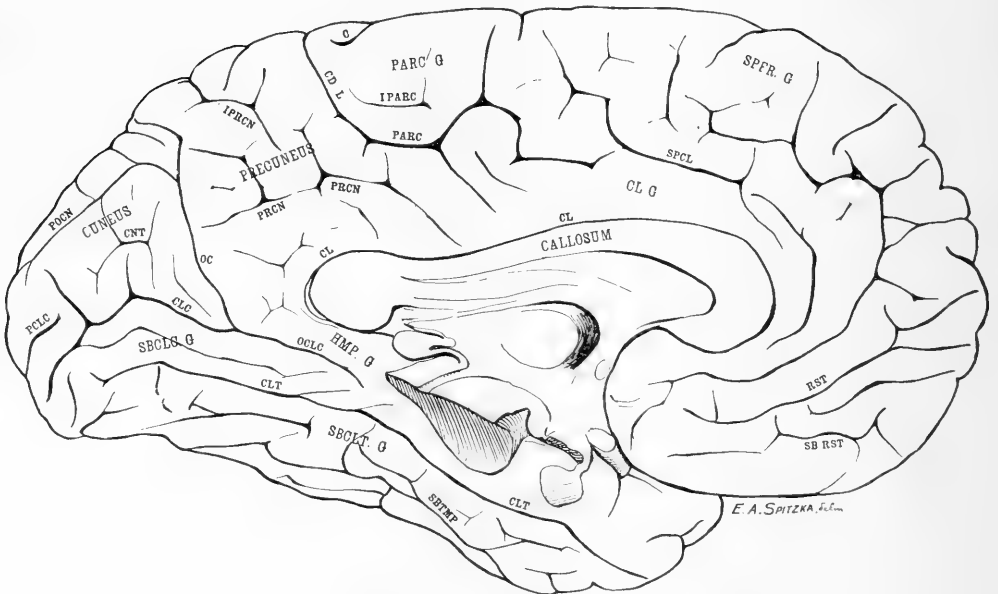


FIG. 8. Brain of "Nooktah;" mesial view of the left hemisphere.

FISSURES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The super-temporal fissure sweeps caudad in bold curves, until, near the region of the marginal gyre, it bifurcates, its dorsal limb joining the intermedial, the ventral limb passing on to join a meditemporal segment. Thus the course of fissural confluence may be followed from the tip of the temporal lobe as far as the exoccipital, and dorsad, by means of the intermedial and parietal to the postcentral.

There are at least three distinct meditemporal segments, the caudal one anastomosing with the exoccipital, supertemporal and the subtemporal.

The subtemporal is of good length (10 cm.) anastomosing caudad with the meditemporal, where the fissure sweeps well upon the lateral aspect of the lobe.

The collateral attains a length of 13.3 cm. and presents many flexuosities. In its caudal part it is particularly ramified. Cephalad it anastomoses with the postrhinal (amygdaline) fissure.

GYRES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The super-temporal gyre is broad in its caudal portion, narrow cephalad. The meditemporal and subtemporal are of good width, and each is fairly well demarcated. The subcollateral and subcalcarine gyres are very wide in their caudal portions, and grow narrower toward the temporal tip. The subcalcarine is notable for its rich fissuration.

The transtemporal fissures and gyres present nothing unusual.

INSULA.—The insula seems a trifle better developed—so far as fissuration is concerned—than that on the left side, but it is on the whole less massive. There is the usual long postinsular gyre, and five preinsular gyres.

2. BRAIN OF "NOOKTAH."

(See Figures 7 to 12.)

The second specimen is that of an adult male, "Nooktah," husband of "Atana." His age is likewise in the neighborhood of fifty-five years. "Nooktah" died on May 14, 1898. The brain was removed on May 16, and weighed, while fresh, 1470 grammes. It was placed in a mixture of formal and alcohol. Its weight on May 25, 1901, was as follows:

Left hemiserebrum (plus a piece of callosum belonging to the right half), 474 grammes; right hemiserebrum, 470 grammes; cerebellum, pons and oblongata, 142 grammes; total 1086 grammes.

The loss in weight during a period of over three years amounts to 384 grammes, or 26 per cent of the original weight.

THE CEREBRUM.

The cerebrum is well preserved and quite firm, so that it is difficult to study in detail the depths of the fissures. In general, the fissuration is fully equal in complexity to that exhibited by "Kishu's" cere-

brum. Transversely directed ramifications and anastomoses are very numerous. In the frontal lobes there is a distinct subdivision into five gyral tiers on the left, and four on the right side.

Viewed dorsally and ventrally, the cerebrum appears wider, and a trifle more intricate, in configuration than that of "Atana," resembling that of "Kishu" in many respects. The insulæ are covered in by the opercula. The callosum, 8 cm. in length, on cross-section is seen to be quite thick in the splenium and genu, but unusually thin in the body of this structure.

The combined calcarine-postcalcarine fissures do not take quite as straight a course as noted in "Atana's" cerebrum.

LEFT HEMICEREBRUM.

THE INTERLOBAR FISSURES.—*The Sylvian Fissure and its Rami.*—The sylvian fissure is 5.7 cm. in length and quite straight. Its depths are: Presylvian depth, 14 mm.; medisylian depth, 17 mm.; postsylvian depth, 24 mm.

The basisylvian, measuring from the temporal pole, is 23 mm. in depth. The presylvian is simple, 20 mm. long, and quite deep. The subsylvian is also simple and 20 mm. in length. The episylvian is exceedingly short (5 mm.) while the hyposylvian is absent.

The Central Fissure.—The central fissure is notably tortuous, and when measured by a wet string laid in its course attains the length of 11.5 cm. There are seven distinct curves, two more than usual. One caudal ramus closely approaches the subcentral fissure, being separated by a slight vadium. Dorsad the fissure reaches the dorsi-mesal margin; ventrad, there is a slight, superficial junction with the sylvian cleft by a vessel-groove.

The Occipital Fissure.—The occipital fissure is deep. Its mesial length is 3.5 cm., its dorsal length, 2 cm. On the mesial surface, near the dorsi-mesal margin, there is an appearance of bifurcation. In reality there springs from out of the true occipital a well-marked adoccipital which extends upon the dorsum for 2 cm., parallel with both the occipital (dorsal part) and the cephalic stipe of the paroccipital. This adoccipital is exceedingly well marked. Its walls slope cephalo-ventrad, so that one may speak of a parietal operculum which partially overlaps a cuneolus.

The Calcarine Fissure.—The calcarine fissure is 3 cm. in length, sends off one dorsal ramus and bifurcates caudally. These limbs embrace a trans-calcarine isthmus, which separates the calcarine from a well-marked, simple postcalcarine ("sulcus extremus" of Schwalbe). The latter fissure, lying almost wholly on the convex surface of the hemicerebrum, is 3 cm. in length. The general direction of the two fissures is less straight than noted in the other hemicerebra.

The occipito-calcarine fissural stem is 2 cm. in length, and completely confluent with both the occipital and the calcarine fissures.

FISSURES OF THE FRONTAL LOBE (LATERAL SURFACE).—*The Precentral Fissural Complex*.—This complex of fissures is of an extremely unusual arrangement, all its parts being independent of each other. First, the supercentral, essentially of zygal type, is situated unusually distant from the central, and anastomoses with the superfrontal only. Dorsad of the supercentral, is another fissure, simple and independent, and running about parallel with the central. The precentral seems to be made up of two segments, both of zygal type. The dorsal one is a true simple, non-anastomosing zygon. The ventral piece anastomoses with both the diagonal and the subfrontal. The transprecentral, 2.3 cm. in length, is independent, and does not dip deeply into the sylvian cleft.

The diagonal is deep and has a common junction with the precentral and the subfrontal.

The superfrontal may be traced uninterruptedly very far cephalad, nearly to the orbito-frontal, from which it is separated by a very narrow depressed isthmus. In the prefrontal region, the fissure passes somewhat further laterad than usual, leaving the superfrontal gyre quite broad in this region. A series of fissural segments lying in the superfrontal gyre (paramesial fissures?) give, with the division of the medifrontal gyre, five fairly distinct frontal gyral tiers.

The medifrontal fissure is very distinct, attains a length of 4.5 cm., is richly ramified, and serves to divide the medifrontal gyre into two nearly equal tiers. The fissure does not anastomose with any other.

The subfrontal fissure, 3.5 cm. in length, bifurcates cephalad and sends a long ramus into the subfrontal gyre corresponding in its position with the radiate fissure.

The orbitofrontal is 5 cm. in length, very well marked, tortuous and ramified. It joins an orbital fissure superficially.

MESIAL SURFACE.—The supercallosal is in three segments separated from each other by very narrow isthmuses. The caudal segment is confluent with the paracentral. Cephalad, the supercallosal and frontomarginal fissures are arranged in so peculiar a manner that one is in doubt as to how to designate each segment. The appearance is one of duplication similar to that observed hitherto by Manouvrier and others.

The paracentral is simple, sweeping caudad gradually to appear on the dorsal surface for 12 mm. Cephalad it joins a segment of the supercallosal. There is an independent longitudinal intraparacentral.

The inflected is absent.

Both the rostral and subrostral fissures are well marked; the former is 5.5 cm. in length, the latter 3.5 cm.

ORBITAL SURFACE.—On the orbital surface, the fissures are complex. There is a lateral triradiate fissure, whose caudal limbs correspond with Weisbach's "transverse orbital," and mesad of this lie a zygal and one sagittal fissure. The last-mentioned anastomoses with the orbitofrontal over a vadium.

The olfactory fissure is 3.8 cm. in length.

GYRES OF THE FRONTAL LOBE (LATERAL SURFACE).—The precentral gyre, in general, is much wider than the postcentral gyre, but is unusually tortuous, and indented by numerous fissural rami.

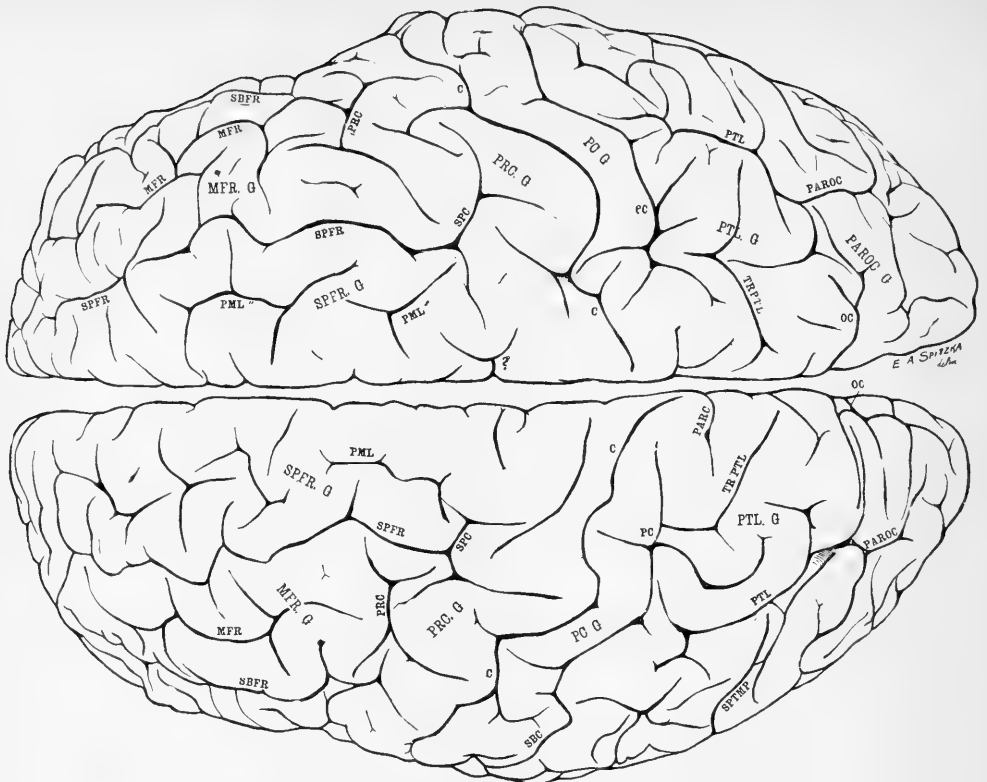


FIG. 9. Brain of "Nooktah," dorsal view.

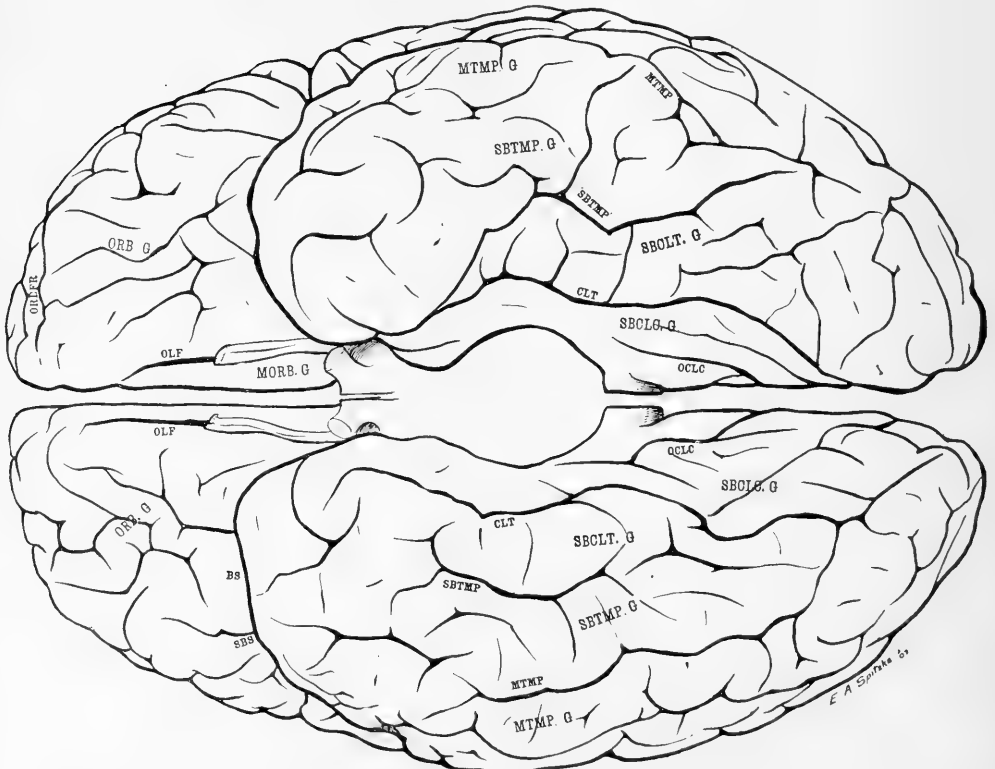


FIG. 10. Brain of "Nooktah," ventral view.

The superfrontal gyre is especially broad in the prefrontal region, and more or less regularly divided into two longitudinal tiers by two parasagittal fissural segments. Between these two are a triradiate and also a zygial segment; still further cephalad there are numerous transverse triradiate and zygial pieces which make this portion of the gyre of an exceedingly complex configuration.

The medifrontal gyre is massive, tortuous and distinctly divided into two tiers by a long medifrontal fissure.

The subfrontal gyre, while small, is well convoluted, and in general exhibits most strikingly the tendency of fissures and ramifications to assume a transverse direction.

MESIAL SURFACE.—The mesial surface of the superfrontal gyre is broad and traversed by a large number of radiating fissures and rami. The dorsomesial margin is particularly marked by numerous fissural segments.

The paracentral gyre is of moderate size, of simple form, marked merely by a short longitudinal intraparasagittal, and slightly indented in its dorsal margin by the central.

ORBITAL SURFACE.—On the orbital surface may be distinguished a postorbital portion, and several sagittal preorbital gyres. The mesorbital gyre is very narrow.

FISSURES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—*The Postcentral Fissural Complex.*—In this hemisphere, the postcentral and subcentral are combined to form a continuous fissure, attaining a length of 8.5 cm. Dorsally, the fissure bifurcates, embracing the gyre indented by the caudal limb of the paracentral. The caudal limb of the postcentral is joined by a transparietal piece. In all, five additional rami spring from the combined fissure. A vadium separates it from the parietal; another from the central.

The parietal, cephalad, is ramified. A narrow isthmus separates it from the supertemporal. Caudad it anastomoses with the cephalic limb of the paroccipital. A deep furcal ramus passes into the parietal gyre.

A transparietal has been described as confluent with one of the postcentral dorsal limbs; another fissure, also confluent with the postcentral, runs somewhat parallel with the parietal.

A quadri-radiate fissure lies in the marginal gyre, just dorsad of the short episylvian. A true intermedial does not seem to be present.

The paroccipital is of the usual zygial shape, with its cephalic stipe passing into the cuneolus, i. e., between the occipital and adoccipital fissures. Laterad in the angular gyre, just caudad of the supertemporal and the cephalic paroccipital ramus, there is a fissure, 3.5 cm. in length, whose walls are markedly inclined caudo-ventrad. If this fissure represents, as it probably does, a segment of the exoccipital, we have here the formation of a partial occipital operculum. There are other zygial pieces on the lateral surface apparently in the course of the primate exoccipital, as well as numerous fissures in the angular gyre and occipital region.

MESIAL SURFACE.—The precuneal fissure is of irregular zygial shape. The ventro-cephalic limb is unusually long. It does not anastomose with other fissures.

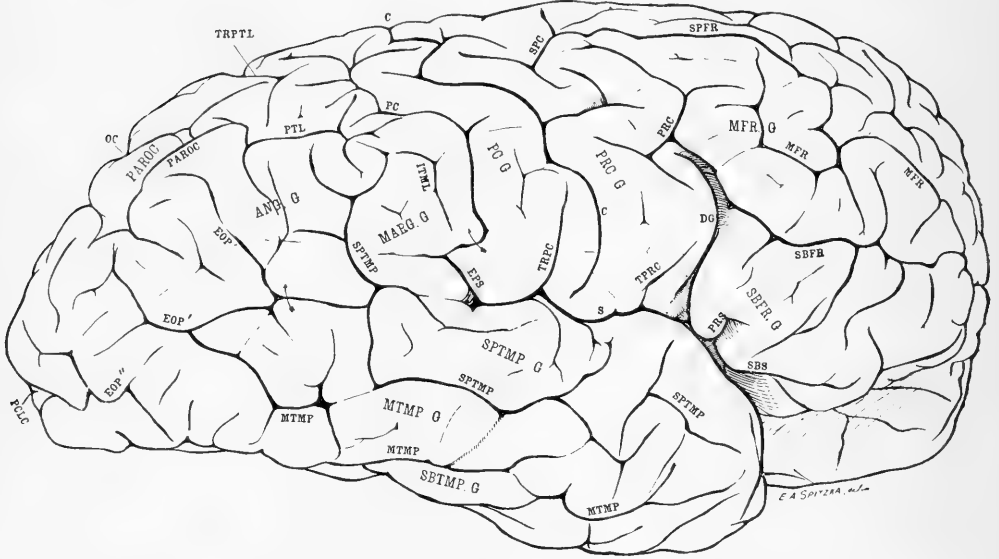


FIG. 11. Brain of "Nooktah;" lateral view of the right hemicerebrum.

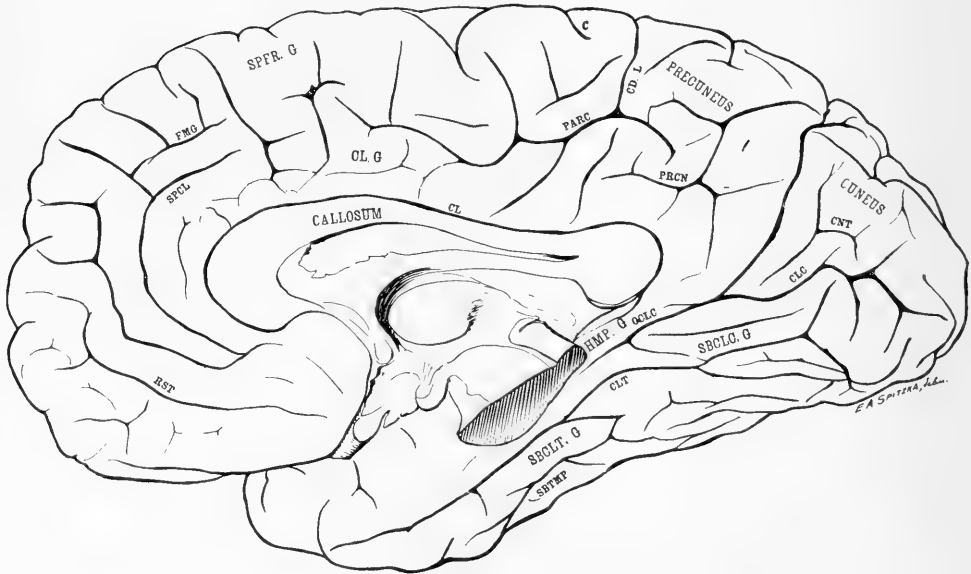


FIG. 12. Brain of "Nooktah;" mesial view of the right hemicerebrum.

There is an irregular zygial intraprecuneal just dorsad of the precuneal, which crosses the dorsi-mesal border.

The cuneal fissure is distinctly zygial. There is an irregular postcuneal fissure which sends a ramus into the paroccipital (possibly a post-paroccipital element).

GYRES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—The postcentral gyre is narrow in its dorsal two-thirds, quite broad in its ventral portion, and quite tortuous. The parietal gyre is shorter than on the right side, but richly fissured. The paroccipital gyre is broad in its caudal arm, but quite narrow in its cephalic portion. A ramus of the postcuneal, possibly a postparoccipital piece, lies caudad of the occipital.

The marginal gyre is unusually broad, and curiously marked by the quadri-radiate fissure described before. The angular gyre is very complex.

MESIAL SURFACE.—The precuneus is rather small, probably owing to the existence of an adoccipital separating off a cuneolus. The cuneus is of good size and richly fissured.

FISSURES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The super-temporal fissure presents a curious arrangement. Cephalad there are two independent zygial segments of which the caudal one anastomoses with the sylvian. The larger part of the fissure attains a length of 9 cm., almost reaching the parietal. In its course it anastomoses with a meditemporal. Further caudad, it anastomoses with the (exoccipital ?) complex in the parieto-occipital transition.

The meditemporal is represented by three segments. The subtemporal is 6.5 cm. in length, and richly ramified. The collateral is a distinct, boldly-curved fissure of a length of 11 cm.

There is a short but distinct postrhinal (amygdaline) fissure.

GYRES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The super-temporal gyre, owing to the odd course and formation of the supertemporal fissure, while massive is unusually tortuous. The meditemporal and subtemporal gyres on the whole, are broad, and richly fissured. The sub-collateral gyre is well-defined, and considerably fissured, especially in transverse directions.

The subcalcarine is of the usual form, and is marked by one long fissural segment lying between the collateral and calcarine fissures, distinctly dividing the gyre into two longitudinal tiers.

THE INSULA.—The insula is of simple configuration, resembling in its general appearances those of the other Eskimo hemispheres, and exhibiting one postinsular and four preinsular gyres.

RIGHT HEMICEREBRUM.

THE INTERLOBAR FISSURES.—*The Sylvian Fissure and its Rami.*—The sylvian fissure is 4.3 cm. in length and of the following depths: Pre-sylvian depth, 13 mm.; medisylian depth, 18 mm.; postsylvian depth, 25 mm.

Its course is irregular. The presylvian is a very short fissure. The subsylvian is simple and 2 cm. in length. The episylvian is 2 cm. in length

and anastomoses with the sub-(post)-central over a slight vadum. The hyposylvian is represented by a mere notch.

The Central Fissure.—The central fissure is 11.5 cm. in length, has the usual five curves and is less tortuous than its fellow on the left side. At about 2 cm. from the dorsi-mesal margin, it anastomoses with a small fissure in the precentral gyre over a vadum 8 mm. deep.

The Occipital Fissure.—The occipital fissure is well-marked, deep, with a mesial length of 4.5 cm., and a dorsal length of 2.5 cm.

The Calcarine Fissure.—The calcarine fissure is exceedingly tortuous and ramified. Its length is 5 cm. Caudally it bifurcates, and in its course sends off three rami. The postcalcarine is triradiate, its two mesial limbs embracing the dorsal limb of the furcal calcarine. The postcalcarine lies almost wholly on the convex surface of the hemiserebrum and anastomoses with an exoccipital piece.

The occipito-calcarine stem is 2.8 cm. in length and sends one ramus into the subcalcarine gyre.

FISSURES OF THE FRONTAL LOBE.—*The Precentral Fissural Complex.*—The supercentral is of a well-formed zygial type anastomosing freely with the superfrontal. The precentral is separated from the supercentral, is also of zygial shape, and anastomoses with the subfrontal. A depressed isthmus separates the diagonal from both the precentral and the subfrontal. The transprecentral springs from the sylvian cleft, but is otherwise independent.

Communicating with the diagonal over a deep vadum, and dipping deeply into the sylvian cleft, there lies an unnamed fissure.

The superfrontal is divided into two segments in the mid-frontal region by a small isthmus. Both pieces are tortuous and ramified. The caudal, larger piece communicates with the distinct medifrontal by a transverse anastomosis.

There are two distinct paramesial segments in the superfrontal gyre.

The medifrontal fissure is in this case exceedingly well marked. It may be described as consisting of two, freely-confluent segments, attaining a total length of 9 cm. It has a sigmoid course, and is richly ramified. It communicates near its middle with the superfrontal and far cephalad with the subfrontal by means of what may be a segmental representative of the orbitofrontal fissure.

The radiate fissure is represented by a short piece.

Several segments, not very typical, are to be observed in the course of what would be the orbitofrontal.

MESIAL SURFACE.—The supercallosal fissure is distinct for 7 cm. in the cephalic region, but, as one approaches the paracentral the appearances become atypical. The continuity of the fissure is broken by two transverse isthmuses. As for the paracentral, whether this is the short caudal piece so marked in Figure 12, with its cephalic limb caudad of the tri-radiate piece traversing the dorsi-mesal margin, or whether it is the entire piece, 4 cm. in length with an intraparacentral ramus is a matter of doubt. The author inclines to the latter explanation, judging from the general relations of neighboring fissures. It still remains an important

question whether the tri-radiate piece at the dorsi-mesal margin represents the inflected. It were the first instance in the author's experience (based on studies especially directed to the inflected fissure in over a hundred brains) that the inflected were other than a simple fissure.

The frontomarginal is represented by two segments, both running parallel to the supercallosal, the longer segment joining the latter just ventrad of the splenium.

The rostral fissure is 5.5 cm. in length, while the subrostral is only slightly indicated.

Owing to the narrowness and comparative insignificance of the mesorbital gyre in this hemisphere, the olfactory fissure becomes visible on the mesial aspect for 2 cm.

THE ORBITAL SURFACE.—Two principal, sagittally-directed orbital fissures, and several smaller segments mark the orbital surface. The olfactory fissure is 5 cm. in length.

GYRES OF THE FRONTAL LOBE (LATERAL SURFACE).—The precentral gyre is of unusual breadth and is very tortuous. Its surface area is fully twice as great as that of the precentral.

The superfrontal gyre is of good width, except near the frontal pole, where the gyre tapers perceptibly and becomes very narrow. One of the paramesial pieces serves to divide a portion of the gyre into two tiers. Further cephalad the gyre is marked by many transverse segments and incisures.

The medifrontal gyre is particularly massive and of a superior complexity. It is notable for its distinct and long medifrontal fissure.

The subfrontal gyre is smaller than its fellow on the left side and in its configuration much less developed.

MESIAL SURFACE.—The mesial surface of the superfrontal gyre, while well supplied with fissures is a trifle less so than on the left side.

The limits of the paracentral, depending upon the identification of the paracentral rami must remain a matter of doubt for the present at least.

ORBITAL SURFACE.—The mesorbital gyre is unusually narrow in this case. The remaining gyres may be resolved into three principal portions, sagittally directed, without any demarcated postorbital gyre.

FISSURES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—*The Postcentral Fissural Complex.*—The combined postcentral-subcentral attains a length of 7.5 cm., is bifurcated dorsally, to embrace the caudal paracentral limb, and anastomosing ventrally with the episylvian over a slight vadium. From it spring two cephalic and three caudal rami. The transpostcentral springing from the sylvian, is otherwise an independent fissure.

The parietal is separated from the postcentral, and is confluent with the paroccipital. Five rami spring from it. There is a well-marked transparietal. The intermedial fissure is small. The paroccipital is a very irregular zygial fissure, confluent with the parietal by its cephalic ramus. The cephalic stipe is bifurcal. The caudal stipe anastomoses with the postcuneal.

Of the exoccipital complex there may be made out one extensive seg-

ment (EOP', Fig. 11) irregular and ramified, curving around the caudal ramus of the paroccipital; another segment (EOP'', Fig. 11) ventrad of this, and whose caudal limbs embrace the lateral end of the postcalcarine. Numerous other fissures mark the angular gyre and occipito-parietal transition.

MESIAL SURFACE.—The precuneal fissure, as in the same half of "Atana's" cerebrum, presents a vertical zygon. One of its dorsal limbs anastomoses slightly with the paracentral. The cuneal fissure is zygal and resembles very much that of the other half of this cerebrum. The same can be said of the posteuneal.

GYRES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—The postcentral gyre is quite narrow, especially in its dorsal portion. The parietal gyre is short, but broad and richly fissured. The paroccipital gyre is of irregular contour, its caudal arm being many times larger than its cephalic portion.

The marginal and angular gyres present a notable complexity as well as considerable extent of surface. The latter is of especial broadness.

MESIAL SURFACE.—The precuneus is rather better developed than its fellow on the left half. The cuneus of this hemiserebrum bears a striking resemblance to that of the other side. The disposition of its intrinsic fissures is practically the very same as in the left cuneus.

The callosal gyre throughout is more fissured than on the left.

FISSURES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The supertemporal fissure, like that of the left side, runs a very irregular and atypical course. There is a cephalic smaller, tri-radiate segment, and a larger, tortuous caudal piece whose length is 8.5 cm. To understand its appearance, the reader must refer to Figure 11. The dorsal end of the fissure is furcal; from here it sweeps ventro-cephalad, sending one ramus into the supertemporal gyre, another across the angular gyre to anastomose over a vadium with the exoccipital. The fissure proceeds well ventrad, then turns sharply to pass cephalad, and divides into two rami, one closely approaching the sylvian, the other passing just a little ventrad of the cephalic supertemporal segment.

The mediotemporal is represented by three segments, the middle one of which is quite long and anastomoses with the collateral fissure far caudad.

The subtemporal is represented by two irregular and much-ramified pieces. The collateral is 11.5 cm. in length and is well-curved. The postrhinal (amygdaline) fissure is slightly indicated.

GYRES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The supertemporal gyre is particularly massive and very broad, especially in its middle portion, owing to the wide ventral sweep in the course of the supertemporal fissure. The mediotemporal and subtemporal gyres are well developed. The subcollateral is comparatively simple. The subcalcarine is narrow in its middle portion but unusually broad and richly fissured caudally.

THE INSULA.—The insula resembles that of the left side. There is a broad postinsular gyre, and four smaller preinsular gyres. In general it is less developed and smaller than its fellow.

3. BRAIN OF "AVIA."

(See Figures 13 to 18.)

The third specimen is that of a young girl, about 12 years old. Her name is variously spelled "Avia," "Ar-wee-ah" and "Aviag"; it is pronounced as if spelled "A-vee-ah." She died in New York City on May 19, 1898, at 7 p. m., and was received at the Anatomical Laboratory, Columbia University on May 21, at 12 m. When fresh, the brain weighed 1227 grammes. It was placed in a mixture of formal and alcohol. (This mixture probably consisted of equal parts of 50 per cent alcohol and 20 per cent formaldehyde solution.) Its weight on May 25, 1901, was as follows:

Left hemisphere, 369 grammes; right hemisphere, 366 grammes; cerebellum, pons and oblongata, 135 grammes; total, 870 grammes.

The loss in weight during a period of three years amounts to 357 grammes, or 29 per cent of the original weight.

THE CEREBRUM.

This cerebrum is as well preserved and firm as that of "Nooktah." As is consistent with the youth of the subject, the external configurations are far simpler than exhibited in any of the brains here described. Viewed dorsally or ventrally, the outline is not so markedly hexagonal, the frontal lobes are less broad and more rounded off, and the cerebrum tapers caudad more sharply than do the other Eskimo brains. An asymmetry of the hemispherical masses is noticeable; the right parieto-temporal region is fuller than the left, and the left subfrontal more massive than that of the right side. Further, the convexity of the left occipital lobe is fuller than that of the right. Viewed laterally, the dorsal curve of the cerebrum is more pronounced than that of either "Atana" or "Nooktah," and the hemispherical mass does not taper so markedly toward the occipital pole. Both insulæ are exposed, the left more than the right. The callosum, whose length is 47.5 per cent of the total cerebral length, presents the same outline on cross-section as noted in the other brains.

The slight curvature and higher dorsal situation of the calcarine-postcalcarine, noted especially in "Atana," is here likewise indicated.

While differing in considerable degree from the other Eskimo brains in that its complexity of fissuration is much less, due doubtless to the subject's youth, this brain must appear to the trained eye as presenting a very different configuration from what one is accustomed to see in the brains of whites. This "cerebral physiognomy"—we may venture

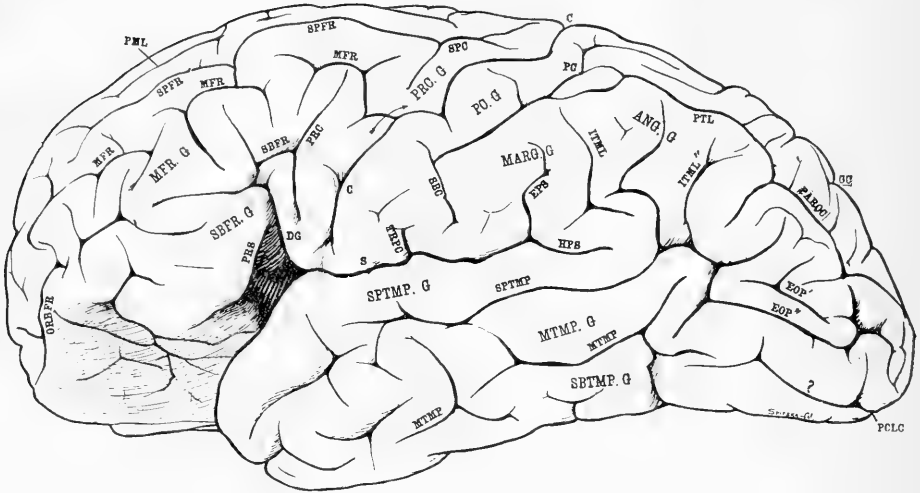


FIG. 13. Brain of "Avia;" lateral view of the left hemisphere.

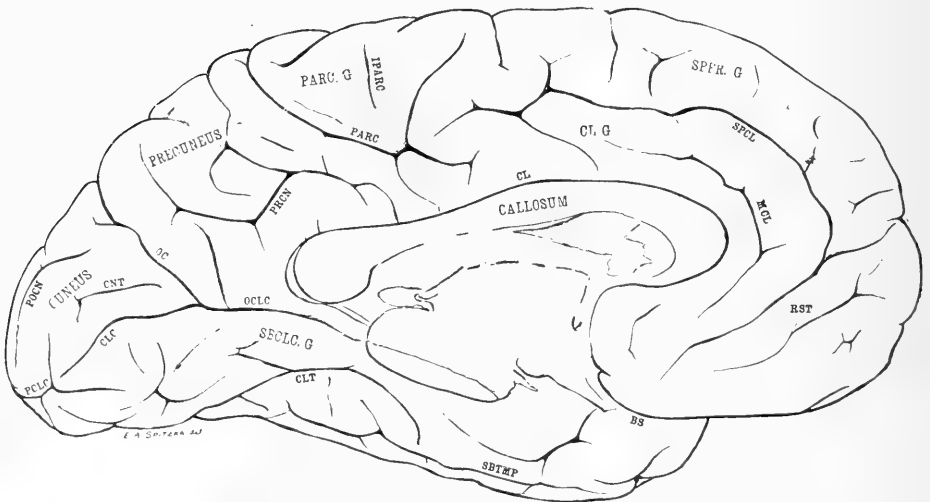


FIG. 14. Brain of "Avia;" mesial view of the left hemisphere.

to call it—seems as distinctive of the Eskimo-type as it is seen, better developed, in the brains of “Atana,” “Nooktah” and “Kishu,” and places it in this category as differing from all other types, quite as the outward characteristics of the race itself do.

LEFT HEMICEREBRUM.

THE INTERLOBAR FISSURES.—*The Sylvian Fissure and its Rami.*—The sylvian fissure is 5 cm. in length, fairly sinuous, opening out cephalad into a distinct sylvian fovea at the bottom of which the insula is visible. The depths of the fissure are as follows: Presylvian depth, 11 mm.; medially depth, 18 mm.; postsylvian depth, 21 mm.

The basisylvian is 20 mm. deep. The presylvian, as determined by its origin from the extreme dorsi-cephalic angle of the insula, is 12 mm. in length and simple. The subsylvian is of the same length. The episylvian is somewhat Z-shaped and 1.5 cm. in length. The hyposylvian is well-marked and of the same length.

Central Fissure.—The central fissure is 11 cm. in length, of the usual contour, anastomosing over a vadium with a precentral-medifrontal segment. It has four short rami, two cephalic, and two caudal.

Occipital Fissure.—The occipital fissure attains a mesial length of 3 cm., and a dorsal length of 1.5 cm. It is deep throughout and of a simple contour. One short ramus is sent into the cuneus, another indents the par-occipital gyre cephalad.

Calcarine Fissure.—The calcarine is an exceedingly simple, slightly-curved fissure, 3 cm. in length. It is separated from the postcalcarine by a narrow but distinct transcalcarine isthmus. The postcalcarine begins on the mesial surface in a furcal piece and is continuous with a fissure (marked by (?)) in Figure 13) upon the ventro-lateral margin of the hemisphere, the whole attaining a length of 7 cm.

The occipito-calcarine fissural stem is simple, 3 cm. in length, and is joined superficially by an independent fissure in the precuneus.

FISSURES OF THE FRONTAL LOBE (LATERAL SURFACE).—*The Precentral Fissural Complex.*—The supercentral is 4 cm. in length, and unusually simple, running parallel with the central. From its middle springs the superfrontal. Ventro-cephalad of the supercentral and separated from it—lies a segment which partakes of the values of a medifrontal and a precentral piece, and corresponds to what Schäfer (Quain) describes as an “anterior ramus of the inferior precentral.” This piece is peculiar in that it is not confluent with the precentral, but anastomoses across the precentral gyre to join the central fissure over a vadium. The third segment is the precentral proper, 3.5 cm. long, from which springs the subfrontal.

The diagonal fissure in this case presents a curious appearance. The fissure is exceedingly deep and opens freely into the sylvian fovea. It completely divides the subfrontal gyre, being deeply confluent with the subfrontal fissure dorsally. Both walls of the fissure are again marked by smaller fissures and grooves.

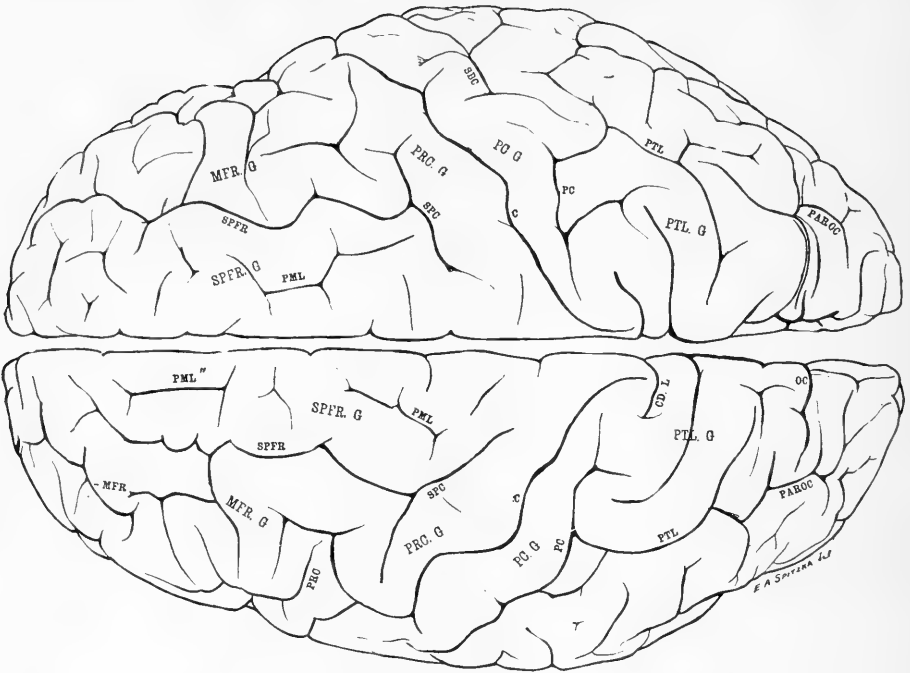


FIG. 15. Brain of "Avia;" dorsal view.

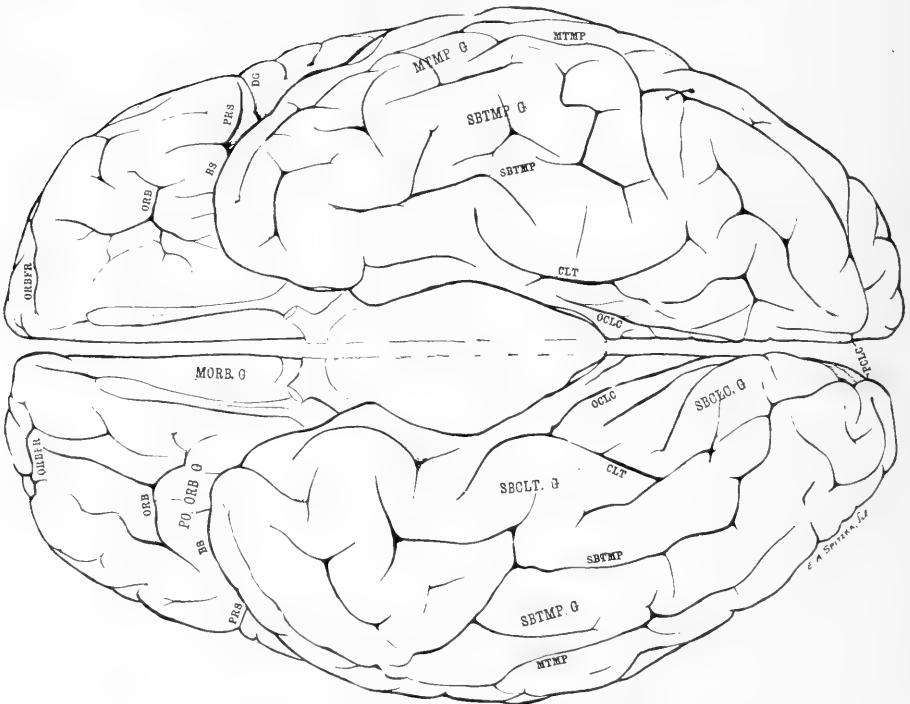


FIG. 16. Brain of "Avia;" ventral view.

The superfrontal fissure is a well-marked one, 7 cm. in length, springing from the supercentral and anastomosing with a medifrontal segment. Its cephalic termination is bifurcated.

The medifrontal is represented by three segments. The caudal one has been described as anastomosing with the central by means of a precentral element. The middle segment has been described as anastomosing with the superfrontal. Its ventral limbs curve around a subfrontal ramus. The most cephalic piece is of a complex, much-ramified contour, anastomosing with the orbitofrontal.

The subfrontal springs from the precentral, terminates in a simple manner at a distance of 2.5 cm. from this origin, and in its course anastomoses with the diagonal. There is one dorsal ramus embraced by the limbs of the middle medifrontal segment. Cephalad of this fissure there is a zygial fissure which, from its topography, might be interpreted as representing an orbitofrontal segment, the radiate, or a subfrontal segment. A distinct orbitofrontal exists further mesad, anastomosing with the medifrontal.

MESIAL SURFACE.—The supercallosal has a total length of 12 cm. Except at its caudal end it has few rami. It is possible that the angular caudal piece is really a segment of the paracentral with its ramus cephalad of the fissure which traverses the dorsi-mesial margin and which possibly represents the inflected. In some respects this arrangement resembles that noted by the writer in the right hemisphere of the assassin Czolgosz. The main part of the paracentral slopes in a nearly straight line toward its dorsal terminus. Its cephalic termination is furcal. There is a short, independent intraparacentral.

The frontomarginal is not present. The rostral is 3 cm. in length. In the callosal gyre, just cephalad of the genu there is a medicallosal fissure, running parallel with and between the callosal and supercallosal fissures.

ORBITAL SURFACE.—The orbital fissural complex may be resolved into a quadri-radiate arrangement of which the two caudal limbs form an arched transorbital, demarcating the preorbital from the postorbital regions.

The olfactory fissure is simple and 4.2 cm. in length.

GYRES OF THE FRONTAL LOBE (LATERAL SURFACE).—The precentral gyre is of regular contour, average width, and interrupted by the vadium described as joining the central with the precentral-medifrontal segment.

The superfrontal gyre is well demarcated, tapers cephalad, and is marked by three fissural segments, two of which are distinct paramesials.

The medifrontal gyre is of notable width, and is marked by numerous fissures whose rami tend to a transverse direction. The subfrontal, however, is very poorly developed; of small size, unusual configuration, and traversed completely by the diagonal. It fails to cover in the insula.

MESIAL SURFACE.—The mesial surface of the superfrontal gyre is simple and unusually narrow. The callosal gyre is of the usual form, except cephalad of the genu where it is wider than common, and is marked by a medicallosal fissure. The paracentral, meaning so much as is defined of it, is small.

ORBITAL SURFACE.—The orbital surface may be divided into pre- and post-orbital regions, fairly well supplied with fissures of irregular types. The mesorbital gyre is unusually narrow.

FISSURES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—*The Postcentral Fissural Complex.*—The postcentral and subcentral pieces in this instance anastomose over a vadium to form a continuous fissure whose total length is 8 cm. The postcentral segment is the longer. It is fairly tortuous, and terminates dorsally in a furcal manner to embrace the caudal limb of the paracentral. Caudally it anastomoses with the parietal by two junctions. Its junction with the subcentral takes place at a depth of 10 mm. over an oblique subgyre. The subcentral itself is tri-radiate. The transpostcentral is independent.

The parietal is a deep and well-marked fissure which anastomoses with the postcentral by means of two limbs, enclosing a gyral islet. It is the ventral one of these limbs which is deeper, and which is the ideal continuation of the fissure. One ramus of the parietal is sent into the parietal gyre, another into the angular. Caudal it anastomoses with the cephalic paroccipital ramus. There is a long transparietal which is confluent with the precuneal fissure on the meson. A second transparietal, tri-radiate, lies in the caudal part.

The paroccipital is zygial, with simple stipes and a bifurcating caudal ramus whose mesial limb is very long.

The intermedial proper is 2.3 cm. in length, independent of other fissures and its ventral end furcal. What may be described as a second intermedial (also named "angular fissure" by some authors) (ITML", Figure 13) lies caudad of the supertemporal, demarcating the angular from the postparietal gyre, and running into the anastomosing fissure which joins the supertemporal and "exoccipitalis secundus" (EOP", Figure 13).

In the parieto-occipital transition there exist several fissures which have the value of exoccipital segments. One of these (EOP') is a small tri-radiate piece. Another larger longitudinal piece (EOP'') anastomoses cephalad with the supertemporal. Ventrad of this is a third segment marked (?) which is confluent with the postcalcarine.

MESIAL SURFACE.—The precuneal is of the usual zygial shape. The dorsicephalic limb anastomoses with the transparietal. The cuneal fissure is short. The postcuneal is a distinct, tri-radiate fissure.

GYRES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—The postcentral gyre is of a simple contour, and rather narrow in its dorsal third; ventrad it is broader. The parietal gyre is of good size, wide, and well fissured. The paroccipital gyre is small. The marginal and angular gyres are much simpler than in the other brains and relatively smaller.

MESIAL SURFACE.—The precuneus is large and presents a richly-fissured surface. The cuneus is small and of rather a simple configuration. The hippocampal gyre is quite narrow.

FISSURES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—In this hemisphere the supertemporal fissure is interrupted at a distance of 3 cm. from the temporal pole by a narrow isthmus. The cephalic segment is quadri-radiate. The longer piece attains a length of 8.5 cm., and anas-

tomoses caudally with an exoccipital (EOP") segment. Its course is in general a simple one.

Four segments, of which three are tri-radiate, and one zygial, represent the meditemporal. The last-mentioned piece sends a ramus well across the subtemporal gyre, and a narrow isthmus separates it from the piece described as confluent with the postcalcarine.

The subtemporal is indifferently represented by four irregular ramified segments.

The collateral is 8 cm. in length and quite sinuous. Its apparent shortness may be due to a division into two segments, the shorter cephalic one being confluent with a small postrhinal.

GYRES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—Especially the supertemporal and to some degree the meditemporal gyres are narrow. The subtemporal is of the usual irregular contour, while the subcollateral is particularly wide in its middle portion owing to the divergence of the collateral fissure. For the same reason the subcalcarine gyre is very narrow in its middle portion but very broad, massive and richly fissured in its caudal part.

THE INSULA.—The insula is small and of simple configuration presenting the usual postinsular gyre and only three preinsular gyres. Owing to the slight development of the opercular parts the insular gyres are well-rounded, not flattened as is usual when encroached upon by the parts which cover them.

RIGHT HEMICEREBRUM.

THE INTERLOBAR FISSURES.—*The Sylvian Fissure and its Rami.*—The sylvian fissure is 5 cm. in length, ends in a simple manner without the usual episylvian or hyposylvian rami. Cephalad, and as described on the left side, the fissure opens out into a sylvian fovea. The depths of the fissure are as follows: Presylvian depth, 12 mm.; medisylvian depth, 16 mm.; postsylvian depth, 23 mm.

Both the subsylvian and the presylvian rami are very short. The central fissure dips into the cleft to a depth of 8 mm. The basisylvian is only 15 mm. in depth.

Central Fissure.—The central fissure attains a length of 10.5 cm., is only slightly tortuous and, reaching the sylvian dips into the cleft to a depth of 8 mm. On the mesial aspect, its dorsal end extends for 1 cm.

Occipital Fissure.—The occipital fissure is of exceedingly unusual form. At a point 2 cm. from its origin at the occipito-calcarine junction, the fissure appears to bifurcate, or what is probably a more correct description, it actually ends here and joins an adoccipital and a posteuneal at once, for the relations of neither arm with the paroccipital justify calling the one or the other the true continuation of the occipital.

Calcarine Fissure.—The calcarine fissure is 3 cm. in length, and is separated from the postcalcarine by a narrow and slightly-depressed isthmus. The postcalcarine is a tri-radiate segment with a long dorsal limb.

The occipito-calcarine stem is 2.7 cm. in length and anastomoses ceph-

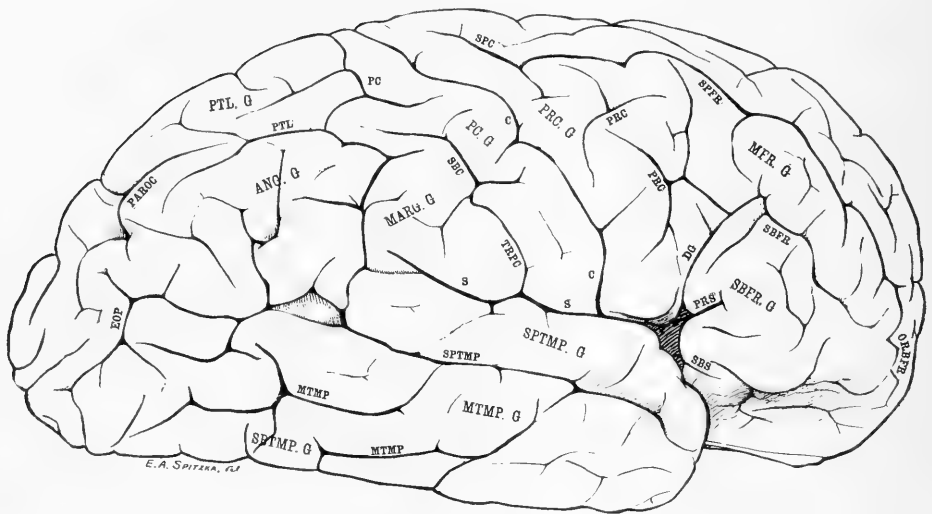


FIG. 17. Brain of "Avia;" lateral view of the right hemisphere.

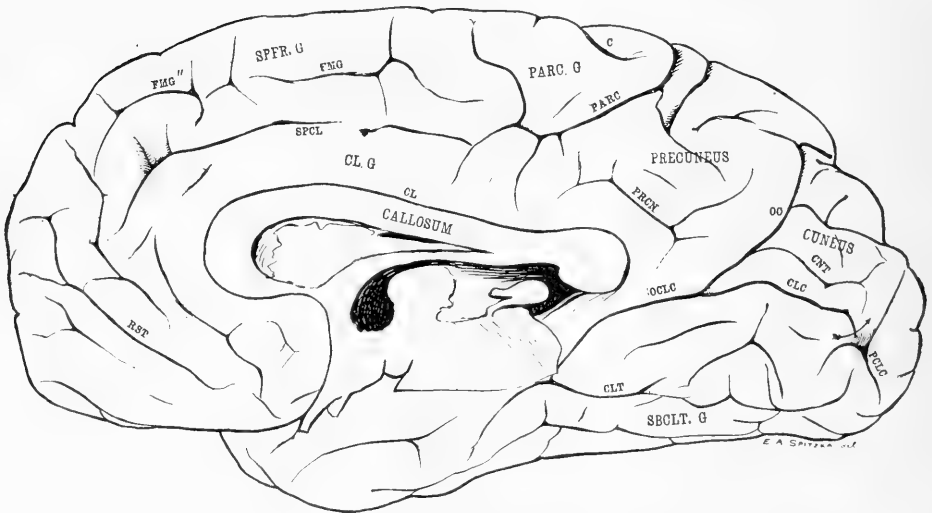


FIG. 18. Brain of "Avia;" mesial view of the right hemisphere.

alad with the collateral. It is deeply confluent with both the occipital and calcarine fissures.

FISSURES OF THE FRONTAL LOBE (LATERAL SURFACE).—The Precentral Fissural Complex.—As may be seen in Figure 15, the supercentral is practically identical with the one on the left side. Furthermore, there is a similar piece at the site of the precentral-medifrontal segment (Schäfer—Quain's "anterior precentral ramus") which does not, however, anastomose with the central as happens on the left side. It is in this case an independent tri-radiate fissure. Ventrad is another precentral, of a zygial shape, with one of its limbs joining the diagonal-subfrontal junction. Throughout, there may be found not a little resemblance between the two sides (compare Figures 13 and 17).

The diagonal dips deeply into the sylvian fovea, and, traversing the subfrontal gyre, as on the left side, to join the subfrontal as well as the precentral limb. The transprecentral is present, but does not appear on the convex surface.

The superfrontal springs from the supercentral in a similar manner to that of the left, and may be traced as a continuous fissure to its junction with the orbito-frontal. Unlike its fellow on the opposite side, this superfrontal fissure sweeps further laterad in the prefrontal region, and comes to occupy a position corresponding to the cephalic medifrontal piece of the left hemisphere. This divergence renders the superfrontal gyre broad and the medifrontal correspondingly narrow. The medifrontal gyre is chiefly traversed by transverse segments.

The subfrontal is a very tortuous fissure springing from the precentral-diagonal junction as described. Its total length is 3.5 cm. The orbito-frontal is a short (2 cm.) piece anastomosing with the superfrontal.

MESIAL SURFACE.—The supercallosal is 7 cm. in length, confluent with the paracentral and ending just cephalad of the genu. (N. B.—The interruption of the fissure in Figure 18 is due to defect in the plate.) Several fissural segments lie in the course of the frontomarginal, of which two are distinct longitudinal pieces. The rostral is 4.5 cm. in length, while the subrostral is quite short and shallow. Between the rostral fissure and the genu lies a medicallosal piece which joins a "transrostral" element. The paracentral fissure is almost the exact counterpart of its fellow on the left side.

ORBITAL SURFACE.—The orbital fissure presents a well-marked transverse stem from which spring two long cephalic rami. Another tri-radiate piece joins the orbitofrontal. The olfactory is 4.8 cm. in length and simple.

GYRES OF THE FRONTAL LOBE.—The precentral gyre is in general wider than its fellow on the left side. The superfrontal is also much broader, while the medifrontal is correspondingly less in width. Both of these gyres are well supplied with fissures tending in a transverse direction. The subfrontal gyre is much larger and better developed in all respects than the left, but like the latter is completely traversed by the diagonal.

MESIAL SURFACE.—On the meson, the superfrontal gyre is broader and more richly fissured than the left. The region marked by the rostral

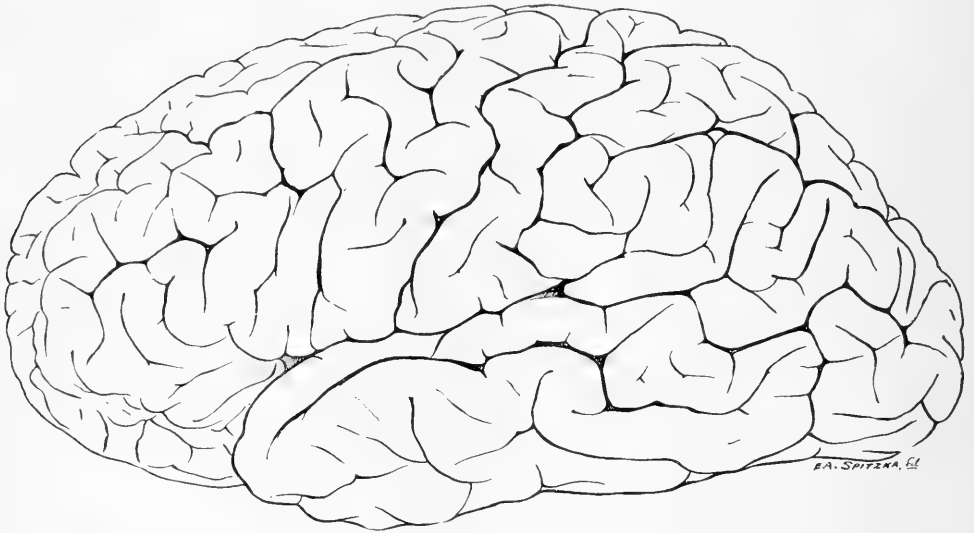


FIG. 19. Brain of "Kishu" (after Hrdlicka; drawn by the author from the specimen); lateral view of the left hemicerebrum.

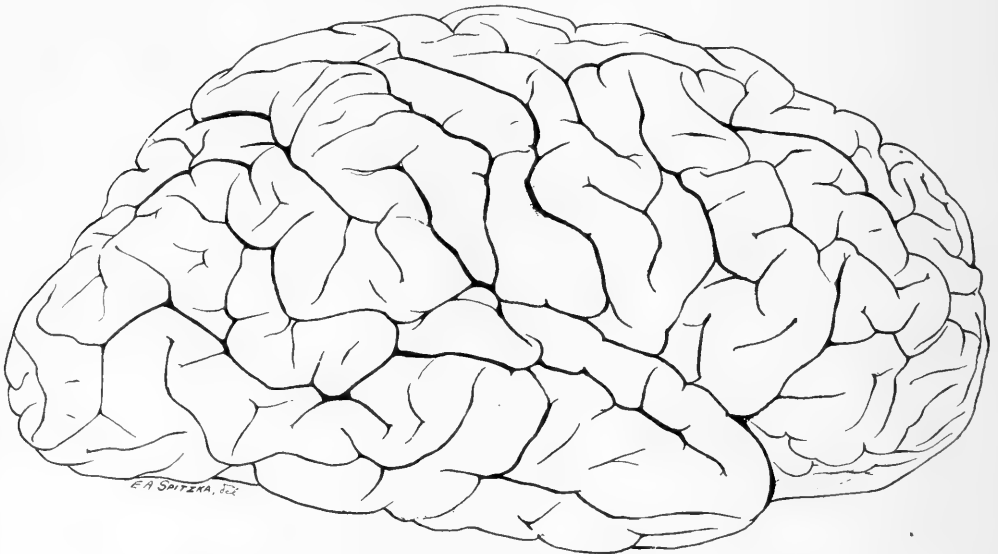


FIG. 20. Brain of "Kishu" (after Hrdlicka; drawn by the author from the specimen); lateral view of the right hemicerebrum.

fissures is also much more intricate in configuration. The callosal gyre is simple. The paracentral gyre is of the same shape and size as its fellow.

ORBITAL SURFACE.—The well-marked transorbital fissure distinctly demarcates the postorbital from the preorbital region. The latter is divided into several sagittal gyres.

FISSURES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—*The Postcentral Fissural Complex.*—In this case the postcentral and subcentral elements are separated from each other. The postcentral is tri-radiate, with its dorsal and caudal limbs embracing the caudal paracentral limb. The longer, ventral limb anastomoses with the parietal. The subcentral and transpostcentral are confluent over a deep vadum, and join the sylvian.

The parietal is a tortuous fissure, 4.5 cm. in length, and separated from the paroccipital. A ventral ramus joins the intermedial and by this the supertemporal superficially. A long dorsal ramus traverses the parietal gyre. There is a transparietal which crosses the margin to join an intraprecuneal.

The paroccipital is an irregular zygial fissure, independent, but with long rami. Its relations to the occipital are difficult to determine with accuracy.

There is one distinct exoccipital zygial fissure which anastomoses cephalad with the supertemporal. A few other irregular, unnamed fissures mark this region.

MESIAL SURFACE.—The precuneal is a simple zygial fissure. Dorsad of this there is an intraprecuneal piece which joins both the paracentral (over a vadum) and the transparietal. The cuneus is marked by a cuneal and a postcuneal fissure, both running parallel with the calcarine and anastomosing with the occipital.

GYRES OF THE PARIETAL AND OCCIPITAL LOBES (LATERAL SURFACE).—The postcentral gyre is of the same form and size as its opposite fellow. The parietal is of moderate size—presenting nothing notable. The paroccipital gyre, though small, is curiously marked by transverse pieces. The marginal and angular gyres are better developed than those of the left half in all respects, the latter being especially massive.

MESIAL SURFACE.—The precuneus is of good size and of the same form as that on the left half. The cuneus is fairly well divided into three longitudinal tiers by the cuneal and postcuneal fissures.

FISSURES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The supertemporal fissure runs in a fairly straight course till, in the region of the angular gyre, it becomes irregular, and turns sharply dorsad. Its total length is 12 cm. In its course it anastomoses with the intermedial, and thence with the parietal, and further caudad with the exoccipital segment.

The meditemporal is represented by several tri-radiate and two longitudinal, ramifying segments. The subtemporal is better defined, attaining a length of 9 cm., and anastomosing with one of the meditemporals.

The collateral is short, and as on the left side there is a separate cephalic segment. The postrhinal is merely indicated by a shallow groove.

GYRES OF THE TEMPORAL LOBE (LATERO-VENTRAL SURFACE).—The super-temporal and meditemporal gyres are much wider and far more massive than on the left. The subtemporal, however, is correspondingly reduced. As on the left, the subcollateral is wide in its middle portion, and the subcalcarine correspondingly narrow. The anastomosis between the occipito-calcarine and the collateral interrupts the latter gyre.

THE INSULA.—The insula presents the same configuration as its fellow on the left, having the same number and arrangement of gyres. It is less exposed, however.

Aside from certain peculiar variations of types too numerous to permit of detailed mention within the scope of this article—and perhaps based on too few observations—the natural grouping of the notable appearances of these Eskimo brains determines the existence of prevailing typical differences which distinguish these from the brains of whites. It is difficult to describe this distinction in so many words and one is justified in employing the metaphoric term “cerebral physiognomy” to convey the idea. Were one to place any one of these Eskimo brains next to that of one of the Papuan brains, yet to be described, it would be—not a comparison—but a contrast of the clearest kind. The marked tendency in all these brains to transverse fissuration, numerous anastomoses in a transverse direction, with frequent interruption of some of the longitudinal fissures is a feature which even the pronounced dolichocephaly of little “Avia’s” head was not able to efface. It is something more than skull-shape which has determined this and other distinguishing characteristics, borne out also by similar observations on Mongolian brains. In the Eskimo brains here studied such features are the different relative topography and boundaries of the cuneus, the exposition of the insula (“Atana” and “Avia”) and the preponderating development of certain features upon the left and of others on the right side. The brain-form in general, too, is of typical kind, if one may judge from the small number of specimens available. The hitherto popular notion that the typical Eskimo skull exhibits a low order of intelligence, and is characterized by a small brain-capacity has been generally refuted, and the fallacy of this idea becomes more apparent with the demonstration of so highly developed a brain as these specimens have shown the Eskimo to possess.

ABBREVIATIONS.

The following abbreviations arranged in alphabetical order, are those of the names used in designating the fissures and gyres in the illustrations:

FISSURES.

<i>AMYG.</i> , Postrhinal (or Amygdaline).	<i>CPH. L.</i> (Cephalic Limb).
<i>BS.</i> , Basisylvian.	<i>CD. L.</i> (Caudal Limb).
<i>C.</i> , Central.	<i>PAROC.</i> , Paroccipital.
<i>CL.</i> , Callosal.	<i>PC.</i> , Postcentral.
<i>CLC.</i> , Calcarine.	<i>PCLC.</i> , Postcalcarine.
<i>CLT.</i> , Collateral.	<i>PML.</i> , Paramesial.
<i>CNT.</i> , Cuneal.	<i>POCN.</i> , Postcuneal.
<i>DG.</i> , Diagonal.	<i>PRC.</i> , Præcentral.
<i>EOP.</i> , Exoccipital.	<i>PRCN.</i> , Precuneal.
<i>EPS.</i> , Episylian.	<i>PRS.</i> , Presylvian.
<i>FMG.</i> , Frontomarginal.	<i>PTL.</i> , Parietal.
<i>HMP.</i> , Hippocampal.	<i>RDT.</i> , Radiate.
<i>HPS.</i> , Hyposylvian.	<i>RST.</i> , Rostral.
<i>IFL.</i> , Inflected.	<i>S.</i> , Sylvian.
<i>IPARC.</i> , Intraparacentral.	<i>SBC.</i> , Subcentral.
<i>IPRCN.</i> , Intraprecuneal.	<i>SBFR.</i> , Subfrontal.
<i>ITML.</i> , Intermedial.	<i>SBRST.</i> , Subrostral.
<i>MCL.</i> , Mediallosal.	<i>SBS.</i> , Subsylvian.
<i>MFR.</i> , Medifrontal.	<i>SBTMP.</i> , Subtemporal.
<i>MTMP.</i> , Meditemporal.	<i>SPC.</i> , Supercentral.
<i>OC.</i> , Occipital.	<i>SPCL.</i> , Supercallosal.
<i>OCLC.</i> , Occipito-calcarine stem.	<i>SPFR.</i> , Superfrontal.
<i>OLF.</i> , Olfactory.	<i>SPTMP.</i> , Supertemporal.
<i>ORB.</i> , Orbital.	<i>TPRC.</i> , Transprecentral.
<i>ORBFR.</i> , Orbitofrontal.	<i>TRPC.</i> , Transpostcentral.
<i>PARC.</i> , Paracentral.	<i>TRPTL.</i> , Transparietal.

GYRES, ETC.

<i>ANG. G.</i> , Angular Gyre.	<i>PO. ORB. G.</i> , Postorbital Gyre.
<i>CL. G.</i> , Callosal Gyre.	<i>PRC. G.</i> , Precentral Gyre.
<i>HMP. G.</i> , Hippocampal Gyre.	<i>PR. ORB. G.</i> , Preorbital Gyre.
<i>INS.</i> , Insula.	<i>PTL. G.</i> , Parietal Gyre.
<i>MARG. G.</i> , Marginal Gyre.	<i>SBCLC. G.</i> , Subcalcarine Gyre.
<i>MFR. G.</i> , Medifrontal Gyre.	<i>SBCLT. G.</i> , Subcollateral Gyre.
<i>MORB. G.</i> , Mesorbital Gyre.	<i>SBFR. G.</i> , Subfrontal Gyre.
<i>MTMP. G.</i> , Meditemporal Gyre.	<i>SBTMP. G.</i> , Subtemporal Gyre.
<i>PARC. G.</i> , Paracentral Gyre.	<i>SPFR. G.</i> , Superfrontal Gyre.
<i>PAROC. G.</i> , Paroccipital Gyre.	<i>SPTMP. G.</i> , Supertemporal Gyre.
<i>PC. G.</i> , Postcentral Gyre.	

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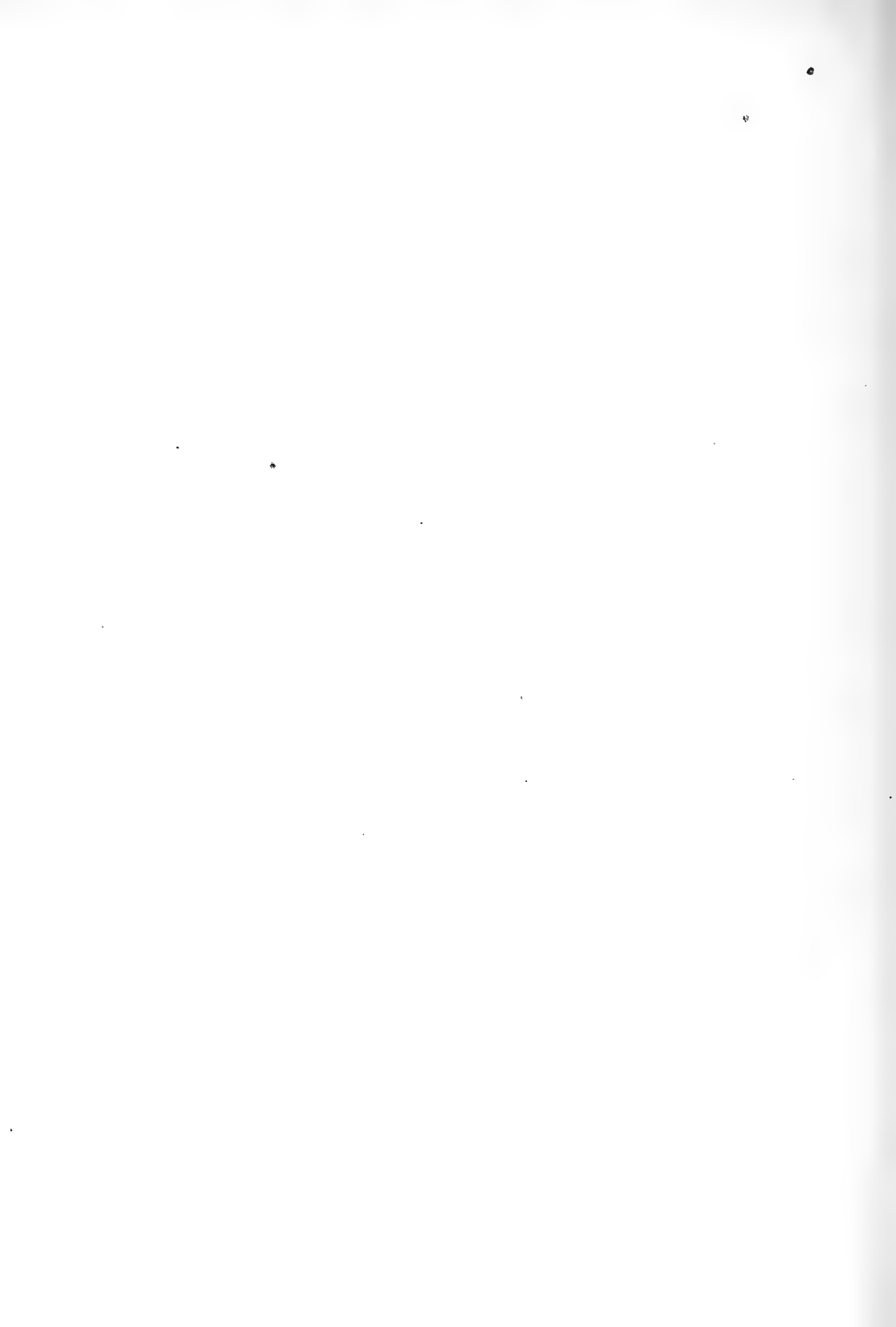
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ON THE STRUCTURE OF THE CORPORA CAVERNOSA IN THE DOMESTIC CAT.

BY

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WITH 7 TEXT FIGURES.

Some years ago in examining sections of the cat's penis, I was surprised to find that the corpora cavernosa are composed of adipose tissue. Having repeatedly observed a similar condition in different specimens, and finding no description of the same in the literature,¹ I have recently made a careful examination of about thirty specimens, from cats of various ages, in order to determine whether this occurrence be normal and constant. The results of this investigation, together with a few observations concerning similar relations found in other domestic animals, are included in the following pages. In this connection, I would express my thanks to Dr. L. F. Barker, of the University of Chicago, in whose laboratory some of the latter part of the work was done.

The specimens examined, 34 in all, were preserved in formalin (5%) or a mixture of formalin and alcohol (formalin 5%, alcohol 70%). The vessels were injected with Grübler's gelatin injection mass. Five specimens were imbedded in celloidin or paraffin and sectioned. The remaining specimens were examined after hardening, by means of free-hand razor sections.

The penis of the cat has the typical mammalian form, as shown in Fig. 1. Within the glans is sometimes found the *os penis* (Figs. 2

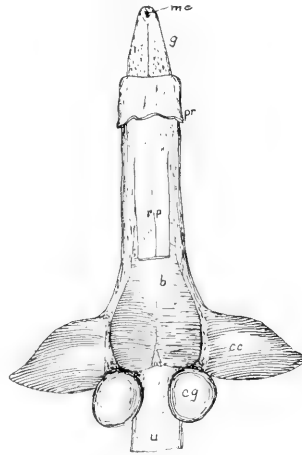


FIG. 1. Ventral surface of the penis of the cat. $\times 2$. u, urethra; cg, Cowper's glands; cc, crura penis, covered by ischiocavernosus; b, bulbourethra, covered by bulbocavernosus; rp, retractor penis muscle; pr, prepuce; g, glans penis; me, meatus urinarius externus.

¹ There is a brief reference in Bonnet's "Entwicklungsgeschichte der Haussäugethiere" to the fact that in the cat the corpora cavernosa are largely transformed into a non-erectile fatty cushion.

and 3). This bone is by no means constant in its occurrence. Of the specimens examined, in 7 kittens (2 half-grown), and 5 small-sized cats, no trace of an os penis was found. In 9 specimens of medium-sized cats, 3 showed a very small rudimentary os penis, the others none. Of 12 large-sized cats, 8 had a well-developed os penis (3 mm. to 5 mm. long); 2 a small or rudimentary bone; and 2 no trace of bone. It therefore appears that the os penis of the male cat is inconstant and acquired relatively late in life, certainly not until long after sexual maturity.

The os penis, when well developed, is about 5 mm. long and shaped like a long tapering cone. It is placed dorsal to the urethra, and the apex extends beyond the meatus externus to near the tip of the glans. The bone is slightly flattened from side to side (Fig. 3). The base of the os penis lies embedded in the septum between the distal ends of the corpora cavernosa, in the base of the glans. At this extremity, the bone is flattened dorso-ventrally, and presents dorsally on each side, a groove in which rests the end of the corresponding corpus cavernosum.



FIG. 2. Os penis of the domestic cat, dorsal view. $\times 15$. d, distal end; p, proximal end.

The os penis is usually a solid bone, but occasionally contains a medullary cavity. Around the bone and forming a conical projection beyond its tip is a strong fibrous periosteal layer, which is a prolongation from the tunica albuginea, and especially from the septum. A similar prolongation exists as a dense fibrous cylinder in cases where the bone is undeveloped, even distinctly in the penis of the new-born cat. The os penis therefore may be considered as the ossified distal prolongation of the septum between the corpora cavernosa. It is not preformed in cartilage, thus differing from that of the dog, as described by Retterer.²

The corpora cavernosa throughout the greater part of their extent are closely united to each other in the median line, the septum being very slight or incomplete (Fig. 5). Distally, however, they become slender and diverge to end in the base of the glans, on each side of the os penis. The structure varies greatly in the different regions. Toward the distal extremity, the corpora cavernosa are composed almost entirely of compact *adipose* tissue, supported by slight fibrous trabeculæ

² Retterer, E., Sur l'origine et l'évolution variable de la charpente qui existe dans le gland des mammifères. C. R. Soc. de Biologie, Paris, 1886.

extending in from the tunica albuginea (Fig. 4). The appearance of the corpora cavernosa in this region is in striking contrast to that of the corpus spongiosum, especially in injected specimens. Still more striking is the appearance of a specimen stained with osmic acid, in which the corpora cavernosa are stained jet black. Passing from the distal extremity, the corpora cavernosa gradually enlarge, and become more fibrous and vascular. The vessels are irregular venous channels, best developed in the center of each corpus, so that the adipose tissue

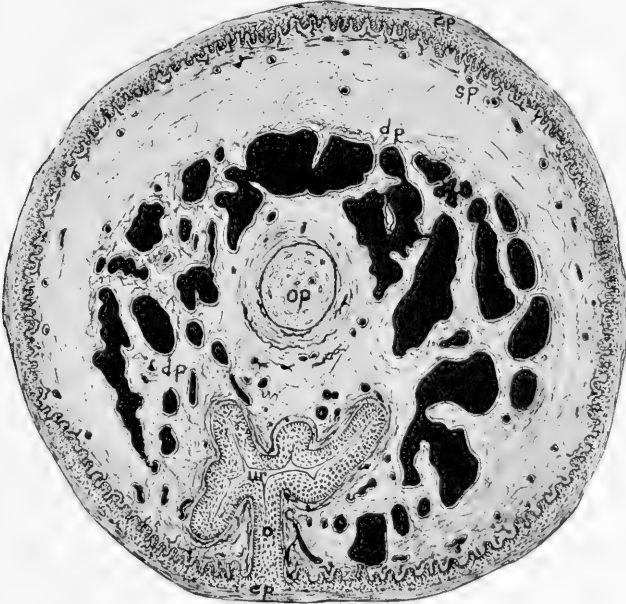


FIG. 3. Cross-section through glans penis of a cat, near external meatus, vessels injected. $\times 40$. Stained with haematoxylin. ep, epidermis; ur, urethra; o, strip of epithelium connecting urethra with surface epithelium; sp, superficial integumentary plexus of vessels; dp, deep venous plexus, forming the cavernous tissue of the glands; op, os penis.

appears to become gradually crowded toward the periphery (Fig. 5). Toward the base of the penis the cavernous tissue increases steadily in amount, and the adipose tissue correspondingly decreases. In the proximal third, as a rule, a very slight amount of adipose tissue is present in the form of a few groups of fat cells, forming an imperfect peripheral layer, especially on the ventral side. Adipose tissue is never entirely absent. The cavernous tissue in this region is composed of typical irregular venous spaces, separated by fibrous trabeculae in which the smaller arteries enter. The cavernous tissue differs from that of

the corpus spongiosum in the greater irregularity in the shape of the venous spaces, and the more frequent anastomoses of the spaces with each other. Longitudinal sections show also that the spaces in general are not extended in a longitudinal direction as they are in the corpus spongiosum. In the crura, the amount of adipose tissue again increases slightly, forming usually a thin, imperfect peripheral layer (Fig. 6). At the proximal extremity the cavernous tissue of the crura is often very largely replaced by adipose tissue.

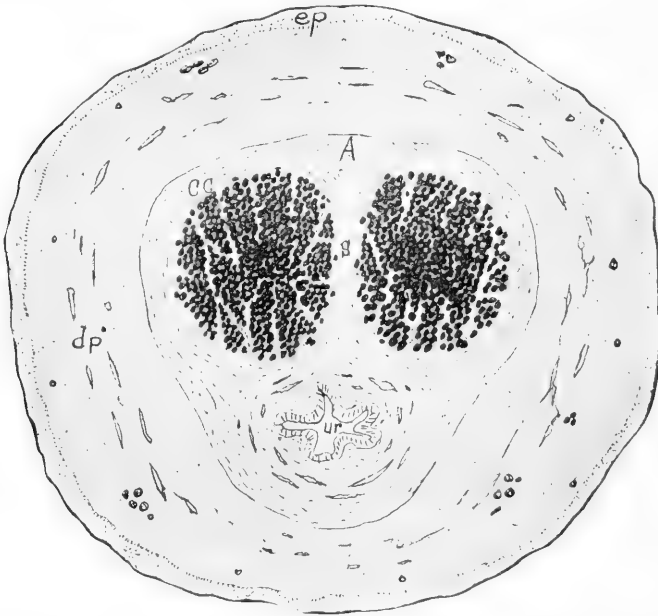


FIG. 4. Cross-section of penis of a cat through base of glans, vessels uninjected. $\times 25$. Stained with osmic acid. ep, epidermis; dp, deep venous plexus; A, tunica albuginea; S, septum; CC, corpus cavernosum; ur, urethra, in corpus spongiosum.

The corpus spongiosum, it should be noted, contains only the typical cavernous tissue of that region. In the peripheral portion of the bulb, however, adipose tissue is occasionally found (cf. Fig. 6).

The presence of adipose tissue in the corpora cavernosa as previously described is fairly constant, although the extent of its development varies somewhat in individual cases. Sometimes the adipose tissue is present in larger amount than indicated, and occasionally it is less well developed. The variation apparently does not depend upon the age of the animal, except during the first few weeks after birth. At birth, there is no trace of adipose tissue in the corpora cavernosa, which con-

sist at this time of compact embryonal fibrous tissue, in which the cavernous spaces are beginning to develop, especially toward the proximal end. The adipose tissue evidently appears shortly after birth, however, for it was found well developed in several instances in kittens only a few weeks old. There is no evidence to indicate that the adipose tissue is formed by a *degeneration* of cavernous or other tissue. Both cavernous and adipose tissue evidently develop directly from embryonal connective tissue, the adipose appearing at a slightly later date than the cavernous tissue.

I have not had an opportunity to make extensive investigation of the conditions in other animals, but have examined several specimens of the penis of the dog, sheep, pig, bull, and man. With the exception of the last, adipose tissue was found in greater or less amount in the corpora cavernosa of all the foregoing animals. In all cases, however, as in the cat, no adipose tissue was found in the corpus spongiosum.

In the dog, the conditions are similar to those in the cat. The corpus spongiosum, including the bulb and glans, contains no adipose tissue. In the corpora cavernosa considerable fat is present, especially in the superficial portions, and toward the distal end. In the dog the

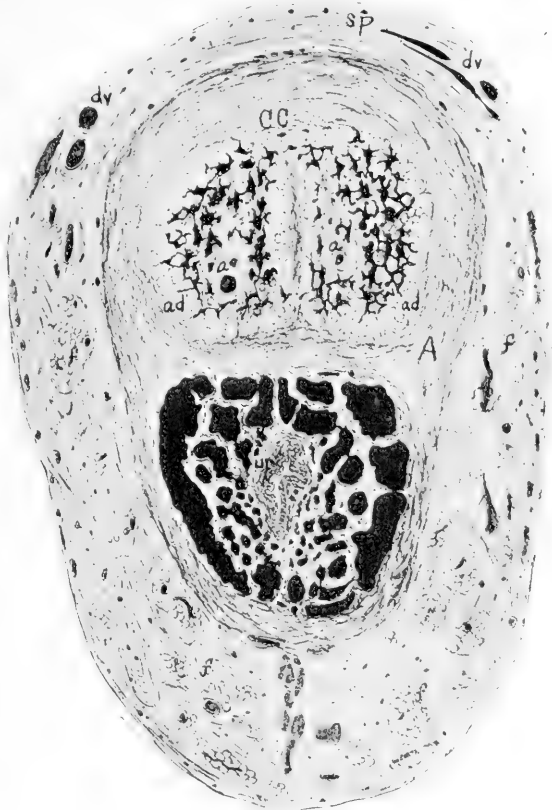


FIG. 5. Cross-section of a cat's penis, near junction of middle and distal thirds. Vessels injected. $\times 25$. Stained with haematoxylin. sp, superficial plexus; dv, dorsal vessels of the penis; f, clusters of fat cells in surrounding fascia; A, tunica albuginea; CC, corpora cavernosa; a, artery of corpus cavernosum; ad, adipose tissue of corpus cavernosum; ur, urethra, in corpus spongiosum.

fibrous trabeculae are much stronger, and occupy relatively a much larger space than in the cat. The amount of adipose and cavernous tissue is reduced in proportion.

In the ram's penis, the condition is similar to that in the dog, except that the adipose tissue occurs chiefly in the *proximal* portion, little or none distally. Wether's penis contains fat in about the same amount as the ram, but less cavernous, and more fibrous tissue. Lamb's penis similar, except that the adipose tissue is less abundant.

In the boar's penis, adipose tissue is likewise found in considerable amount in the proximal region, especially in the crura. Fibro-caver-

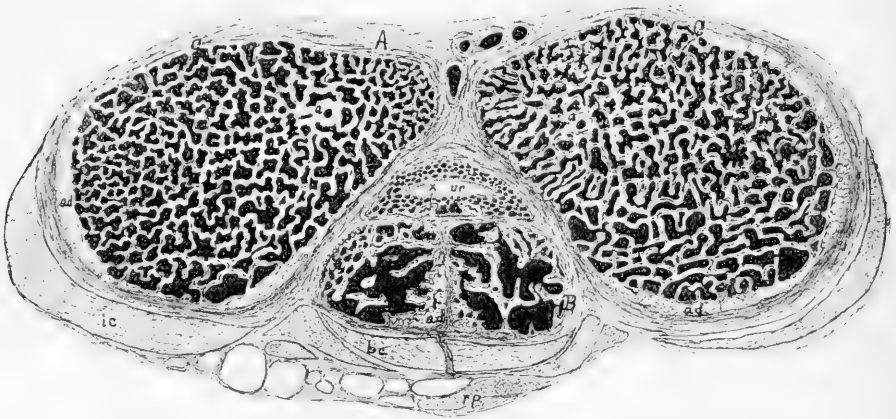


FIG. 6. Cross-section of injected penis of the cat, through crura and bulb. $\times 10$. A, tunica albuginea; C, crus penis; B, bulbus urethrae; ad, adipose tissue; a, artery of crus; ur, urethra; x, duct of Cowper's gland, between urethra and bulb; ic, ischio-cavernosus; bc, bulbo-cavernosus; rp, retractor penis.

nous structure throughout. In the barrow the cavernous tissue is reduced, but the adipose tissue remains in about the same amount.

Sections of the bull's penis show the corpora cavernosa to be strongly fibro-cavernous throughout, from crura to distal extremity. Some scattered adipose tissue proximally, none distally. The corpora cavernosa of both sides are united into a single body. From the thick tunica albuginea fibrous trabeculae extend inward, and unite in the center to form a fibrous core on each side. The corpus spongiosum has the usual cavernous structure.

The penis of the steer shows a marked change, however. The fibrous tissue remains, being even more strongly developed. The cavernous tissue almost entirely disappears, and is replaced by adipose tissue, especially in the proximal region. Sometimes little or none is found in the

distal region. In no other animal observed did castration apparently increase the amount of fat present. No observation was made on castrated dogs or cats.³ An investigation of the histological changes in the penis of a eunuch would be of much interest since, so far as I know, no observations have been made upon this point.

The adipose structure of the clitoris, which is interesting in this connection, has been observed in various animals. Bonnet⁴ mentions the dog, cat,

pig, cow, guinea-pig, sheep, goat, and states that the adipose structure is fully established in the 3 months' old pig, and 4 months' dog. The latest reference to the subject which I have seen is found in Ellenberger and Günther's textbook,⁵ p. 197, from which the following is quoted, referring to the clitoris: "Beim Pferde sind dieselben wie das Corpus cavernosum urethrae gebaut, werden aber von einer starken

Albuginea umgeben. Bei allen anderen Tieren findet man in den Maschen des Balkengerüstes Fettzellen, die beim Hunde in so grossen Mengen zugegen sind, das die Corpora cavernosa einem derben Fetts-trange gleichen. Ein Septum teilt die Fettmasse in zwei Hälften. An

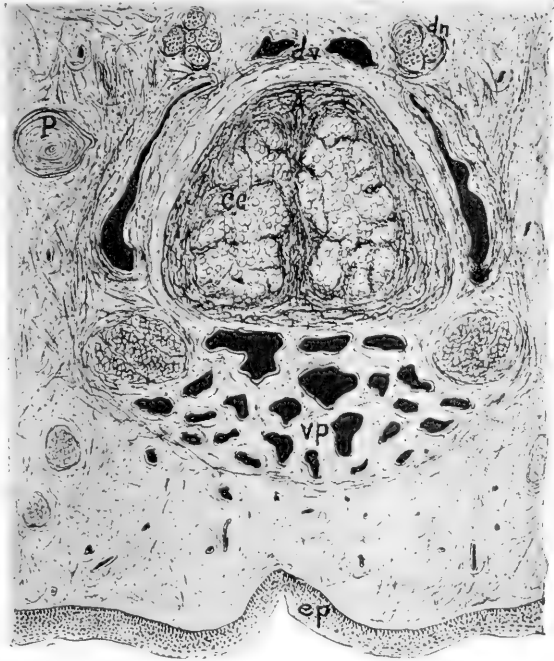


FIG. 7. Cross-section through the injected clitoris of a cat. $\times 25$. Stained with haematoxylin. A, tunica albuginea; CC, adipose corpora cavernosa; dv, dorsal vessels; dn, dorsal nerve of clitoris; P, Pacinian body; vp, venous plexus; ep, surface epithelium.

³ Retterer observed that in castrated cats the numerous recurved spines of the glans disappear, but makes no statement concerning changes in the corpora cavernosa.

⁴ Bonnet, R., *Grundriss der Entwicklungsgeschichte der Haussäugethiere*. Berlin, 1891.

⁵ Ellenberger and Günther, *Lehrbuch der vergleichende Histologie*. Berlin, 1901.

der Spitze fehlt das Fettgewebe, so das dieselbe nur von der Albuginea, und den von ihr abgehenden, sich innig verflechtenden Bälkchen gebildet wird. Bei den anderen Tieren sind die Fettzellen niemals so massenhaft zugegen als beim Hund. Es folgen Schwein, Rind, Katze, bei welchen Tieren die Fetteinlagerung fast nur auf die peripheren Teile beschränkt, dann Schaf und Ziege, welche nur wenig Fettzellen in dem Corp. cav. enthalten."

There is, however, in the work cited, no reference whatever to a similar adipose structure in the penis. A cross-section through the clitoris of the cat, illustrating the adipose structure, is shown in Fig. 7. In the clitoris of the new-born kitten, like the penis, I find only embryonal connective tissue, slightly vascular, and containing no adipose tissue. In this connection it may be remarked that in the human species the penis, like the clitoris, contains no adipose tissue.

Résumé.—1. The os penis is inconstant in the cat, is rarely found except in old animals, and occurs as an ossification within the distal prolongation of the septum between the corpora cavernosa.

2. The corpora cavernosa in the cat are peculiar in that the cavernous tissue is largely replaced by adipose tissue, especially in the distal portion.

3. A similar condition is found to a greater or less extent in various other mammalia (not in man) and also in the clitoris, the adipose tissue occurring always in the corpora cavernosa, and not in the corpus spongiosum.

4. As a result of castration, the cavernous tissue of the corpora cavernosa is greatly reduced in amount, and the fibrous tissue correspondingly increased. The amount of adipose tissue is greatly increased in the steer, but not in other animals, so far as observed.

THE NEUROGLIA OF THE SPINAL CORD OF THE ELEPHANT WITH SOME PRELIMINARY OBSERVATIONS UPON THE DEVELOPMENT OF NEUROGLIA FIBERS.

BY

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WITH 4 TEXT FIGURES.

The material from which is made the following contribution to the comparative study of neuroglia has been on hand several years. It consists of a portion of the spinal cord of a 21-year old bull elephant killed in Bridgeport, Conn., in 1897. Through the kindness of Prof. H. H. Donaldson, the specimen was finally allotted to me and a partial description of its gross and microscopic anatomy is contained in a previous paper.¹ The material was removed a few hours after death and fixed in 10% formalin in which the unused portions have been preserved ever since.

The medullated axones of the spinal cord of the elephant have an appreciably larger diameter than those of man or of any of the mammals more usually studied. Measurements, inclusive of the medullary sheaths, of fifty axones in an average field of a transverse section of the cervical region stained by the Weigert hæmatoxylin method give diameters ranging between 25 μ and 8 μ with an average diameter of 19 μ . Similar measurements from the human specimen, prepared in the same way, give diameters varying from 17 μ to 6 μ with an average of about 11 μ . The larger axones of the spinal cord of the elephant result, of course, in larger inter-axone spaces. These larger spaces being occupied by the neuroglia allow, in consequence, larger areas for its study. This fact suggested the spinal cord of the elephant as a favorable field for the study of the neuroglia cells in that larger areas in the vicinity of the neuroglia nuclei were to be expected.

The study has been suggestive of several conclusions, the validity of which must be further tested by recourse to developing material. Aside from these, however, the tissue in itself may be of interest.

¹Hardesty. Observations on the Medulla Spinalis of the Elephant, with some Comparative Studies of the Intumescencia Cervicalis and the Neurones of the Columna Anterior. Jour. Comp. Neurology, Vol. XII, No. 2, 1902.

Several of the methods devised for the staining of neuroglia allow the use of formalin-preserved tissue and the two methods by which the best general results are to be obtained (those of Weigert² and Benda³) require fixation in formalin. Thus the elephant material on hand, having been fixed in formalin, was suited to the purpose.

I have found paraffin sections much better for the study of neuroglia than celloidin sections. The celloidin itself will at best hold a certain amount of the stain and thus, under transmitted light, give a murky property to the section detrimental to the sharpness of both image and contrast. The Weigert method, as originally given, is a celloidin method. Also it is more applicable to human tissue, having been especially devised for such. For purposes of comparison the material here in hand was prepared by each of two methods, both of which give fairly good results with animal as well as human tissue. These two methods are, first, a modification of the Weigert procedure as given by Aguerre⁴ and, second, the method of Benda as adapted and employed by Huber in his comparative "Studies on the Neuroglia."⁵ Of the two methods the latter gave the better results, both with the elephant tissue and with that of the other animals to be mentioned. Though the modification of Weigert's method of staining neuroglia gave preparations in which could be observed all to be noted in sections stained by the latter method, yet for sharpness of outline and distinctness of differentiation, the procedure given by Huber resulted in a decided excellence. Also, with it thinner sections are possible than with the Weigert method. Very thin sections, however, are not always necessary nor even best. To get an idea of the complexity of the networks of neuroglia fibers, the shape of the cells, and the extent of single neuroglia fibers, fairly thick sections are desirable. Paraffin sections of 5 μ and 8 μ in thickness proved efficient for the study. Both transverse and longitudinal sections were made, and mounted and stained on the same slide. Certain of the sections were made from small pieces from a known locality of the spinal cord, others from large pieces involving one-half of its lateral diameter. All pieces were taken from within the cervical enlargement.

² Weigert, C. Beiträge zur Kenntniss der normalen menschlichen Neuroglia. Festschrift, Frankfurt a. M., 1895.

³ Benda, C. Erfahrungen über Neurogliafärbungen und eine neue Färbungsmethode. Neurologisches Centralblatt. Vol. XIX, 1900.

⁴ Aguerre, J. A. Archiv für Mikros. Anat. und Entwicklungsgesch. Vol. LVI, 1900. Also Neurological Technique (Hardesty) Method XIV, The University of Chicago Press, 1902.

⁵ Huber, G. Carl. The Am. Jour. of Anat., Vol. I, No. 1, 1901.

As used by Huber, the Benda method applied to the elephant's cord gave remarkably sharp contrasts. The neuroglia fibers stain a deep bright blue against a slightly pink but almost transparent background. Their contour is even and threadlike. On the other hand, white fibrous connective tissue, the pia mater, its ingrowths and the walls of the blood-vessels, stains a light brownish-red. The endoplasm (when present) of the neuroglia cells appears brownish-red with distinct granulations; the nerve cell-bodies and the chromatin of their nuclei, a dead grayish-blue; axones (axis cylinders), light brownish-red with sometimes a tinge of blue. The outlines of the neuroglia nuclei and their chromatin masses stain a black-blue. In the various blood-vessels the blood corpuscles may be noted. The red corpuscles color a greenish-blue. In sections prolonged in the differentiating fluids the red corpuscles become a light greenish-red or practically colorless. Of the white corpuscles, the eosinophiles and polymorphonuclear types generally stain very dimly or not at all, while the small lymphocytes show a deep blue nucleus with a pinkish granular cytoplasm. The myelin portion of the medullary sheaths does not stain at all, but the general framework of the sheaths takes a light pink like the fibrillæ of white fibrous connective tissue.

As an additional test of the selective power of the stain for neuroglia, the Benda method was applied to pieces of formalin-fixed lung, salivary gland, spleen and skin (human and dog). In all the steps these tissues were subjected to the identical procedure employed with the sections of the spinal cord. The result was highly satisfactory as to the value of the method. No blue-stained fibers were found in any of the sections. Both white fibrous and elastic tissue stained the same light brownish-red as found in the pia mater and the walls of its blood-vessels. In the salivary gland, for example, the white fibrous framework between the alveoli and the basement membranes about them, showed in beautiful detail but were stained a pale red with no trace of blue. The chromatin in the nuclei of the connective tissue cells stained blue but seldom so deeply as in those of the neuroglia cells. Some nuclei, however, were remarkably like certain of those found in sections of the spinal cord. The endoplasm about the nuclei stained the same color as that about neuroglia nuclei but with a much less evident granular structure. Lymphocytes could be distinguished with their thin rim of granular cytoplasm. Many apparently "free nuclei" could be noted. As a test for neuroglia fibers the experiment indicated at least that the method is selective since in none of the tissues did either white fibrous or elastic tissue show the blue reaction.

Although neuroglia was discovered by Keuffel in 1811, the distinctive nature of the tissue was not considered until 1846 when Virchow described it under the name it now bears. The study of neuroglia, however, did not really begin till the advent of the silver method of Golgi. This method, though described by its inventor as early as 1873, remained practically unnoticed and unused till after 1885, when Golgi's more voluminous work appeared. This method not only was the means of certain important additions to our knowledge of the development of the tissue, but also through it the fibrous nature of neuroglia was established. Previous to 1895, however, our knowledge of neuroglia as a tissue consisted almost entirely of what could be shown by the precipitation of the silver salt. The investigators, chief among whom were Golgi himself, Kölliker, Cajal, Ranvier and Lenhossèk, had no means of confirming their observations by adequate control methods and, as the natural consequence of a precipitative method, the later daylight upon its results has shown that certain of their conclusions were erroneous. The appearance of Weigert's paper in 1895, giving the results of a new method he had devised, marked the beginning of a new epoch in the study of neuroglia. Since Weigert's publication no less than twenty-three papers have appeared giving results obtained either by the application of his method or of others newly devised. Most of these papers do little more than confirm Weigert's results. While certain of them add a few details to the knowledge of the tissue, on the whole they have strengthened rather than detracted from Weigert's original conclusions. The more important of these papers and the literature on the subject in general, have been repeatedly reviewed and so thoroughly by Aguerre⁶ and Reinke⁷ and more recently by Huber,⁸ that it is considered unnecessary to attempt here anything like a detailed review of the literature. The more important and commonly accepted statements may be summated as follows:

1. Structurally, neuroglia as a tissue consists of neuroglia cells and neuroglia fibers.

2. The neuroglia cells vary in size and shape. They usually possess branched cytoplasmic processes. The cytoplasm, however, is present in varying amounts, many of the cells having but a small quantity which closely invests the nucleus or sometimes occurs only on one side of it. Most of the neuroglia nuclei are described as free from cytoplasm. The nuclei are of the vesicular type but vary greatly in shape and size.

⁶ Aguerre. *Archiv f. Mikros. Anat.*, Vol. LVI, 1900.

⁷ Reinke. *Archiv f. Mikros. Anat.*, Vol. L, 1897.

⁸ Huber. *Loc. cit.*

Usually spherical or oval, they may assume any of the shapes ascribed to polymorphic nuclei. Their chromatin is of the granular arrangement and stains deeply. It usually occurs as one or more larger masses of irregular outline situated among a number of smaller granules. The smaller nuclei stain more deeply than the larger. Now and then neuroglia cells are found which are appreciably larger than the ordinary. These "colossal glia cells" (Monstrezellen of Weigert or the "Monstreastrocytes" of the Golgi method) often contain two or more nuclei. These "Multinucleated glia cells" (Aguerre and Krause⁹) are thought to be a special type of neuroglia cell and constant structures for all the higher mammals. Further they may have to do with the multiplying of the cells.

3. The neuroglia fibers, at one time regarded as processes of the neuroglia cells (Deiters' cells), are not identical with the cytoplasm of the cells, but are morphologically, physically and chemically different from it. By the selective stains, the fibers appear completely differentiated from the cell protoplasm and therefore cannot be considered as processes in the ordinary sense of the word. Further, a single fiber may often be observed pursuing an unbroken course through the domain of the cell-body, thus involving two outgrowths which could not be the case were each fiber a process arising individually from the cell-body. The differentiated fibers appear to pass through the cell chiefly along its outer zone, but often cross above or below the nucleus and sometimes directly through the cytoplasm surrounding the nucleus when such is present. They are quite small, are thread-like in contour and vary somewhat in thickness. They frequently anastomose. They form a true supporting tissue for the nervous elements and in the substantia alba, the greater number course in the general direction of the nerve fibers about which they form loose plexuses. They are of unknown length. In the spinal cord they are more abundant about the blood-vessels, about the central canal and in the posterior white commissure than among the nerve fibers. The number of neuroglia nuclei in a given locality is no index of the abundance of neuroglia fibers to be found there.

4. Neuroglia fibers may be regarded as differentiated intercellular structures since they bear no fixed relation to the neuroglia nuclei nor to the cells themselves, though in certain cases the neuroglia fibers are not completely emancipated from the cytoplasm of the cells. They are produced at the expense of the cell protoplasm and are later differentiated from it but by a process the steps of which are unknown.

⁹Krause. Anhang. z. d. Abh. der Königl. Akad. der Wissenschaften zu Berlin, 1899.

Embryologically, all neuroglia is generally considered as derived from ectodermal cells.

5. The neuroglia nuclei have been variously classified according to both their shape and size, but they may be sufficiently described under the two divisions originally made by Weigert:

a. Large. Sometimes attain a diameter of 16 μ . Usually spherical or oval in shape but may vary. Very vesicular. Granular chromatin usually accumulated in one or two larger masses (nucleoli) surrounded by smaller granules.

b. Small. Diameter 4 μ or even less. Various shapes but usually spherical. Compact chromatin a deeply staining almost homogeneous mass.

There are to be found all transition forms between the two varieties.

I have arranged what seem to me the principal findings of the literature under the above five heads because such observations as I have been able to make on the neuroglia of the spinal cord of the elephant and collaterally of that of man seem to fall under one or the other of these heads.

After a brief general description of the neuroglia of the elephant I shall confine myself to one or two less generally emphasized points suggested by a study of the preparations, and the figures given are intended to illustrate features less usually described. To avoid slight confusion, the description will better be based upon appearances resulting from the application of the Benda method alone.

The neuroglia of the spinal cord of the elephant as seen in both transverse and longitudinal sections may be described as follows: The neuroglia fibers stain a deep bright blue, whereas cytoplasm of the neuroglia cells, when present, takes a pale brick color with rarely a slight tinge of blue. The cytoplasm is distinctly granular, while the neuroglia fibers have a smooth, even contour and each a practically constant thickness. Thus the fibers differ both physically, and in their chemical reaction to the stains, from the cytoplasm of the cell-bodies, and so agree with one of the general statements made by Weigert for human neuroglia and confirmed by subsequent investigators of neuroglia both human and comparative. The neuroglia fibers in the elephant are in general somewhat larger than in the human specimens I have examined and, judging from the descriptions found in the literature, they are larger than those found in other animals. On the whole, they do not vary greatly in size. Very few seem under 0.5 μ in thickness and the average is somewhat over that figure. Occasionally what seems an exceptionally large fiber is noticed. On measurement these often acquire

but seldom exceed $1\ \mu$ in breadth. The fibers are of unknown length. Short fibers are common, but they are undoubtedly pieces, cut by the knife. Frequently in the thicker sections one fiber may be traced intact through the domain of two or more neuroglia cells (Fig. 3, *k*) and then the ends appear as cut by the knife rather than as terminations of the fiber. Anastomosis is to be observed but not as a very frequent occurrence. Both transverse and longitudinal sections of the specimens distinctly show many fibers obliquely and transversely cut, in fact cut in all conceivable planes. The fibers run tortuous courses in the inter-axone spaces of the white substance or form a general complex plexus in the gray. They may be seen to form loose feltworks about the medullated axones often quite closely investing the medullary sheaths, the membranous portions of which stain a pale red in contrast. Generally, however, they seem to merely course freely in the spaces among the nerve fibers showing a preference for none. Comparing the transverse section with the longitudinal, it is immediately evident that while the fibers course in all planes, more have a tendency to course in the direction of the nerve fibers than transversely to them (Fig. 4). They show no fixed relation to the neuroglia nuclei, merely running indifferently in the spaces occupied by them.

In the gray substance the neuroglia fibers either do not hold the stain so well or are less abundant than in the white substance. While, as Aguerre noted for the human spinal cord, they are abundant in the commissura alba posterior and in the substantia grisea centralis, they do not show so abundantly through the general gray figure as one would expect. Occasionally areas may be noted quite rich in neuroglia fibers but these are more often in the vicinity of the blood-vessels. Though the periphery of the columna posterior is rich in well-stained neuroglia fibers, the column itself, which contains a great amount of substantia gelatinosa, appears as a brownish-red, compact granular mass filled with innumerable nuclei, most of which are of the small deeply-staining variety. Neuroglia fibers can scarcely be distinguished except about occasional blood-vessels and entering nerve fibers. What are supposed to be neuroglia nuclei are more abundant in any given area of the gray substance than of the white as is to be expected because in the former they are less dispersed by the presence of medullated axones within it. On careful examination the oil immersion reveals many fine fibers in the gray substance but these are pale red in color. The preparation gives the impression that if these are neuroglia fibers their staining properties have been influenced by some other tissue constituent in which they are imbedded. Throughout the entire gray figure many

neuroglia nuclei may be observed with the characteristic investment of granular cytoplasm in varying amounts but the majority of the nuclei are seemingly "free" and mostly of the small, compact, deeply-staining variety. The cytoplasm, when present, never shows the branched processes found in the substantia alba.

In the white substance in general, the neuroglia fibers are colored deep blue and stand out in sharp distinctness against their environment. This contrast is most striking in sections involving the periphery of the

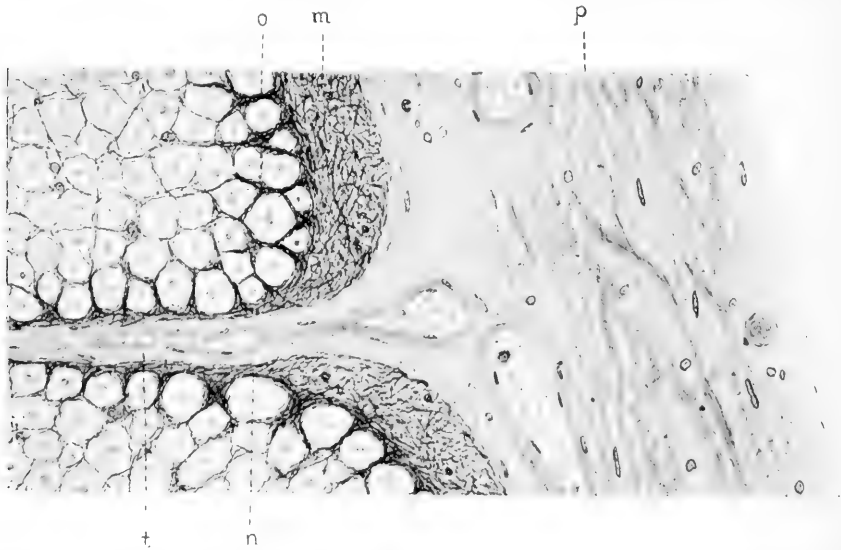


FIG. 1. Portion of dorso-lateral periphery of transverse section from spinal cord of elephant showing a blood-vessel passing into the tissue of the cord proper and the relation and contrast in staining of the white fibrous tissue of the pia mater (*p*) to the neuroglia fibers forming the marginal veil (*m*) of the cord, together with the structure of the latter and the dense trabeculae of its fibers (*o*) passing in among the adjacent nerve fibers of the cord. Deep black in the drawing represents blue in the original, other shades represent pale brownish-red. The blood-vessel is seen to be accompanied not only by pial tissue (*t*) but also by a thick sheath of neuroglia (*n*) acquired in passing through the marginal veil. $\times 370$.

spinal cord. Here the cortex of the cord or marginal veil (*Randschleier* of His) stands out as a deep blue, thick feltwork against the adjacent pia mater as shown in Figure 1. The pia (*p*) sends in a few thin strands of white fibrous tissue which interweave with the sharp blue neuroglia fibers but these strands are so thin as to be almost colorless. Being entirely void of nerve fibers to disperse them, the neuroglia fibers of the marginal veil (*m*) course thickly in all directions, forming a dense, intricate and admirable feltwork. It sends in processes (*o*) among the nerve fibers along its inner border in which the neuroglia fibers run

parallel and so thick as to obscure their individuality under the microscope. Intermingling with the nerve fibers along their course, these processes rapidly decrease in size as they pass inward with the result that areas in the periphery of the white substance are more richly supplied with neuroglia fibers than those farther in.

The marginal veil is interrupted by no appreciable ingrowths of the pia mater except those accompanying the blood-vessels. Figure 1 is given to illustrate a locality showing this. The blood-vessel (artery in this case) leaving the pia mater, carries with it an investment of pial tissue which, together with the tissue of its own walls, stains brownish-red (*t*). In passing through the marginal veil the blood-vessel appears to take with it an additional investment of neuroglia fibers (*n*). This neuroglia investment remains continuous with the marginal veil and though gradually decreasing, is maintained as far as the blood-vessel can be followed into the specimen—in some instances to the substantia grisea itself. It has been frequently observed that the neuroglia fibers are especially abundant about the blood-vessels, occasionally even reaching into their walls. This behavior has been considered as having to do with processes of nutrition. The well-differentiated preparations I have examined, both of man and the elephant, show no neuroglia fibers actually reaching into the walls of the blood-vessels and whether their greater abundance about the blood-vessels has to do with nutrition or not, the appearances suggest that their presence is the result of neuroglia tissue having been carried in from the marginal veil by the blood-vessels as they pass through it. Therefore, if for a physiological purpose, their presence is due to a physical process. The blood-vessels grow in for the most part during the early stages of development, and at a time when the marginal veil, and the whole organ, is in a more plastic condition than it is after the nerve fibers grow in and the processes of medullation have begun. No neuroglia fibers are formed at the time the blood-vessels begin to enter and the neuroglia tissue carried in from the (then relatively thick) marginal veil simply remains about the blood-vessels and later develops into the adult form of neuroglia. This development is no doubt facilitated because of the nutritive conditions afforded there.

In the early stages of growth the marginal veil (*Randschleier* of His) in man is described as formed of the fused distal ends of the epithelial (later ependyma) cells lining the central canal. At first it contains no nuclei but appears as a sort of reticulated protoplasmic continuum, the fusion of the cell processes having resulted in an obliteration of all cell boundaries. Later, as the walls of the neural tube thicken still more,

nuclei appear in the marginal portion resulting from the division of those lying nearer the central canal. In the adult, after the application of the ordinary hæmatoxylin methods, for example, the marginal veil (cortex) of the spinal cord appears as a thin, lightly-stained homogeneous, granular zone void of medullated nerve fibers and containing a few small spherical nuclei scattered in it and certain fine colorless fibrillæ which are perhaps neuroglia fibers. In the literature I have been unable to find any detailed descriptions of the adult marginal veil after treatment by any of the differential neuroglia stains. In the elephant after this treatment, it appears as a dense feltwork of neuroglia fibers coursing in all directions and but slightly intermingled with white fibrous connective tissue from the adjacent pia mater. It contains no nerve fibers and is thicker on the dorsal and lateral aspects of the spinal cord than on the ventral. At best it is a relatively thin mantle, on measurement seldom showing a thickness of over 80 μ . In proportion to the abundance of neuroglia fibers, it contains remarkably few nuclei (see Fig. 1) and very seldom are any of these of the large vesicular variety. In this respect, when compared with other localities of the transverse section, it conforms to Aguerre's observation that the number of neuroglia nuclei in a field is in inverse ratio to the abundance of neuroglia fibers. In their abundance, length and arrangement, the fibers have all appearances of having been formed from a common syncytium rather than from or with reference to any arrangement of individual neuroglia cells.

The entering radix posterior contains no fibers whatever which take the neuroglia stain until its nerve fibers penetrate the marginal veil. This fact is well differentiated by the Benda stain. The radix posterior, as it enters the cord, even apparently depresses the marginal veil on coming in contact with it. Once it breaks through this mantle, however, its nerve fibers become richly intermingled with the blue staining neuroglia fibers. The nerve fibers of the radix anterior on the other hand, as they emerge through the marginal veil are accompanied a short distance beyond the confines of the spinal cord, by a few blue-staining fibers. My preparations, not being made with this point in mind, unfortunately do not allow satisfactory observations as to how far these neuroglia fibers accompany the fila of the radix anterior nor how abundant they are. The radix anterior of the elephant arises by innumerable small fila radicularia, most of which in the preparations were torn off close up to the surface of the cord. The fila of the radix posterior are considerably larger and in several sections quite an extent of a filum of this root remained attached to the cord.

The study of the neuroglia cells was made from both longitudinal and transverse sections. In general it may be said that the great majority of nuclei are entirely free from cytoplasm or possess a very small amount. Of such as do possess cytoplasm, a comparison of appearances in the two planes indicates that the longest diameter is generally in the direction of the long axis of the spinal cord (Fig. 4, *c*). Sometimes two, and rarely even three, nuclei may be found with a common cytoplasm (Fig. 2). Krause¹⁰ found glia cells with more than one nucleus in the apes, and Aguerre (*loc. cit.*) describes such for the half apes and for man.

In all my preparations the neuroglia is better studied in the white substance than in the gray.

The study of the neuroglia cells and the neuroglia nuclei with reference to their relation to the neuroglia fibers, has suggested a series of changes which may probably indicate some of the steps in the development of the neuroglia fibers. The accompanying drawings are taken from fields especially chosen as suggestive of these changes. They are all camera drawings and Figures 2, 3 and 4 are on the same scale (oc. 4, 1/12 oil immersion, Zeiss). The drawings represent the areas chosen except in case of one cell, noted in the explanation, which was drawn from an adjacent field. This cell merely substitutes another of the more common type and otherwise does not affect the normal appearance of the area represented. Neuroglia cells similar in appearance to those shown may all be found on the same slide, and therefore the various forms evident can hardly be due to variations in the application of the staining method.

The cells and nuclei, as found in the spinal cord of the elephant, may be described together. To indicate the series of changes suggested, they may be taken up in the following order:

1. Cells with a large amount of cytoplasm which is largely present in the form of extensive, branched processes. The cytoplasm is sufficient to fill the inter-axone space occupied by the cell—the processes being sent out between the adjacent nerve fibers, give the impression that the shape of the cell is the result of its position—it merely fitting into the space it occupies. For obvious reasons this shape is best observed in transverse sections. The cytoplasm is granular after the technique employed, and, by the Benda method, stains a brownish-red, with occasionally a tinge of blue. The nucleus is always of the large vesicular variety, *i. e.*, with a diameter of from 10 μ to 16 μ and with granular

¹⁰ Krause, R. Untersuchungen über die Neuroglia des Affen. Abhandl. der Königl. Akad. der Wissenschaften zu Berlin. Anhang, 1899.

chromatin loosely distributed, usually showing one or two larger masses (nucleoli) situated in the midst of smaller granules. When two cells of this type occur in adjacent inter-axone spaces, their processes anastomose, forming a common cytoplasm surrounding the nerve fibers involved, or rather, perforated by them. This type of cell is of less frequent occurrence than any of those that follow, and in sections sufficiently differentiated for the study of the neuroglia fibers, it often requires some search to find two near enough together to clearly show the fusion of their processes. Figures 2 and 3 illustrate such cases and

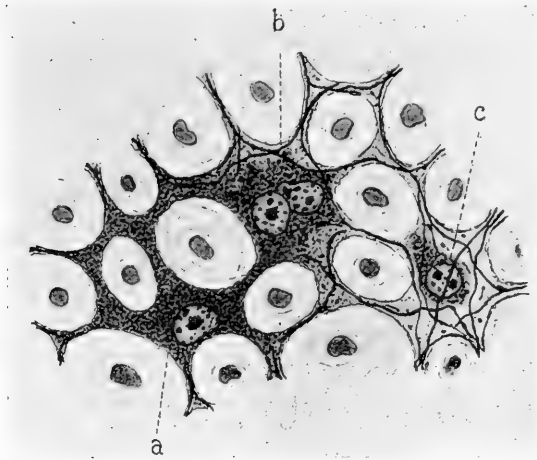


FIG. 2. Small area from transverse section showing two neuroglia cells (*a* and *b*) with anastomosing cytoplasm and a third cell (*c*) with cytoplasm much less abundant. The varying relationship between the neuroglia fibers and the "neuroglia cell" is shown in the three cases. In the original, the neuroglia fibers and the chromatin of the nuclei are stained deep blue; the granular cytoplasm of the cells, dark brownish-red, while the axones and fibrous constituents of their medullary sheaths are colored a pale brownish-red. + 940.

The cytoplasm of the processes always appears less compact than that more immediately surrounding the nucleus (endoplasm) and in the extreme portions of the processes neuroglia fibers can always be found, but such appear as continuations of fibers which may be traced from confines of the neighboring cells of the more common type. If the process is long, i. e., if it may be traced some distance before becoming a part of the domain of another cell, its stainable cytoplasm rapidly becomes more and more attenuated till the neuroglia fibers alone are to be seen; or, conversely, one of these neuroglia fibers may be traced back to the cytoplasm in which it disappears. If the inter-axone space occupied by the cell is large, the cell may contain two nuclei.

cell *c* in Figure 4 might be considered as presenting the same condition in longitudinal section.

In thin sections the brownish-red cytoplasm allows sufficient light to pass through it to easily observe its structure.

Examination shows that such a cell may be entirely void of neuroglia fibers (Fig. 2, *a*) or, if fibers are discernible, they occur only in the peripheral portion (exoplasm) of the cell in close proximity to the nerve fibers (Figs. 2 and 3, *b*).

As before noted, cells of this type are less frequent in my preparations and such have been very infrequently noted in the literature. Brodmann¹¹ noted what were evidently cells of this type in a glioma of the thalamus opticus stained by Weigert's neuroglia method. He describes such cells as especially abundant in the zone of growth of the tumor and refers to them as "Bindungszellen der Gliafasern." Reinke (loc. cit.) in one of his illustrations shows two of the larger cells with joining processes. His stain, however, does not show the abundance and nature of the cytoplasm marking the type as is shown by the Benda method.

2. The second type of cell to which I wish to call attention (*b*, Figs. 2 and 3) is apparently a transition form of the first. It possesses the large vesicular nucleus as in the first type, but its cytoplasm is modified. About the nucleus the cytoplasm is as compact as in the first type but in the outer zone of the cell it grades into loose scattered granules which may be quite absent from the processes. Thus the cell is partially a phantom of the first type, having for its outline the boundaries of the inter-axone space it occupies. Neuroglia fibers are easily distinguished passing through the cell. They may be followed into it by way of one process, then usually along one side in the less obstructed outer zone, and out by way of another process. Or, in passing through the cell, a fiber may involve a portion of the more dense cytoplasm about the nucleus. It cannot be said with confidence that fibers are interrupted in passing through the cytoplasm. Fibers often appear as if having been spun out of the cytoplasm and often appear to terminate in it, but such appearances must more generally be considered as being due to the knife. No fibers have been observed terminating in the cytoplasm in a cone-like end as noted by Yamagiwa¹² in his preparations, which cone was described by him as a part of the cell cytoplasm and as an evidence that the fibers are processes of the cell. The cytoplasm about the nucleus possesses short branches. These always point toward, and sometimes into, the spaces between the neighboring nerve fibers and thus represent portions of the original processes of the cell.

3. More often a much smaller amount of cytoplasm is present (stains) and this is always in the immediate vicinity of the nucleus forming an irregularly-shaped, granular zone about it. Such cells never fill the inter-axone space. Usually short projections are maintained and these,

¹¹ Brodmann. Ueber den Nachweis von Astrocyten mittelst der Weigertschen Gliafärbung. Vortrag in der Naturwissenschaftlichen Gesellschaft zu Jena. Jan., 1899.

¹² Yamagiwa. Eine neue Färbung der Neuroglia zugleich ein Kleiner Beitrag zur Kenntniss der natur von den Glia-fasen. Virchow's Archiv, Bd. 160, 1900.

as above, point toward the spaces between the neighboring nerve fibers. The balance of the inter-axone space is clear and the neuroglia fibers coursing through it are sharply differentiated. The fibers occupy the clear area chiefly, but often they penetrate the cytoplasm and even cross the nucleus (*c*, Figs. 2 and 4). When the mass of cytoplasm (endoplasm) is quite scant it sometimes appears on one side of the nucleus only but is usually pointed, suggesting one of the projections of a previously more abundant cytoplasm. The nucleus of this type is also of the large vesicular variety. Representatives of this type of cell may

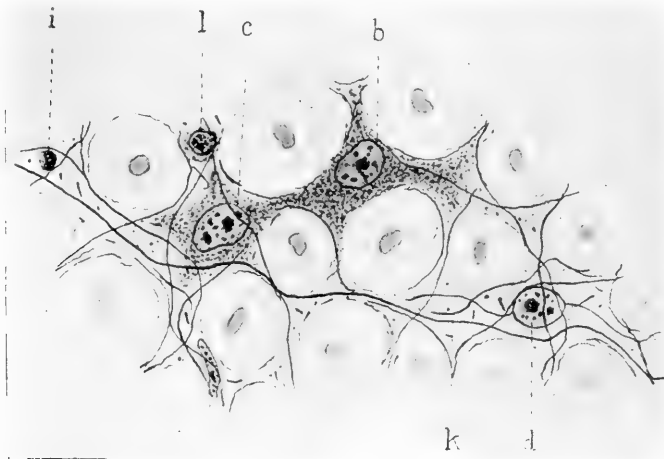


FIG. 3. From transverse section showing four types of neuroglia cells (*b*, *c*, *d*, and *i*) and the arrangement of the neuroglia fibers with reference to the cell and the inter-axone space. One neuroglia fiber (*k*) appears continuous through the domain of several neuroglia cells. The colors represented by the different shades of black are the same as those in Figures 1 and 2. *l* = leucocyte. $\times 940$.

be seen in most any field of the microscope. In his comparative "Studies on the Neuroglia," Huber (*loc. cit.*) describes this type, and I think also the second type I have mentioned, for the dog, cat, rabbit, dove, tortoise and frog, and such have been noted in the human.

4. Cells with but a very small amount of cytoplasm about the nucleus forming a sort of granular halo about it (*d*, Figs. 3 and 4). Projections are seldom apparent. Neuroglia fibers traverse its inter-axone space indiscriminately, frequently crossing the nucleus above or below it. The fibers are more abundant in these areas than in any of the above types. They enter and leave by way of the spaces between the adjacent nerve fibers and often one may be traced through the domain of a neighbor-

ing cell. This variety is about as numerous as the third variety mentioned and is evidently a transition form. The nucleus though of the vesicular type appears at times somewhat smaller than that of any of the preceding varieties.

There should be mentioned under this class a variety of cell which is questionably a neuroglia cell at all (*l*, Figs. 3 and 4). Though surrounded by a definite rim of cytoplasm, the nucleus of this cell is con-

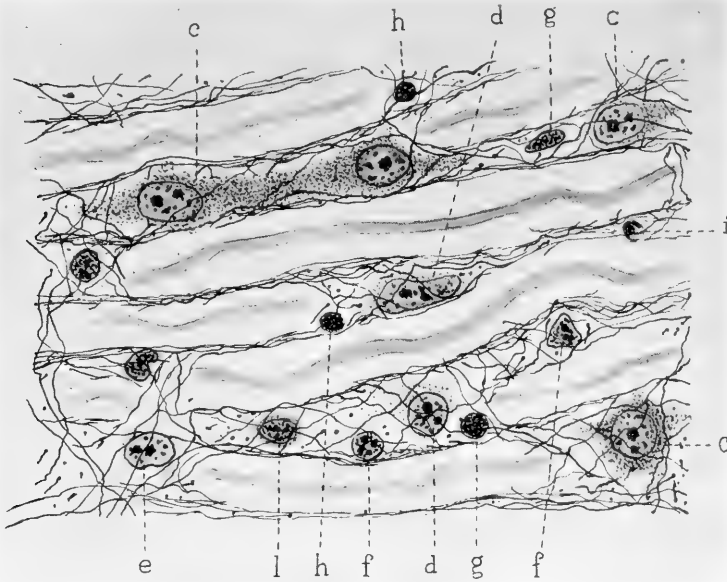


FIG. 4. Small area from longitudinal section showing different types of neuroglia cells and the general direction and arrangement of the neuroglia fibers with reference to the nerve fibers and "neuroglia cells." The colors represented are the same as in the preceding figures. Nucleus *i* is transplanted from a neighboring field and substitutes a nucleus of type *e*. *l* = leucocyte. $\times 940$.

siderably smaller (4μ to 6μ in diameter) than that of any of the above varieties. The chromatin of its nucleus is more evenly granular and more compact and therefore the nucleus stains more deeply than those referred to as vesicular. The cytoplasm forms a thin ring about the nucleus, sometimes thicker on one side, and its granules are not so coarse as in the cytoplasm of the neuroglia cells. In quite a few instances cells resembling these have been noted in the blood-vessels, at times situated among the red blood corpuscles (Fig. 1) but more often close to their walls. A study of the white blood corpuscles in the prepa-

rations reveals the fact that the nuclei of the eosinophiles and of the polymorphonuclear varieties generally stain very lightly or not at all by the Benda neuroglia method. The cells in question having a single nucleus with even contour and a relatively small amount of cytoplasm, must be considered as lymphocytes. Outside the blood-vessels this variety of cell may be found in all conceivable positions among the nerve fibers and often without reference to the amount of space. Usually its nucleus is spherical but when pressed between other structures it may be rod-shaped. There is reason therefore for considering these cells as other than neuroglia cells. They are looked upon as small mononuclear lymphocytes which, outside the blood-vessels, may be called "wandering cells."

5. Most of the neuroglia nuclei appear free from cytoplasm. These free nuclei vary greatly in size, ranging from the truly vesicular type with a diameter equal to those possessing cytoplasm, through the various degrees of compactness and density in staining, to a type with a diameter of 4μ and less. In general it may be said that the smaller the nucleus the more compact is its chromatin and therefore the more deeply does it stain. None of the more deeply-staining nuclei ever have a vestige of cytoplasm about them. The free nuclei are generally spherical or oval in the elephant but may be polymorphic. They vary in size from 15μ to 3μ in diameter and the smallest always stain as one compact mass. All transition forms may be observed between the smallest and the large vesicular type, suggesting that the one may be derived from the other. What are considered some of these stages of transition are shown in Figures 3 and 4. The nuclei *e* to *h* taken in their order illustrate the diminution in size accompanied by the increased density in staining.

6. Now and then a nucleus of the smallest type may be noted which appears as though in the process of disintegration. All the stages of karyolysis usually described for other tissues have not been observed in these nuclei, and little more can be said of them than that the compact chromatin seems to undergo fragmentation and occurs as a small jagged mass either in the center of the nucleus or more often at one side of its outline (*i*, Figs. 3 and 4), while the rest of the nuclear area appears practically clear. Nuclei which may be considered as belonging to this type are by no means so numerous as the other types of free nuclei. They occur at the rate of about one in every two fields under the oil immersion. They are generally under 4μ in diameter. They sometimes resemble the transverse sections of the smaller axones and but for the deep stain and the absence of the structures belonging to

the medullary sheath, might be taken for such. At first it was thought they were artefacts or nuclei injured by the knife but a close study of their occurrence and appearance lends more to the idea that they are constant structures. They always occur in the midst of a network of neuroglia fibers.

For purposes of comparison and in order to test how far the special technique of the neuroglia method affects the shape, size and structure of the neuroglia nuclei, sections of the elephant's cord were examined after preparation by other methods. Without previous treatment, other than the action of the formalin in fixation, the tissue was imbedded in celloidin and sectioned. Some of these sections were stained with Ehrlich's hæmatoxylin and counterstained with congo red, others with erythrosin and toluidin blue. In these sections all of the above types of neuroglia cells and nuclei may be identified by careful examination under the oil immersion. The nuclei are not only the same as to size and structure, but stain in much the same way as by the toluidin blue in the special neuroglia stain. The large (Deiters') cell with cytoplasm sufficient to fill the inter-axone area and sending processes between the adjacent nerve fibers is readily found. This is the identical neuroglia cell often pictured in the older text-books and is no doubt one of those described later by Ranvier.¹³ I consider it as corresponding to types 1 and 2 described above, the differences in the appearance of the cytoplasm and the lack of differentiated neuroglia fibers being due to differences in the method of treatment. Also, in these sections cells with but a small amount of cytoplasm about the nucleus are of frequent occurrence. However, owing to the diffuse manner in which the counterstains act, a small quantity of cytoplasm is not so easily distinguished as after the Benda neuroglia stain. The majority of the nuclei are as evidently "free" as in the Benda preparations. As to be expected, neither of the ordinary methods mentioned give any distinction between pia mater and neuroglia, but though undifferentiated, the neuroglia fibers may be distinguished after one is familiar with their size and distribution when stained by the special methods.

I have classified the neuroglia cells and neuroglia nuclei in the above order because a study of them in the spinal cord has suggested that in this sequence they may illustrate some of the phases in the development of the neuroglia fibers. The phases suggested may be presented as follows:

1. "Neuroglia cell" is a misnomer if the term is considered as ex-

¹³Ranvier. De la Névrogliæ. Arch. de Physiologie, 1883.

pressing an individuality of the cell as is ordinarily implied. In the embryology of the spinal cord it is found that the spongioblasts are individual cells only during the earliest stages of their development. Shortly after the cells of the neural tube are differentiated into those which will develop into neuroblasts and those which will produce the neuroglia (spongioblasts), there occurs a fusion of the latter resulting in the formation of a somewhat reticulated protoplasmic continuum or syncytium. After this fusion, the cytoplasm (syncytium) grows more rapidly than the nuclei divide and this results in the appearance of a marginal veil (*Randschleier*) about the inner, nucleated portion of the tube. The marginal veil at first contains no nuclei and appears as but an excrescence of the syncytium. Nuclei pass into it later.

If attention be now confined to the marginal veil, which occupies the position of the future white substance of the spinal cord, it will be seen that it thickens, the reticulated syncytium continuing to grow, and later appears as larger bands of protoplasm in which are dispersed frequent nuclei. Though the nuclei have increased rapidly, their increase is not in proportion to that of their common cytoplasm.

Soon the nerve axones begin to grow in and occupy the meshes of the syncytium and perhaps perforate it to a more reticulated condition. As the presence of the axones increases and as they grow in size, the bands of the syncytium necessarily become more and more attenuated. Finally when the axones acquire their medullary sheaths, the syncytium is simply moulded in the inter-axone spaces, the larger of which usually contain its nuclei. The nuclei are so distributed that, in transverse sections of the spinal cord, usually but one nucleus will appear in a given inter-axone space, but two or even more may be so caught. In sections passing in the direction of the nerve fibers, there will of course be found many nuclei scattered along the third dimension of the space, appearing as a column of nucleated protoplasm.

The syncytium may now be considered in two portions; that which more intimately surrounds the nuclei (endoplasm) and that which constitutes the attenuated bands or "processes" between the more closely arranged nerve fibers (exoplasm). If two of the inter-axone spaces containing nuclei are near together, the endoplasm may be continuous, and the two areas of nucleated syncytium thus seen in transverse section may be considered as two neuroglia "cells" with anastomosing processes. Two such cells are shown in Figure 2.

2. The exoplasmic portion of the syncytium becomes more homogeneous while the endoplasm remains granular. In the more attenuated portions of the exoplasm (processes of neuroglia cells), neuroglia fibers

begin to take the characteristic stain. In a cell with considerable endoplasm, neuroglia fibers are never found except in the more remote portions of its processes (see Fig. 2). The processes, it must be remembered, are continuous with those of neighboring cells which usually possess less endoplasm, for in the adult material, the great majority of the nuclei possess either a very small amount of endoplasm or none at all.

3. The endoplasm continues to disappear or rather to be converted into exoplasm, and neuroglia fibers appear nearer and nearer the nucleus. This gradual conversion of endoplasm into exoplasm results in the well-known isolated masses of nucleated granular protoplasm which are usually described as neuroglia cells. Depending upon the extent to which transformation has taken place, these masses may be stellate, the processes pointing toward the spaces between the neighboring nerve fibers (Fig. 3, *c*), or fusiform (Fig. 2, *c*), or the nucleus may retain but a granular halo of endoplasm about it (Figs. 3 and 4, *d*). Remembering that the conversion of endoplasm into exoplasm takes place from all directions, the mass becoming surrounded by exoplasm, one expects to find neuroglia fibers passing both above and below a "cell" in this phase. Often, however, neuroglia fibers seem to actually pass through the endoplasm and sometimes even to terminate in it.

4. Continued transformation of the endoplasm results in its complete disappearance giving the often described free nuclei with neuroglia fibers passing over and about them in all directions and forming the characteristic loose feltwork among the nerve fibers. Since the neuroglia fibers are formed out of a common syncytium rather than from individual cells, the fact that a single fiber may be traced through the domain of several "neuroglia cells" is nothing more than is to be expected.

The question whether the fibers are intercellular or intracellular in origin has been often discussed. It is seen at once that they can be considered intercellular only when one looks upon the free nuclei or nuclei with a small quantity of endoplasm about them, as neuroglia cells. Otherwise they are intracellular, or better, intrasyncytial in both origin and position.

The nerve fibers of the spinal cord do not occupy the whole of the *Randschleier*. There is always left a thin marginal veil about the periphery immediately underlying the pia mater. This zone or cortex of the cord, varies in thickness for different animals. In this the neuroglia fibers develop undispersed by the nerve fibers and the result is a thicker feltwork of fibers, which in the elephant and human spinal

cords, is capable of being seen with the unaided eye, showing as a thin blue margin when stained by the Benda method. It should here be inserted that in a series of preparations (to be mentioned below) of the spinal cords of developing pigs, neuroglia fibers do not begin to appear or do not stain by the Benda method, till after the myellation of the nerve fibers has begun.

Like the other connective tissues of the body, it is probable that neuroglia fibers, after they are differentiated as such, may still have the power of further growth, thickening, and expansion. If so, a continuous conversion of endoplasm into exoplasm must not be necessary for the process.

5. Further changes to be noted occur in the neuroglia nuclei alone. A classification of these is difficult and unnecessary for they merely present one series of transitions or phases of activity. All nuclei with endoplasm about them are of the large vesicular type. Many without endoplasm are of this type also. The remainder show different phases of shrinkage, increased density in staining and perhaps very gradual karyolysis (*f, g, h, i*, Fig. 4).

The neuroglia is capable of growth after adult life is attained. It is capable of hypertrophy. The gliomatous tumors are considered to result from this power. Exactly what type of the nuclei takes part in the process is unknown. In sections of such tumors, the large vesicular type predominates greatly, and Brodmann describes "cells" possessing an unusually large amount of cytoplasm. Also, at need, neuroglia may take part in the formation of scar tissue. The connective tissues as a whole gradually increase normally with age after adult life is reached. "A man is as old as his arteries" or as the meninges of his central nervous system. If the above observations made from the spinal cord of a practically adult elephant have to do with phases in the formation of neuroglia fibers, it is probable that neuroglia also continues slowly to grow with the age of the animal. Observations made from adult material, however, are neither wholly adequate nor conclusive.

To verify impressions obtained from the adult spinal cord as to the processes by which the neuroglia fibers are developed, the study must necessarily be transferred to the developing material. For this purpose a set of preparations is now nearly completed. The pig was chosen as the source of this material because of the greater ease with which a series of embryos of this animal may be obtained. The set of preparations involves transverse sections from the cervical region of the spinal cords of a series of embryos and fœtuses ranging from 5 mm. to 30 cm. in length, and likewise from a suckling pig of two weeks and from the

adult. The series comprises sixteen stages in the growth of the animal. Four separate methods are employed upon each: 1. Fixation in Zenker's fluid, thin paraffin sections stained with Ehrlich's hæmatoxylin and congo red; 2. Zenker's fluid, paraffin sections, Mallory's stain for white fibrous connective tissue;¹⁴ 3. Fixation in 10% formalin, and prepared by the Benda neuroglia method as employed by Huber (*loc. cit.*) and the same as used upon the elephant material; 4. Pieces were fixed in Van Gehuchten's (Carnoy's) fluid, subjected to continued extraction with ether in the Soxhlet apparatus, and digested by pancreatin according to the method devised by Flint.¹⁵ For stages occurring earlier than found in embryos of 5 mm. the work of other investigators, chiefly that of His, will be accepted and drawn upon.

The study of this series of preparations is now underway and the results obtained will be given in an early paper together with certain observations which I now feel sure of being able to add and with illustrations showing the principal phases in the development of the neuroglia fibers. At present it may be said that the study of the developing material has so far corroborated with considerable certainty the impressions obtained from the adult tissue as to the method by which the neuroglia fibers are formed.

Neuroglia, the chief fibrous supporting tissue of the central nervous system, when compared with the other connective tissues of the body is more similar to white fibrous than to any other variety. The resemblance, of course, is a morphological rather than a chemical one, and, from the nature of the case, is more apparent in the looser frameworks of organs than in the more compact arrangements of white fibrous tissue. That neuroglia fibers differ in their chemical properties from those of white fibrous tissue is the chief means by which the one is distinguished from the other. Like adult neuroglia, white fibrous tissue consists of fine fibrils in the meshes of which occur "cells" either in the form of free nuclei or as nuclei with varying amounts of cytoplasm about them. When this cytoplasm is sufficiently abundant it usually shows branches, giving the cells either a spindle-shaped or irregularly stellate form. Such cells appear to assume the general shape of the space they occupy, and the branches of neighboring cells usually anastomose through the channels uniting the contiguous cell spaces. The fibrils of white fibrous tissue are found, according to locality, either as anastomosing bundles or as finer feltworks, varying in arrangement

¹⁴Mallory. *Journal of Experimental Medicine*, Vol. V, 1901.

¹⁵Flint. *Johns Hopkins Bulletin*, Vol. XIII, Nos. 131-132, 1902. Also *Am. Jour. of Anatomy*, Vol. I, No. 3, 1902.

as is best suited for the elements of the organ they support. Neuroglia, unlike white fibrous tissue, is found in but one organ and its fibers are therefore found in but one general arrangement. Its peculiarities in arrangement, then, may be largely imputed to peculiarity of purpose.

During the latter part of the preparation of this paper, Mall's interesting and most necessary paper appeared "On the Development of the Connective Tissue."¹⁶ This paper deals with all the connective tissues except neuroglia. If, after studying the neuroglia in developing material, one reads Mall's paper, especially the part dealing with the development of white fibrous tissue, it will be found that one can cull statements from it which, when arranged in sequence, will quite fully describe the phases in the development of the neuroglia fibers. For the study of developing white fibrous tissue Mall chose the subcutaneous tissue of the back of the embryo. In its final arrangement this, of course, differs from neuroglia.

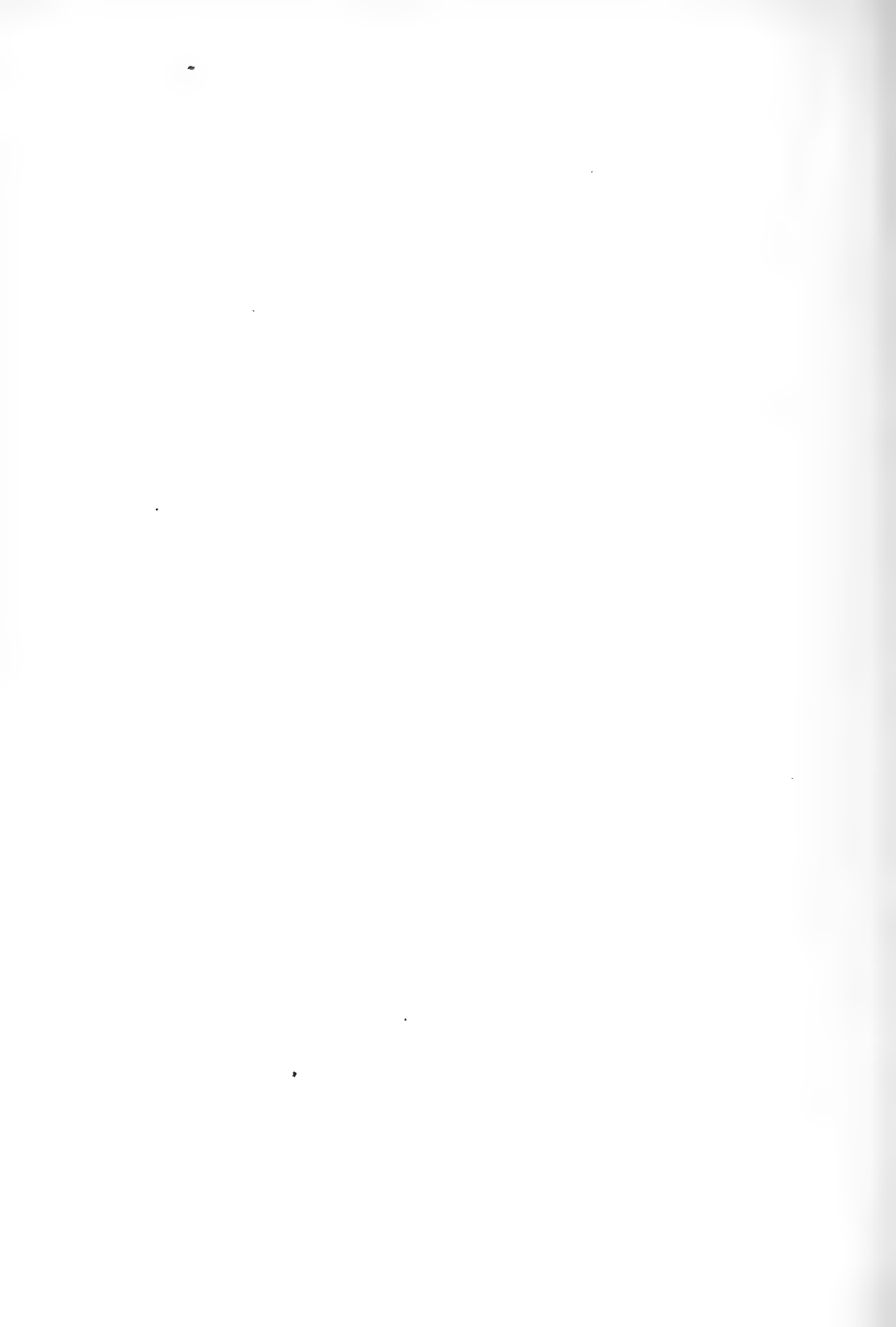
Mall does not mention changes in the connective tissue nuclei similar to those above described for neuroglia. His observations, however, were necessarily made upon embryos and fetuses alone. Concerning the later stages in these he states: "After the activity of the nuclei and endoplasm has produced enough exoplasm to give rise to all the white fibers of the skin, which is the case in embryos from 20 to 30 cm. long, they cease to be so prominent and sink back into the form of irregular cells." All of the neuroglia nuclei of pigs of 21 cm. and below are of the large vesicular variety. In larger fetuses the other types begin to appear. At 21 cm. all the nuclei apparently possess more or less endoplasm, and nuclei with a large amount of endoplasm are much more common than in the adult. Between 16 and 21 cm., the neuroglia fibers first begin to take the characteristic stain and it is during this period that the processes of myelination go on most rapidly, though there are signs of beginning myelination somewhat earlier. Pigs at term measure from 26 to 32 cm.

The dura and pia mater as stainable and indigestible membranes are evident long before the neuroglia fibers make their appearance. In pigs of 4 cm. they show the characteristic fibrillar structure and though thin they both stain by Mallory's method and resist digestion. Up to 21 cm. the whole spinal cord digests out leaving only a thin cuff—the pia mater. At 28 cm. the entire gray figure digests out clean, while in the white substance the digestion is less complete. The series of digested preparations is not yet finished.

¹⁶ Mall. *Am. Jour. of Anatomy*, Vol. I, No. 3, 1902.

With the exception of those accompanying the blood-vessels, the pia mater sends but few ingrowths into the white substance and these are very delicate. Many nuclei are present which, without doubt, enter the spinal cord from the outside, and are therefore mesodermal in origin but whether any of these take part in producing neuroglia is difficult to determine because a neuroglia cell may not be designated as such till it acquires certain characteristics.

[NOTE.—In Dr. Hardesty's original drawing for Fig. 1 the black neuroglia fibers of the marginal veil appear in a transparent, white area invaded by a few faint strands from the pia. The half-tone reproduction here shown fails to give the desired contrast, since the screen carries considerable color into the marginal veil, confusing this somewhat with the gray pia which lies immediately outside of the black felt-work of neuroglia fibers.—ED.]



THE CARDIAC GLANDS OF MAMMALS.

BY

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WITH 16 TEXT FIGURES.

When we consider the immense amount of energy that has been expended on the investigation of the gastric glands since the discovery of the chief cells by Heidenhain and Rollet in 1870, it is a matter for some surprise that so little interest should have been aroused in the small zone of glands surrounding the cardiac orifice of the stomach, now generally known as the cardiac glands. This fact is all the more surprising when we remember that, in some mammals, these glands are by no means restricted to the narrow zone mentioned above, but may equal or even exceed in number the ordinary fundus glands composed of chief and parietal cells.

In examining the literature of this branch of research, it is difficult to decide to whom belongs the honor of discovering the glands in question, because the older anatomists employed the term to designate all the glands of the proximal portion of the stomach including the fundus glands. This example is followed in some recent text-books of Histology, the authors not recognizing that there are glands of more than two kinds in the stomach. In the interest of uniformity it seems desirable to employ the nomenclature adopted by Oppel, 96, in his compilation of the literature dealing with the stomach, and to designate the complex glands, composed of chief and parietal cells, fundus glands, reserving the expressions cardiac and pyloric glands for those which surround the respective orifices of the stomach.

Cobelli, 66, seems to have clearly recognized the cardiac glands in man as early as 1866, when he published a description in which they are referred to the same category as the pyloric glands, which he had studied some two years before, as gastric mucous glands.

The next contribution of importance is the account of the structure of the stomachs of two kangaroos, *Macropus* and *Dorcopsis*, published by Schäfer and Williams, 76, in 1876. These authors describe a very extensive region of the mucous membrane in these animals as being formed of simple glands, containing one kind of cell which resembles closely the cells of the submaxillary gland.

Ellenberger, **88**, was the first to recognize the importance of the cardiac glands as indicated by their great extent in the pig, and the first to dissent from Cobelli's view that they are mucous glands. In his text-book he expresses the opinion that they are serous glands of a special kind, differing from both the fundus and the pyloric glands. This view is shared by Edelmann, **89**, the author of the most important contribution on the cardiac glands. Because of the importance of this work as containing the only comprehensive discussion of the cardiac glands, and because we owe to Edelmann most of our knowledge of the nature and distribution of these structures in mammals, it seems desirable to quote at some length his conclusions:

“Im Magen der Säugethiere giebt es eine besondere Schleimhautregion mit belagzellfreien Drüsen, welche sich durch ihre Lage und durch histologische Eigenthümlichkeiten von der Pylorusdrüsenregion unterscheidet.

“Die Cardiadrüsenregion liegt entweder dort, wo die Schlundschleimhaut mit der Verdauungsschleimhaut des Magens Zusammenstosst, oder sie kleidet besondere Säcke aus oder liegt auch zum Theil isoliert in Vormägen ganz von cutaner Schleimhaut umgeben. . . .

“Eine Cardiadrüsenregion scheint bei den meisten Säugethiern vorzukommen. Sie fehlt sicher bei den fleischfressenden Cetaceen und den Wiederkäuern.

“Die Drüsen der Cardiadrüsenregion unterscheiden sich von der Fundusdrüsen nicht nur durch das Fehlen der Belagzellen, sondern auch von diesen und den Pylorusdrüsen durch die Anordnung und den Verlauf der Tubuli und die Eigenthümlichkeiten ihrer Drüsenepithelien.”

This difference on which Edelmann lays much stress consists in the fact that the cardiac glands subdivide at the neck of the gland, are arranged in groups, and have not so tortuous a course as the pyloric glands.

Edelmann's conclusion that the glands are present in all Mammalia with the exception of the carnivorous Cetacea and the Ruminants, is opposed by Fleischmann, **91**, who refers to their absence in three of the suborders of Rodentia, the Lagomorpha, Hystricomorpha and the Sciuromorpha, and concludes that they were certainly absent in the ancestral Rodents.

Further research, however, tends to support Edelmann's conclusions as to their wide distribution in mammals and as to the great extent of the mucous membrane which they may occupy. For example, the investigations of Boas, **90**, Pilliet, **85**, and Cordier, **93**, on the structure of the camel's stomach seem to indicate that the greater part of the cylindrical segment of the stomach in this animal is occupied by cardiac glands, and that the glands of the so-called water cells may properly be

referred to the same category. Cardiac glands have also been demonstrated by Oppel, **96**, in *Dasyurus* and *Perameles*. The glands described by Salomon in the cœcal sac of *Cercopithecus* and *Inuus* are also in all probability cardiac glands, although the author did not recognize them as such.

Ellenberger, **88**, not only dissented from the commonly accepted view that the cardiac glands are mucous glands, but went farther and attempted a solution of the question of their physiological rôle. He found, in conjunction with Hofmeister, **85**, that the cardiac glands of the pig contained a diastatic ferment. Negrini, **86**, also asserts the presence of an amylolytic ferment in the cardiac mucosa of the pig, in greater quantities than could be accounted for by the amount of blood present in the organ. The results of Ellenberger and Hofmeister are confirmed by Edelmann who tried many of the so-called mucin stains with negative results. Edelmann's explanation of the function of the cardiac glands is as follows:

“Die physiologische Bedeutung der Cardidrüsenregion beruht in der Bildung einer Art Vorraum im Magen, welcher keine Säure, dagegen Fermentquellen enthält, und in dem die Verdauung der Stärke vor sich gehen kann.” “Als Schleimbildende Drüsen sind die Cardidrüsen nicht aufzufassen.”

Schaffer, **97**, also, in his recent studies on the human cardiac glands, ranges himself on the side of Edelmann and Ellenberger as to the serous nature of the cardiac glands. Using the more precise mucus stains recently devised by Mayer, he was unable to obtain any reaction in the cells of the cardiac glands, which he, therefore, compares to the chief cells of the fundus glands, and to the pyloric gland cells.

There is some danger of attaching too much importance to these negative results of Schaffer and Edelmann. In the first place, mucin is not a single chemical substance for which it is possible to establish definite staining reactions, which will enable us to demonstrate it wherever it occurs. There are on the contrary good reasons for supposing that, as Huppert, **96**, points out, the number of mucins belonging to a single class, the glycoproteids, are as numerous as the albumens which are available for entering into such a combination with a sugar. In the second place, the morphological evidence adduced by Krause, **95**, and Langley, **84**, in the salivary glands and the chemical experiments of Hammarsten, all point to the conclusion that there are several stages in the elaboration of mucins in secreting cells. It is probable also that there exist in mucin-forming cells differences of secretory equilibrium analogous to those which have been noted by Langley in pepsin-form-

ing cells, and that, for example, one cell may store its mucin in a more elaborated form than another cell which is its morphological equivalent. It is unreasonable to expect that the different mucins and different stage of elaboration of mucin would present always the same staining properties.

The importance of this point of view is clearly recognized by Mayer, 97, in his recent paper "Ueber Schleimfärbung" in which he points out that, in relation to his muchæmatein solution, it is possible to construct a graded series beginning with mucins which stain only with difficulty and passing by imperceptible gradations to mucins which stain rapidly and deeply. He was also able to obtain in the cells of the submaxillary gland of the hedgehog, the secretion of which, according to Krause, does not contain mucin, a typical mucin reaction.

It may be pointed out, also, that the obtaining of mucin reactions in secretory cells is to a certain extent dependent on the technique of the individual investigator. The writer, for example, as will be indicated in the more special portion of this paper, has had little difficulty in staining the cells of the cardiac glands in every instance with mucicarmine and muchæmatein, and, in some cases, with other mucin stains such as indulin and methyl blue.

It is clear from the foregoing that *negative* results with mucin stains are absolutely without value as evidence of the serous nature of secreting cells, and that positive results are only of value in so far as they are confirmatory to evidence derived from other sources. Some caution is even necessary in drawing conclusions from the structure of the cell. The submaxillary gland of *Erinacæus* is a case in point, where the cells have both the structure and staining properties of mucous cells, although no mucin is secreted by the gland. Another case is that of the pyloric gland which was for many years interpreted as a serous gland, simply because the nucleus is often spherical instead of crescentic, and because the cells may contain considerable residual protoplasm.

Edelmann's theory of the function of the cardiac glands would be a simple and sufficient explanation of the occurrence of these glands in herbivorous mammals, but for the extraordinary fact that they are absent or feebly developed in the most highly specialized of herbivores, the ruminants. The occurrence of large areas of cardiac glands in all Perissodactyls and in the pigs, camels and llamas among the Artiodactyls, precludes the possibility of supposing that they were absent from the stomachs of the herbivorous ancestral types, in which their original occurrence is rendered more probable by the discovery by Zimmermann and Sal, 94, of what may prove to be remnants of cardiac glands along

the œsophageal groove in the sheep. If the glands are really of importance as sources of a digestive ferment, it is difficult to understand why they have disappeared in a group of animals in which their presence would be such an immense advantage. One would rather expect that the processes of natural selection would tend to preserve and perfect them. The importance of the occurrence of an amylolytic ferment in the cardiac mucosa is materially reduced by many recent researches which go to show the widespread occurrence of sugar-splitting ferments in the blood and tissues of mammals, and by the observation of Ellenberger and Hofmeister that a diastatic ferment is present in the fundus mucosa of the pig where, owing to the acidity of the gastric secretion, it could be of very little service in digestion.

In the present state of our knowledge it does not seem possible to assign any definite function to the cardiac glands, nor does investigation by physiological methods appear to offer much hope of solving this problem. It seems to the writer that the first step in the further elucidation of these glands must consist in the comparison of them, as regards structure, staining, and microchemical reactions and mode of regeneration, with the other glandular elements of the stomach. It is true that both Edelmann and Schaffer have instituted comparisons of this kind, but at the time of the publication of Edelmann's paper, no adequate description of the structure of the chief cells and pyloric cells existed, and Schaffer's comparison of the cardiac gland cells with the chief cells as well as the pyloric gland cells shows clearly that he was unaware of the important differences between the two.

Another problem which must be considered in connection with the question of the histology of the glands is that of their phylogeny. The fact that only fundus and pyloric glands are represented in reptiles and batrachians makes the question of the source of the cardiac glands a very interesting one. Are they to be regarded as derived from pre-existent structures, for example, as œsophageal glands which have been taken over into the stomach, or fundus glands which have been peculiarly modified, or finally as cœnogenetic structures which have arisen in Mammalia in response to a new functional demand? Oppel, 96, has suggested, but in a tentative rather than an assertive mood, that they may represent the simple glands of lower vertebrates, which have not all been differentiated into the complex fundus glands of mammals, but admits that the great structural differences are scarcely compatible with such a view. Edelmann contents himself with stating their possible sources of origin without attempting to decide between them. More recently Oppel, in a brief discussion of Schaffer's discovery of parietal

cells in the cardiac glands of man, suggests the possibility that these structures may have been derived from the fundus glands by the gradual disappearance of the parietal cells and that this change may be the initial phase of the process by which the glands are replaced by stratified epithelium.

It will be observed that, with the exception just noted, the only attempts which have been made to explain the occurrence of cardiac glands in mammals have been based on the *a priori* assumption that they have a useful function to perform in digestion. The alternative hypothesis that they constitute a stage in an advancing process, and that their production and subsequent disappearance in some forms is the result of the continued and consistent action of the same causes, has scarcely been discussed at all.

The basis for comparison adopted in this paper is the structure of the chief cells as described by the writer and confirmed by Zimmermann, 98, Cade, 01, and others. In 1896, in a preliminary note, 96, and subsequently in a more extended paper, 98, I pointed out that the chief cells of the body of the fundus glands in common with certain other serous glands possess structural and microchemical characters which enable one to distinguish with ease between them and all other glandular elements of the stomach. These are briefly as follows: The cell is divisible into a proximal and distal zone. The distal zone next the lumen contains granules of zymogen inclosed in protoplasmic trabeculæ. The proximal zone, of variable extent at the attached end of the cell, exhibits an indistinct radial striation (basal filaments of Solger), and stains strongly in nuclear dyes, owing to the presence in it of a kind of chromatin, prozymogen, which, like the chromatin of the nucleus can be shown by Macallum's microchemical methods to contain iron in a masked form as an organic compound. MacCallum, 98, has since shown that this substance as well as the zymogen granules contains phosphorus. I found that the chief cells of the neck of the gland were the homologues of the large clear cells of the corresponding portion of the fundus gland of lower vertebrates and of the cells of the pyloric glands, all of which differ in fundamental points from the ferment-forming chief cells of the body of the gland. They contain neither basal filaments nor granules of zymogen and their protoplasm gives only a faint microchemical reaction for iron. These neck chief cells and pyloric gland cells I found to pass into the surface epithelium by a gradual transition, the mean of which is reached at the deep end of the gastric pits or foveolæ where actively dividing cells are found which are probably engaged in replacing, in accordance with the "wander"

theory of Bizzozero, the surface epithelium and to some extent these peculiar neck cells and pyloric gland cells. Because of this relationship to the surface epithelium, which is undoubtedly muciparous, and because of the fact that it stains readily with Mayer's mucin stains and with certain other distinctive stains such as indulin, I regard the secretion of the neck chief cells and pyloric gland cells as of a mucous nature.

The first section of this paper will be devoted to the extension of the same methods of research to the cardiac glands. The second section will be devoted to a discussion of the phylogeny of the cardiac glands and of some points in the evolution of the complex forms of mammalian stomachs, with which, in the writer's opinion, these glands are intimately connected.

THE HISTOLOGY OF THE CARDIAC GLANDS.

I. THE CARDIAC GLANDS OF MAN.

I have chosen the cardiac glands of man for preliminary description because of the importance of the structure of the human stomach from the physiological and pathological standpoint and because of the fact that an opportunity, like that which I have fortunately met, so rarely presents itself of securing the normal gastric mucous membrane of man in a good state of preservation. The cardiac glands of man also illustrate very well the points which I regard as of histological and phylogenetic importance. My material was secured at a necropsy on the body of an executed criminal, a young man of about thirty years of age, at which I was enabled to be present through the kindness of Professor A. Primrose. Pieces of the mucous membrane of the cardiac orifice and from the important regions of the stomach were fixed in alcoholic bichromate sublimate and in absolute alcohol. The whole of the regions surrounding the cardiac and pyloric orifices were similarly fixed in the bichromate sublimate mixture and the rest of the stomach then preserved in seventy per cent alcohol for topographical study. On examination, all of this material proved to be in an excellent state of preservation although the superficial epithelium was lost in some places and somewhat altered in others. The necropsy occurred about forty-five minutes after death.

The cardiac glands of man have been recently the subject of a very careful research by Schaffer, 98, whose descriptions, in so far as they are concerned with the topography and general structure of the glands leave little to be desired. According to Schaffer the cardiac gland zone begins from one-half to four mm. above the termination of the œsophageal epithelium, and extends a distance into the stomach which

varies with different individuals and in different portions of the zone in the same individual. The maximum extent is given by Kupffer, 83, as 1.5 cm., the minimum as .5 cm. That the maximum may be much greater than this is indicated by the present case in which the cardiac glands begin nearly 3 mm. above the termination of the œsophageal epithelium and extend a distance of 4.3 cm. into the stomach. The latter measurement is following the various folds of the mucous membrane, the length in a straight line being 3.4 cm.

The mucous membrane at different points in this region is of very unequal thicknesses, the differences in this respect being partly due to the size and mode of aggregation of the glands, partly to the number and size of the lymphatic follicles which, as Schaffer indicates, are very numerous. In general it may be said that the greatest thickness occurs at or near the œsophageal epithelium and the minimal at the point where the cardiac gland zone passes into the fundus gland zone. In a zone comprised within a distance of 2 mm. from the œsophageal epithelium the thickness of the mucous membrane, not including the muscularis mucosæ, varies from .99 mm. to 1.326 mm. Three millimeters from the œsophagus in one section which is fairly representative the thickness is .969 mm. From this point onward there is a gradual diminution in thickness until at a point 11 mm. from the œsophageal epithelium the minimum thickness of .5 to .6 mm. is reached, which is maintained, with slight variations probably due to different degrees of contraction of the intrinsic muscle fibers, for the rest of the cardiac zone.

This great difference in the relative thickness of the mucous membrane of the proximal and distal portions of the zone is due to a difference in the nature of the glandular aggregates, not to a fundamental difference in their structure. Just at the termination of the œsophagus, the glands consist for the most part of freely branched and tortuous tubules, derived from a narrow duct which ascends in the direction of the free surface of the mucosa to open alone, or more frequently in common with others, into a depression of the surface which corresponds to the ducts or foveolæ of the glands of the rest of the stomach. Several such tubulo-racemose glands are commonly grouped together into a sort of lobule more or less definitely separated from adjacent groups by a sort of septum of collagenic fibers containing bands of smooth muscle. The ducts of these glands are frequently the seat of retention cysts which may be of such a size as to be readily recognized without the aid of a microscope. These may occur near the opening of the gland into the foveolæ or deeper in the mucosa. The cysts appear as large oval ampullæ into which the branches of the gland open. The glands and ducts are lined throughout by secreting cells.

As the distance from the œsophageal epithelium increases and the mucous membrane diminishes in thickness the tubules become less and less branched and the peculiar grouping disappears, although an apparent grouping may sometimes be observed, caused by the regular occurrence at intervals of lymphoid follicles. The cysts also become rare and the number of foveolæ opening on a given area more numerous. In the distal thin portions of the mucous membrane there is little difference between the cardiac glands and the adjacent fundus glands as regards their shape and mode of branching.

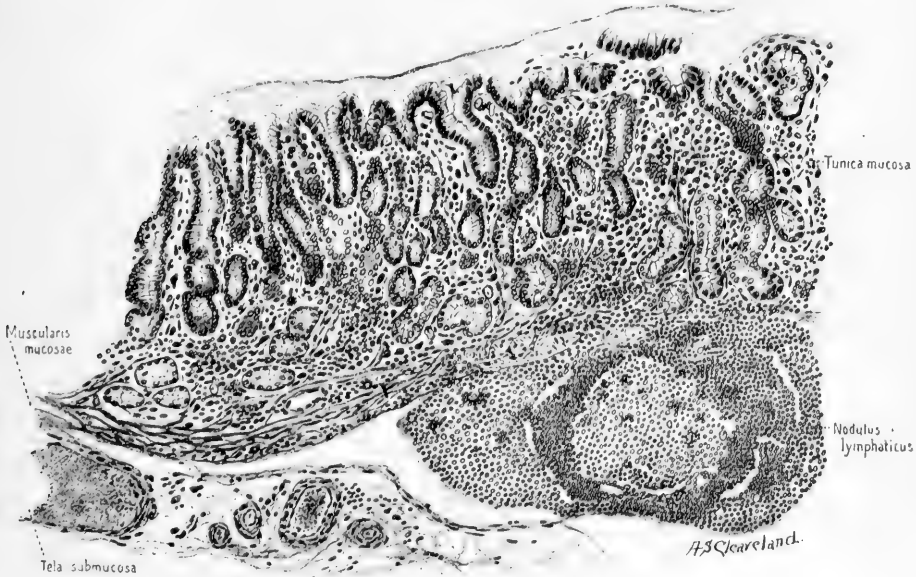


FIG. 1. Longitudinal section of the tunica mucosa of the cardiac region of man, 2.5 cm. from the edge of the œsophageal epithelium. $\times 70$. The leucocytes and plasma cells are considerably more numerous than in the figure.

Throughout the area there is considerable interglandular tissue of a reticular character, the meshes of which are filled with leucocytes of various types. Considerable collagenic tissue is also present between the bases of the glands and the muscularis mucosæ. Many bands of smooth muscle fiber ascend from the region of the muscularis mucosæ in the direction of the epithelium. The structure of this interglandular tissue will be discussed at greater length in a paper on the "Structure of the Human Stomach," now in course of preparation.

Lymph follicles are very numerous in the proximal thicker portion. They occur at fairly regular intervals and are situated in the mucosa,

but as the membrane becomes thinner they become first restricted to the deeper portion of the mucosa and finally break through the muscularis mucosa to extend into the submucosa. In the latter case the muscularis mucosæ is interrupted opposite the follicle, the superficial tissues of which are continuous through the gap with the diffuse adenoid

tissue of the mucosa (Fig. 1).

There are reasons, which will be discussed later, for regarding the cardiac glands as decadent structures. On this account it is desirable to select for preliminary description those glands in which this feature is least apparent. Such are the glands of the thinner distal portion of the mucous membrane of the cardiac zone. To avoid confusion, I shall call the funnel-shaped depressions of the surface into which the glands open, foveolæ, as being a preferable term to the compound expressions gland-duct

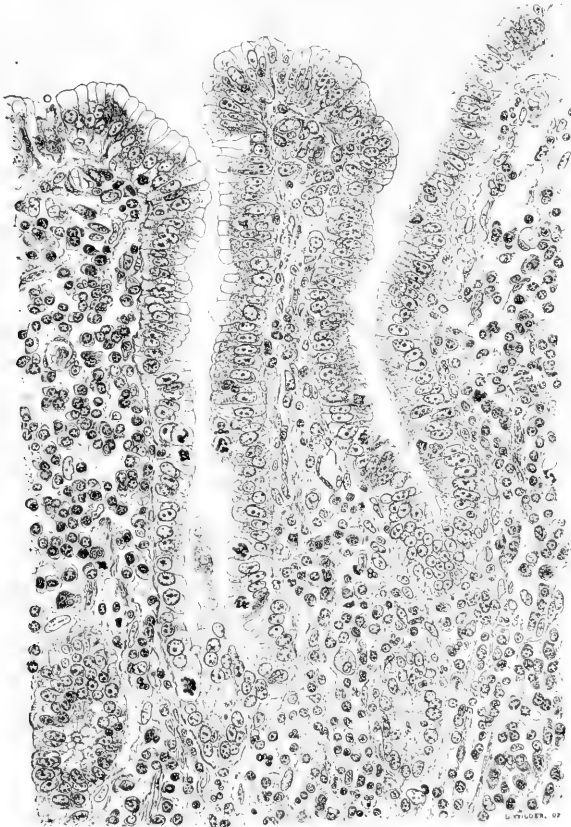


FIG. 2. Two foveolæ gastriciæ from the cardiac region of man, $\times 280$. The mucous theca becomes reduced, in the lower half of the foveola, to a very narrow margin along the lumen. The cells in this position are shorter and a number of deeply staining mitotic figures are seen. A few polymorphonuclear leucocytes and lymphocytes are to be seen in the epithelium. The cells of the interstitial tissue are largely Unna's plasma cells with a few polymorphonuclears and eosinophiles.

and stomach-pit, commonly employed.

The epithelium of the free surface was lost in most of the material at my disposal, but where it was retained resembled in all essential points that of other stomachs. The epithelium of the upper portion of the foveola is represented in Fig. 2 and is very similar to the epithelium of

similar portions of the stomachs of other mammals. The cells are elongated conical structures. A well-defined mucous theca occupies the outer third of the cell, an oval nucleus the inner protoplasmic portion. Passing down the sides of the foveolæ there is observed a gradual reduction in size, from cell to cell, of the mucigenous border, and for a variable distance at their lower ends foveolæ are lined by columnar cells in which only a very narrow band of mucin can be distinguished along the free border. The spherical or oval nuclei of these cells are, as compared with the nuclei of the cells of the surface epithelium and those of the glands, exceedingly rich in chromatin and are frequently seen in the process of mitotic division, from one to four or even more mitoses being seen in each foveola. Many leucocytes, both lymphocytes and polymorphonuclear cells, could be seen in my material, within the epithelium of the foveolæ, in most cases occupying spaces between the cells but occasionally intracellular.

For a short distance at their upper ends, the glands are lined by cells similar in all respects to those of the deep ends of the foveolæ, but at a short distance from the foveola the cells begin to give evidence of greater activity in secretion inasmuch as the portion of the cell so engaged increases in size and the protoplasmic portion containing the nucleus becomes correspondingly reduced. This feature becomes more and more prominent as the bottom of the gland is approached, where the cells may be entirely filled with secretion. In such cells the nuclei are compressed, flattened or crescentic, and are found at the base of the cells. As a rule, there is considerable variability in the cardiac glands as to the degree of loading exhibited by the individual cells of a terminal tubule or of different terminal tubules, some cells being completely filled with secretion, others only partly so. In the latter type, the cell is sharply divided into two zones, a proximal protoplasmic zone in which a fine reticulum may be seen, and a distal zone which appears transparent in ordinary preparations and contains the stored-up secretion (Fig. 3, A).

The outer zone does not contain basal filaments, nor is it markedly chromophile. Examined for masked iron by the usual methods, a slight reaction is obtained, but no greater than that exhibited by the protoplasm of the cells of the surface epithelium, the pyloric gland cells, and the neck chief cells of the fundus glands. The inner zone of these cells stains but faintly in hæmatoxylin and eosin, but one can readily recognize a wide-meshed alveolar structure, the meshes of which correspond to the protoplasm between the droplets of secretion. The apparent thickness of these protoplasmic meshes is increased by the precipitation on them of the solids of the secretion. Frequently the

mass of secretion contained within a cell is incompletely divided into two masses by a strand of reticular protoplasm stretching across the cell (Fig. 3, A). In such cases the proximal mass of secretion usually contains a protoplasmic network composed of thicker trabeculae than the distal mass. This transverse band is particularly obvious in specimens stained by Heidenhain's iron hæmatoxylin method and is of frequent occurrence in all the mucin-forming elements of the stomach as well as in the cells of the glands of Brunner (Zimmermann,

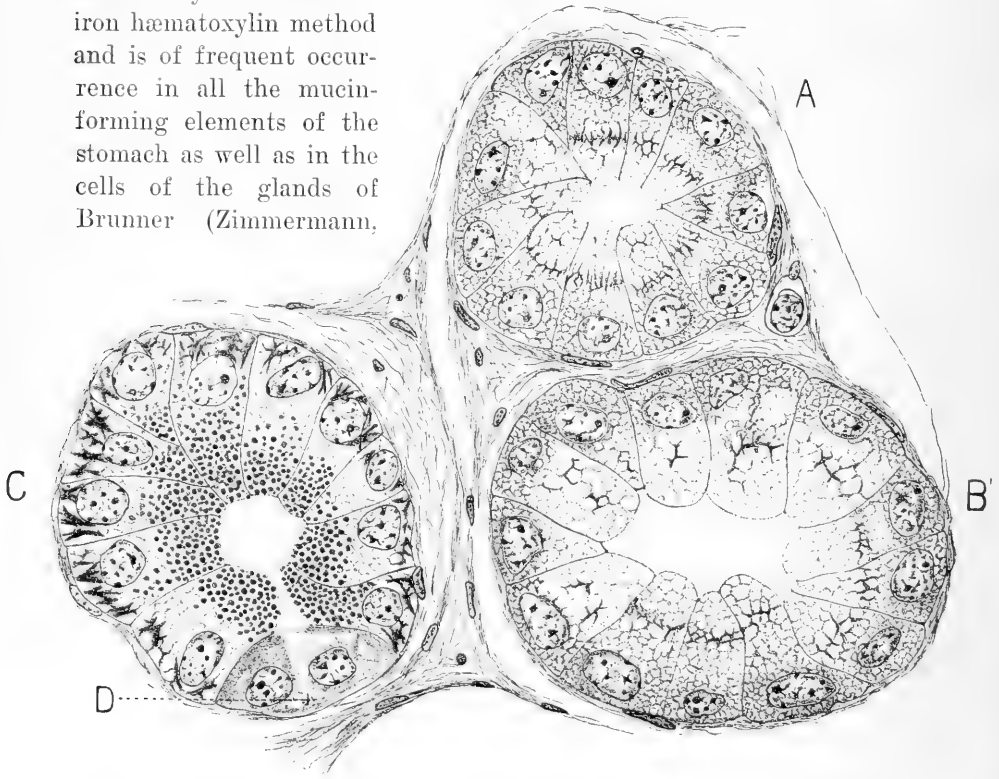


FIG. 3. Three tubules from cardiac glands of man. $\times 1000$. A, Mucous tubule in which cells are in early stage of mucin formation. B, Mucous tubule showing cells in various stages of mucin formation. Subdivision of mass of secretion into two masses by transverse bridge of protoplasm and the gradual disappearance of the latter as the proximal mass increases in size. C, Tubule formed of cells of the type of the chief cell of the body of the fundus gland, showing zymogen granules in the distal zone and prozymogen (basal filaments) in the proximal zone. D, Binucleate parietal cell with intracellular secretion channels.

98) and in mucous cells from other sources, Maximow, 01. As the cell fills with secretion (Fig. 3, B), the distinction above referred to between the protoplasmic framework of the two masses of secretion gradually disappears and the transverse band which separates them becomes disintegrated and may finally disappear, although, as a rule some slight re-

mains of it may usually be recognized in the interior of the cell. In some cases the proximal mass of secretion only is present so that the cell has a protoplasmic distal border along the lumen, and reminds one strongly of Krause's figures of the mucin-forming cell of the retro-lingual gland of *Erinaceus* at an early stage of mucin formation.

The mitoses seem to be entirely confined to the cells of the bottom of the foveolæ and adjacent portions of the gland. I have not observed a single instance of cell division in the surface epithelium nor in the cells at the bottom of the gland, although cells near the foveolæ may divide even when they contain a good deal of secretion. The great mitotic activity at the junction of gland and foveola, as well as the gradual transition from this point in both directions leads me to believe that this is the site of the reproduction of both the surface epithelium and the glandular epithelium, both of which are probably replaced when lost by a gradual migration of cells from the point at which they are reproduced.

Passing on, now, to the complex glands of the beginning of the area this simple relation of the cellular elements to one another is found to be by no means the rule. Many anomalies are seen. The cells of the lower ends of the foveolæ while similar in the majority of cases to those already described may lose their mucigenous border altogether and appear protoplasmic throughout. Again the transition into the gland may not occur at all or be little marked, the secretion filling only a small portion of the free border of the cell even in tubules remote from the main duct. Thus, one may see side by side in the same gland, cells or tubules equally remote from the duct which exhibit the two extremes of secretion, some filled with stored-up product, others containing but little. These are, obviously, differences of physiological equilibrium and do not introduce any new difficulties in the way of interpreting the glands. In this region the mitoses, as in the case of the more typical glands, are practically confined to the upper portions of the ducts and the adjacent portions of the gastric foveolæ. There is also in the complex glands near the œsophageal epithelium a great variability in the size of the terminal branches of the tubules which compose the gland, some being many times as large as others.

The important question now arises, what is the nature of the stored-up secretion in these cells? The transition to the surface epithelium and the probable mode of reproduction of the glandular elements as indicated by the mitoses, both suggest that the secretion may be chemically, as the cell is genetically, related to that of the surface epithelium, that is to say, may consist largely of mucus. On the contrary Schaffer,

97, and Edelmann, 89, agree that the contents of the cells do not stain with mucin stains. In view of the fact that Schaffer used for this purpose mucicarmine and muchamatein as recommended by P. Mayer, and that my results with similar solutions are directly opposed to his, inasmuch as I succeeded in staining the secretion in the cells of the cardiac glands as well as those of the surface epithelium, it may be of interest to discuss briefly the reasons of the discrepancies in our results. Some reference has already been made to the probably great chemical diversity of the mucins and to the work of Mayer on their staining properties. In the course of this paper he says:

“Ich selber habe bisher das Wort Mucin geflissentlich vermeiden und dafür stets von Färbung des Schleimes gesprochen. In der That wissen wir vom Schleime der höheren Thiere chemisch noch recht wenig und von dem der allermeisten Wirbellosen so gut wie gar nichts. Oben habe ich bereits angedeutet dass die Schleime sich gegen einen und denselben Farbstoff sehr verschieden verhalten, indem ich bei Besprechung der Lösungen von Hämatoxylin oder Hämatein sagte: In der Regel färbt sich der Schleim, oder: in der Regel färbt er sich nicht. Das sollte heissen: die von mir geprüften Arten Schleim sind je nach ihrer Provenienz verschieden. Man könnte da eine förmliche Reihe aufstellen, die mit solchem Schleime zu beginnen hätte, dessen Färbung kaum zu verhindern ist, und mit solchem enden würde, der sich kaum noch färben lässt. Jener ist z. B. bei Muscheln vertreten dieser findet sich im Darm von Homo.”

I have found that not only do different mucins stain with different degrees of readiness in Mayer's solutions, but that by modifying the composition of the solution or the mode of applying it, many mucins which stain with difficulty in the ordinary method may be made to take the color readily. For example, if a longitudinal section in celloidin of the pylorus of man be placed in Mayer's muchamatein (Hæmatein .2 grammes, aluminium chloride, .1 gramme, 70% alcohol, 100 cc.), only the goblet cells of the surface epithelium and of the glandulæ intestinales stain. If the strength of the solution in hæmatein and aluminium chloride is doubled, then the goblet cells stain strongly and a faint reaction is obtained in the epithelial cells of the stomach and of the pyloric foveolæ. If the strength of the solution is increased fivefold, so that it contains one per cent of hæmatein and one-half per cent of aluminium chloride, both the secretion of the goblet cells in the intestine, and of the epithelium in the stomach, stains intensely and an equally vigorous stain is obtained in the cells of the duodenal glands (glands of Brunner) and in the cells of the pyloric glands. Practically the same result was obtained with mucicarmine. With the diluted solution recommended by Mayer, only goblet cells were stained, but if

the strength of the solution were increased, the gastric epithelium stained. With Mayer's undiluted stock solution of mucicarmine, we find in addition the pyloric glands and duodenal glands stained. Thin sections from which the imbedding mass has been removed and which are allowed to float freely in the solution will give positive results with much less concentrated solutions than sections in celloidin, or sections attached to the slide. For example, I obtained positive results in the pyloric gland cells of the cat and in the neck chief cells of the fundus glands of the same animal, by simply transferring thin sections, cut after imbedding in paraffin, from alcohol to the diluted solutions recommended by Mayer.

If the undiluted mucicarmine solution of Mayer or the muchæmatein solution of fivefold strength be employed, positive results may be obtained with perfect certainty in the glandular cells of the pyloric glands, the duodenal glands of Brunner, the cardiac glands, and in the neck chief cells of the fundus glands of a great many mammals. Material fixed in alcohol or in bichromate sublimate has yielded the best results in my hands, but other fixing agents do not materially alter the character of the reaction. Sections cut in celloidin stain perfectly in the above solutions, although the time of staining with muchæmatein must not be too prolonged or the celloidin mass will take the stain. With mucicarmine, the celloidin stains somewhat, but in the tissues the color is entirely confined to the secretory contents of the cells.

In cardiac glands so treated, the inner portion of the cell, which remains unstained in sections stained by other methods, is deeply colored blue or red according to whether muchæmatein or mucicarmine is employed. The protoplasm of the cells and the nuclei remain unstained. Schaffer's failure to obtain this reaction was probably simply due to the fact that his solutions were too dilute or that he did not take advantage of the greater rapidity of action of the dilute stains on sections unattached to the slide and free from any imbedding mass.

There can be very little doubt that the cardiac gland cells of man are muciparous structures. Their relation to the cells of the surface, the staining reactions which I have observed, the compression phenomena observed in the nuclei in the completely filled cell, and the absence from them of zymogen granules and prozymogen (with certain exceptions to which I shall refer presently) all clearly point to this. I should hesitate to assert, however, that this is the only kind of activity in which the cardiac gland cell is engaged although, indeed, it is the most conspicuous and impresses itself most clearly on the structure of the cell.

A point remains to be discussed which is of the greatest importance in deciding the origin of the cardiac glands, namely, the occurrence in them of the other characteristic elements of the fundus gland, the parietal cells and the pepsin-forming chief cells. Schaffer has shown that the former occur in the cardiac glands of man in varying numbers. This observation I can confirm. The parietal cells of the human cardiac glands exhibit the characteristics which have been described for those of the fundus glands by Zimmermann, 98, are frequently binucleated, and contain distinct intracellular ducts. The parietal cells are not confined to any special region of the cardiac mucosa nor to any definite part of the gland, although I have not observed any in relation with the cylindrical epithelium of the foveolæ.

Schaffer also saw among the usual transparent cardiac glands certain more deeply staining tubules which he describes as follows:

“Daneben findet man Drüsenschläuche welche nahezu cubische Zellen mit compactem stark gefärbtem Protoplasmakörper und kugeligem Kern besitzen; dies sind offenbar im Gegensätze zu der vorigen durch das Reagens nicht veränderte oder ruhende Zellen vor oder nach der Secretentleerung.” These may have been resting cells, as Schaffer suggests, or zymogenic chief cells, which I have found to be of quite frequent occurrence in my preparations. In Müller's fluid preparations the distinction between these two kinds of cells is not obvious owing to the solvent action of the fluid on the granules and prozymogen.

In my material these zymogenic chief cells occurred even more frequently than parietal cells. Their presence served to throw into strong relief the differences between them and the ordinary cardiac gland cells. Like the parietal cells they showed no special preference for any part of the cardiac region but occurred in the highest as well as the lowest portion of it. In the simple tubular glands of the distal region, they were usually found at the deep end of the tubule, but in the complex tubulo-racemose glands near the œsophageal epithelium their arrangement was less definite. Sometimes they occupied in common with a few parietal cells the terminal tubules of a gland. Some of the large compound glands at the margin of the œsophagus were almost exclusively zymogenic, in others some of the tubules were mucous, the rest zymogenic, while in the majority of cases one or two tubules only or a few cells in some of the tubules presented the structure of chief cells. The tubules formed of zymogenic chief cells are as a rule narrower and have a smaller lumen than those formed of mucous cells.

In sections stained in toluidin blue it is possible to distinguish the two kinds of tubules in the cardiac glands with a very low power, owing

to the intensity with which the prozymogen (basal filaments) in the outer zone of the ferment-forming chief cell stains. Fig. 4 shows a group of such tubules surrounding the ampulla-like duct of one of the compound gland groups at the margin of the œsophagus.

By staining in Heidenhain's iron hæmatoxylin the structure of these cells can be shown to be exactly like that of the chief cell of the body

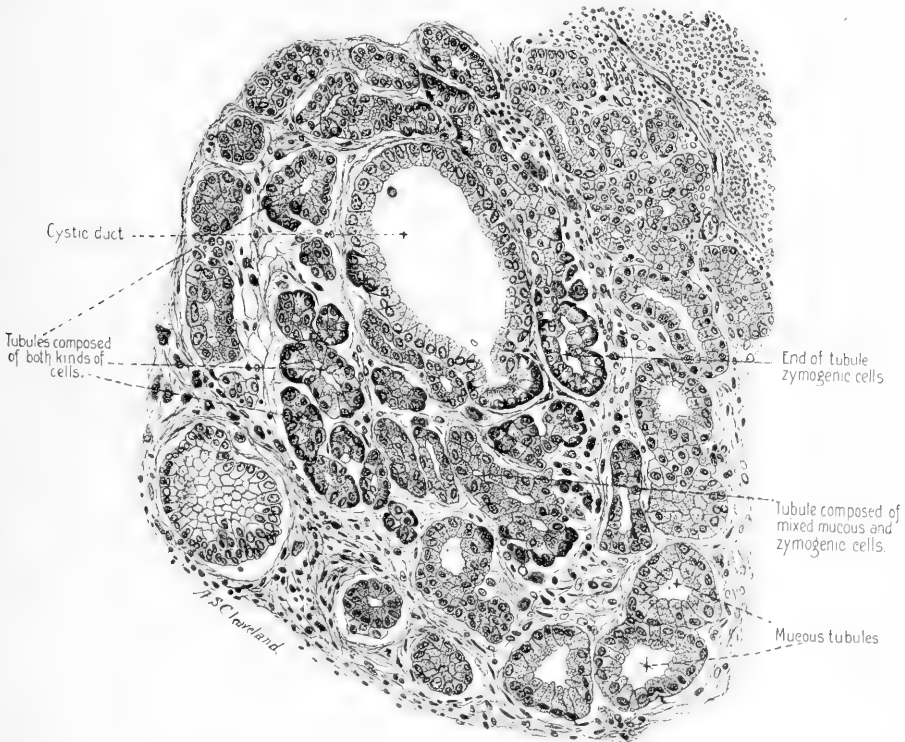


FIG. 4. Portion of compound cardiac gland from the edge of the œsophagus of man, showing the two kinds of secreting cells of which it is composed. $\times 100$.

of the fundus gland (Fig. 3, *c*). The outer zone of the cell is deeply stained and indistinctly striated owing to the presence of prozymogen. The inner zone contains well-defined zymogen granules which were fortunately fairly well preserved in my material. The zymogen granules were slightly smaller and less closely aggregated than in the chief cells of the fundus glands.

There was no constant relation between the point of occurrence of the parietal cells and the zymogenic chief cells in these glands.

The transition from the cardiac gland zone to the fundus region is a gradual one. As the fundus region is approached chief cells and parietal cells begin to be of frequent occurrence in the deep ends of the glands. These gradually increase in number and occupy more and more of the gland until all but the neck and foveola is formed by them. The change takes place thus by a reduction in number of the mucous cardiac gland cells and a substitution for them of chief cells and parietal cells in the body of the fundus gland. This transition, as well as the relationship of the cardiac gland cells to the epithelium of the gastric foveolæ strongly suggests a relationship of the cardiac gland cells to the mucous chief cells of the neck of the fundus glands and the pyloric gland cells which I have shown to be closely related (see also Cade, 1900). On examination, it is found that they closely resemble both of these elements without being actually identical with either. The neck chief cells and pyloric gland cells stain more intensely in mucicarmine and muchæmatein than the cardiac gland cells; the cells are more completely filled with secretion and more uniform in this respect in the fundus and pyloric glands. In the cardiac glands, on the other hand, the cells vary within wide limits as to their degree of physiological loading, but as a rule exhibit a proximal protoplasmic zone of some extent. Still, if one compares the more loaded and deeply-staining cardiac gland cells with the cells from the two other sources, the distinction disappears completely.

In one of his cases, Schaffer made an observation which is of considerable interest if it should prove to be well founded and the clearness of his figures and the confirmations recently furnished by Hari, 01, and Boekelmann, 02, leave little room for doubt. He found among the usual crypts certain others in which well-defined goblet cells could be recognized among the usual cylindrical mucous cells. He also saw cylindrical cells with a well-defined striated cuticle with basal granules and all stages of transition between the latter and mucin-forming gastric epithelial cells. This suggests the possibility, in which, however, Schaffer does not concur, that the resting epithelial cells of the stomach are morphologically identical with the cells of the intestinal epithelium. Schaffer rather prefers to regard the gastric epithelium as specific and the cell types described as dislocated intestinal epithelium. It is difficult to comprehend how this developmental feat could have been accomplished and the mere presence of a striated cuticle is not in itself sufficient to stamp an epithelial cell as intestinal in nature. I have not found any such cells in my preparations, but I have seen some structures which could be readily mistaken for a striated cuticle. The gastric

epithelial cells frequently show a peculiar radial striation in the mucigenous border due to the optical projection into this border of structures which are really on the surface of the cell. Carlier, 99, has shown that in the gastric epithelium of Triton the cement substance is not confined to the contiguous margins of the cells but extends in radiating lines over their free surfaces. This may be particularly well seen in sections of the newt's stomach stained by the iron hæmatoxylin method. Similar features are also exhibited by the cement substance of the gastric epithelium of mammals. In longitudinal sections of the cells in iron hæmatoxylin preparations the cement lines are seen as black dots between the free edges of the cell, or as a line stretching across the cell near its free end, according to the focus. In the latter case fine lines of cement may be traced from the intercellular line in the direction of the end of the cell over the convex surface of the mucigenous border. At the point where these vertical lines join the cement line, there is a granule-like thickening, which might readily be mistaken for the basal granule of a striated cuticle. The same appearances may be made out by careful focussing in a surface view of the ends of the cells where it is seen that the lines of cement over the surface of the cell form an irregular network with nodal thickenings (Fig. 5). This is undoubtedly the explanation of the appearance represented by Schaffer in his Fig. 44, where a row of granules is shown along the free border.



FIG. 5. Surface view of cells of the surface epithelium of the human stomach. $\times 1500$. Stained in iron hæmatoxylin to show cement lines between the cells and the fine lines of cement substance which are continued over the free surface of the cell.

From the foregoing facts it is obvious that the differences between the fundus glands and cardiac glands are not fundamental. This is indicated by the occurrence in the cardiac glands of all the characteristic glandular cells of the fundus glands. Only the relative frequency of the various cells is altered. The cells which are most numerous are muciparous cells morphologically equivalent to the chief cells of the neck of the fundus gland and to the pyloric gland cells, although physiologically much less active than these. In view of the fact that the highly branched glands may be to a large extent formed of zymogenic chief cells which are the morphological equivalents of the chief cells of the body of the fundus gland but little importance can be attached to the mode of branching as a specific character of the cardiac glands.

It now remains to be seen to what extent these conclusions can be supported by data derived from the examination of other mammalian stomachs.

II. THE CARDIAC GLANDS OF THE PIG.

It is in this animal among placental mammals that the cardiac glands reach their greatest extent. They occupy fully one-third of the available surface of the mucous membrane, comprised in a triangular area at the left extremity of the stomach. The mucous membrane of this area is only a fraction of the thickness of that of the middle or fundus gland region and contains throughout glands composed of but one kind of cell.



FIG. 6. Vertical section of tunica mucosa of the cardiac gland zone of pig. $\times 72$.

As regards the general arrangement and shape of the glands and the nature of the interglandular tissue, little can be added to the admirable descriptions of Ellenberger, 88, and Greenwood, 85. Fig. 6 shows a section of the mucous membrane of this region as seen under a low power objective. The superficial portion of the mucous membrane is occupied by the closely-set foveolæ of the glands, which are much narrower and more numerous than in the fundus region. The foveolæ descend in the mucous membrane, becoming narrower as they go and at their lower ends receive one or two glands. These are wavy tubules branching but slightly, usually very narrow at their upper ends but frequently presenting at their lower ends a bulb-like expansion containing a larger lumen.

The surface epithelium of this stomach, while similar in all important details to that of other mammals is unique in one respect; the theca of mucus is of extraordinary size and as a result nearly fills the cell, the nucleus being flattened by compression in the base of the cell. Similar cells line the upper portions of the foveolæ, but it is seen that on going down the sides of the latter the mass of mucus becomes relatively smaller and the nucleus rapidly expands to its normal spherical shape.

The character of the cells lining the deep ends of the foveolæ and the glands differs according to whether the animal is mature or otherwise. Fig. 7 represents the upper end of a cardiac gland and the adjacent portion of its infundibulum from an animal about six weeks old. The preparation was stained with Mayer's muchæmatein followed by acid rubin. The upper cells present two distinct zones; a larger distal zone filled with closely-packed granules of mucigen, black in the figure, which were stained blue by the muchæmatein, and a proximal protoplasmic zone containing the slightly flattened nucleus. Proceeding down the gland it is presently observed that the mass of mucigen exhibits an hour-glass constriction in the center, owing to a concentration of the protoplasm of the cell at that point, and still further down, is completely divided into two masses, one of larger size near the nucleus, and a smaller band along the free border.

On close inspection, the bridge of protoplasm separating these two masses is found, in sublimate preparations to be studded with minute granules which stain intensely in eosin or rubin S. At the lower ends of the foveolæ the proximal or internal mass of mucigen disappears altogether and in the whole of the gland proper only a slightly blue stained band is discernible along the free borders of the cells. As the internal mass of mucigen diminishes in size there is, however, a corresponding increase in the number of rubinophilous granules which occupy, in the upper portions of the glands one-third or more of the cell near the lumen.

These granules are not zymogen granules, because they are not visible in the fresh cell and because Greenwood, —, has shown that the cardiac mucous membrane of the pig yields, when tested by Grützner's method only one-eightieth as much pepsin as the fundus region. The

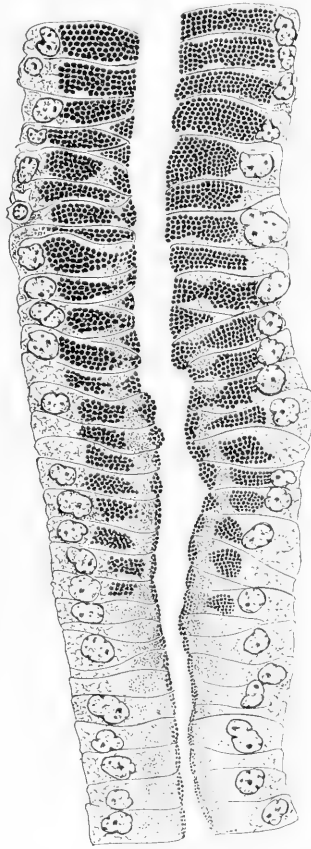


FIG. 7. Lower end of foveola gastrica and adjacent portion of cardiac gland of the young pig. $\times 1000$. From a preparation stained in strong muchæmatein and rubin. Portions stained blue in muchæmatein are indicated black in figure.

gradual disappearance of the granules as the internal mass of mucigen increases in size points to the probability that the latter is to some extent formed at the expense of the substance of which the granules are composed. Similar granules have been observed after fixation in sublimate solutions, by Carlier, 99, in the epithelial cells of the stomach of Triton, and I have myself observed them in many of the mucous cells of the stomachs of different vertebrates, more particularly in the actively dividing cells at the bottom of the foveolæ. As to their nature, the researches of Krause, 95, on the retrolingual gland of Erinaceus seem to be conclusive. He found that at a certain stage of secretion the cells contained no mucin but, in sublimate specimens, were studded with minute rubinophilous granules. These granules were not visible in the fresh salivary gland and their presence was explained by the assumption that the cell juice, preparatory to secretion was rich in dissolved proteids and that these were precipitated in the granular form by the corrosive sublimate employed for fixation.

The narrow tortuous upper portion of the gland in the young pig is entirely composed of cells of this type, exhibiting in such preparations a proximal protoplasmic clear zone containing the spherical nucleus, and a distal zone filled with granules of precipitated proteid. The expanded lower end of the gland is formed of small cubical cells with nearly spherical nuclei (Fig. 8A). The protoplasm of these cells is similar to that of the proximal zone of the cells last described, and may be quite devoid of rubinophilous granules, although a few may usually be seen along the lumen.

Examined for masked iron by Macallum's method, the protoplasm of these cells gives a very feeble reaction, indicating that prozymogen is present only in traces. Treated with muchæmatein or mucicarmine solution, the cells of the lower expanded extremities of the glands of the young pig like those cells which contain numerous rubinophile granules, either remain unstained or show a faintly-stained distal margin as in Fig. 8A, although the cells of pyloric glands of the same animal are filled with mucin in the various stages of its elaboration, and stain intensely in the solutions mentioned. There is thus at this stage apparently very little ground for assuming any relationship between the cardiac and pyloric glands.

The examination of the cardiac glands of the adult animal, however, shows that the failure of the muchæmatein test in the young pig is but an example of delayed and imperfect functional activity.

In the adult animal the cells of the duct and free surface are much of the same character as those of the young pig, and the same gradual

transition may be observed between the cells of the various parts of the gland, but the cells of the gland have altered considerably in character.

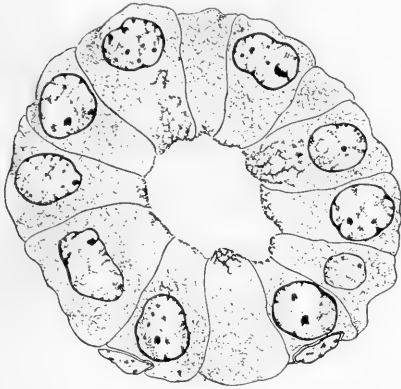


FIG. 8A and 8B. Transverse sections of deeper end of cardiac glands: A, from young pig; B, from adult pig. $\times 1000$. From preparations stained in paracarmine and strong muchæmatein. The deeply shaded portions of the cells next the lumen represent the extent of the mucus stain.

The mucus in these cells stains muchæmatein, if employed in the manner described for the human cardiac glands.

The cells of the lower ends of the glands are much the same as in the young animal, but always show a considerable amount of mucin in their distal zone (Fig. 8B) which stains strongly in mucicarmine and muchæmatein, although less readily in the latter than the cells of the surface.

Comparing these cells, now, with those of the pyloric glands, the difference although still striking, is not so great as in the young animal, for while the pyloric gland cells are much larger than those of the cardiac glands and are quite filled with mucin or its antecedent substances, they are nevertheless engaged in the same kind of activity as the cardiac

In the upper portion of the gland where are found in the young animal cells with a large distal zone filled with rubinophilous granules, the adult gland contains cells with a distinct mass of mucus. This mass may be confined to the interior of the cell in which case, a protoplasmic portion filled with granules intervenes between it and the free border of the cell, or it may reach the free border in which case the granules are clustered around the proximal end of the mass; or, finally, it may be partially or completely divided into two masses by a strand of granular protoplasm stretching across the cell.

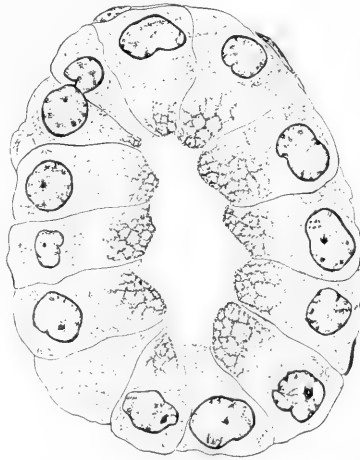


FIG. 8B. Transverse section of deeper end of cardiac gland from adult pig. $\times 1000$. See Fig. 8A.

gland cells and are related to the surface epithelium through a similar perfect transition. The difference is one of degree rather than kind, the cardiac gland cell discharging at a later period of development and with obvious reluctance, the mucin-forming function which the pyloric gland cell assumes early and performs perfectly throughout life.

I have not made an exhaustive comparison of the reactions with synthetic dyes of the cells composing the pyloric and cardiac glands, but so far as I have gone, they have been similar. I should not be surprised, however, if further experiment revealed differences of staining capacity, because it is hardly to be expected that imperfectly functioning secreting cells like those of the cardiac glands would always correspond, in the phase of elaboration to which they carried their stored-up product, with such active elements as the cells of the pyloric glands.

The fundus gland zone of the pig is of great interest owing to the fact that the glands of a very considerable portion of it may be reasonably regarded as intermediate between cardiac glands and true fundus glands. These fundus glands are unique among mammalian gastric glands in the fact, first noted by Greenwood, that the mucous chief cells are not confined to the neck of the gland, but extend into the body and many of the glands may be formed of mucous cells and parietal cells to the exclusion of zymogenic chief cells even in their deepest portions. The ferment-forming chief cells are thus relatively reduced in number.

Thus the cardiac glands of the pig correspond with those of man in their muciparous function, in their relation to the surface epithelium, and in their comparative inactivity in secretion as indicated by the structure of the cell. They differ from those of man in the complete absence of parietal and ferment-forming cells except in the intermediary zone.

III. THE CARDIAC GLANDS OF RODENTIA.

In the guinea-pig, the œsophageal epithelium terminates at the opening of the œsophagus into the stomach in a sort of irregular fringe which bears a superficial resemblance to the Grenzfalte of the Myomorpha but on microscopic examination proves to be composed of the corneous layer of the epithelium only.

The cardiac glands in this animal are confined to a narrow zone about one-third of a millimeter in width. The glands of this area are devoid of both parietal and zymogenic chief cells. The cells of which they are composed resemble very closely in structure those of the human cardiac glands although the distal portion which contains secretion

stains much more intensely in muchæmatein and mucicarmine. As in the human subject, the mucigenous distal zones of the cells vary in extent, from a narrow border along the lumen to one-half or two-thirds of the cell. Rarely the whole cell is filled with secretion but not to such an extent that the shape of the nucleus is materially altered by compression.

The transition from this area to the fundus gland area, appears under a low magnification to be an abrupt one, but closer inspection shows that this is due to the sudden appearance of the parietal cells in great numbers. The glands which immediately succeed the cardiac glands are composed entirely of mucous cells and parietal cells. The ferment-forming chief cells make their first appearance at the very bottom of the glands, increasing rapidly in number and displacing the mucous cells until the latter are confined to the neck of the gland. Thus, there is, if one leaves the parietal cells out of consideration, a gradual transition between the cardiac glands and fundus glands. There is also a gradual transition in the nature of the cells composing the gland to the cells of the free surface similar to that shown to exist in the pig and in man.

In *Arctomys monax* the cardiac glands occupy a zone about 2 mm. in width around the opening of the œsophagus. They are for the most part simple tubular structures slightly expanded at the lower extremities, and opening at the upper end into wide and deep depressions. Neither parietal nor zymogenic chief cells are present in these glands and the cells differ from those of the animals already considered in the fact that the secretion completely fills the cell, the nucleus on this account exhibiting a basal position and a crescentic form. The transition to the fundus zone is as in the guinea-pig except that the parietal as well as the chief cells *gradually* increase in number as the fundus gland region is approached. The secretion of the cells stains readily in muchæmatein, mucicarmine and particularly in methyl blue, enabling one to distinguish readily the cells from the ferment-forming cells which in *Arctomys* as in the Rodentia generally, exhibit a very well-developed proximal zone filled with prozymogen.

In the *Myomorpha*, with the exception of *Myoxus*, the stomach is divided into a right and left portion. The glands are entirely confined to the right division of the stomach, the left being lined by a non-glandular stratified squamous epithelium similar to that of the œsophagus. The line of junction of the two divisions is marked internally by a well-defined fringe, the Grenzfalte, which is really a fold of the mucous membrane. Corresponding to this externally there is a more or less

obvious constriction. In connection with the formation of this left non-glandular region there is an enlargement of the cœcal left extremity of the stomach, in some cases to such an extent that it exceeds in size all the rest of the stomach.

In *Mus musculus*, both the "Grenzfalte" and the external constriction are little marked and the stomach of this form, therefore, represents, with the exception already noted, the simplest type known in the Myomorpha.

The extensive cardiac gland zone described by Toepfer, 91, adjoining the opening of the œsophagus on the lesser curvature of the mouse's stomach, did not occur in any of the numerous specimens examined by me. The glands of this region are relatively short, it is true, but they

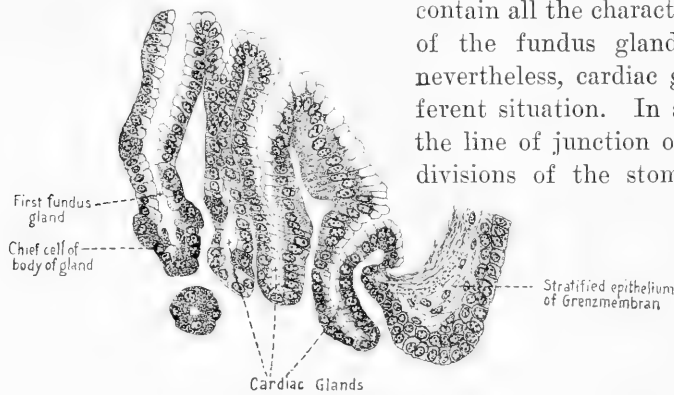


FIG. 9. Section across the junction of the right and left divisions of the stomach of *Mus musculus*. $\times 500$. Iron hæmatoxylin.

contain all the characteristic elements of the fundus glands. There are, nevertheless, cardiac glands in a different situation. In a section across the line of junction of the two main divisions of the stomach it is seen that there are along the "Grenzfalte" two or three rows of glands which may, I think, on account of their structure, be properly designated cardiac glands. The epithelial and glandular portions of such a section are represented in Fig. 9. The gland nearest the "Grenzfalte" is usually a simple crypt lined by cells like those of the surface epithelium, but not infrequently there are two or three glandular cells at the lower end of the tubule. These cells exhibit the usual structure of mucous cardiac gland cells and their contents stain readily in mucicarmine and muchæmatein. The simple crypt above described does not occur with the same frequency along the "Grenzfalte" as the other glands, and if serial sections are not examined may be readily overlooked.

The transition between these cells, when present, and the surface epithelium is usually abrupt, but this probably is due to the shortness of the glands. The parietal and ferment-forming chief cells make their appearance in the third or fourth tubule, the former being usually the first to appear.

The limited cardiac gland area extends all along the junction of the two divisions of the stomach, separating the stratified epithelium from the glandular area.

The stomach of the American water-rat or Muskrat, *Fiber Jibethicus*, resembles closely in structure that of *Arvicola arvalis* as described by Retzius, 41, Toepfer, 91, and others. The stratified epithelium which is confined in the mouse to the left division of the stomach, in the muskrat passes over into the right division, replacing the glands of the lesser curvature, ventral and dorsal surfaces and most of the pyloric glands. The fundus glands are confined to a small isolated oval area on the summit of the greater curvature, surrounded on all sides by a non-glandular mucous membrane covered by stratified squamous epithelium which forms a particularly well-marked "Grenzfalte" on all sides.

The pyloric glands are not so completely displaced as in *Arvicola*. A small ring-shaped area still remains around the pylorus, from which a tongue-shaped mass extends along the lesser curvature in the direction of the oesophagus. These pyloric glands are separated from the adjacent cutaneous region of the stomach by a "Grenzfalte" somewhat less developed than that surrounding the islet of fundus glands.

As in the mouse, there is between the "Grenzfalte" and the fundus area on all sides a narrow strip of cardiac glands. These glands have neither parietal cells nor ferment-forming chief cells. The cells composing them contain next the lumen a mass of secretion which stains readily in the usual mucin stains. The secretion does not fill the cells, a large protoplasmic proximal zone containing a spherical nucleus being usually present. Occasionally, as in the human subject, the glands are cystically dilated, in which case the cells are almost wholly protoplasmic.

The pyloric glands of the muskrat are scarcely distinguishable from the cardiac glands, but on the contrary, differ from the glands of Brunner inasmuch as the cells composing the latter are quite filled with mucin, and possess a flattened crescentic or irregular nucleus.

An interesting fact in connection with the stomach of the muskrat is that the fundus glands which are nearest the pylorus exhibit a structure similar to that of the fundus glands of the pig, inasmuch as mucous cells occur not only in the neck of the gland but are frequent among the ferment-forming chief cells of the bottom of the gland.

In addition to the animals included in the preceding description, which were selected because they have an important bearing on the discussion of the phylogenetic significance of the cardiac gland with which this paper will be concluded, I have examined the cardiac glands of a number of other placentals and of one marsupial, for example, the

cat, dog, rabbit, hedgehog and opossum. The results in these instances correspond so closely with those in the animals selected for description that it was not considered desirable to prolong the histological portion of the paper by further description. In every case I was able to satisfy myself that the cardiac gland cells were mucin-forming elements, staining in the modified solutions of Mayer and related in the usual way to the surface epithelium.

In the opossum, the only marsupial at my disposal, there is a narrow zone of cardiac glands, around the cardiac orifice of the stomach. These are tortuous tubules entirely composed of mucous cells which stain readily in muchæmatein and mucicarmine.

It should be remarked that as a rule in those animals in which the cardiac zone is extremely small the cells are relatively more active in secretion than in animals in which the cardiac zone is large.

SUMMARY OF RESULTS IN THE HISTOLOGY OF THE CARDIAC GLANDS.

As regards the nature of the cardiac glands, my results are directly opposed to those of Ellenberger, Edelman and Schaffer, who concur in the conclusions that they are not mucous glands. Ellenberger contrasts them with the pyloric glands which he regards as mucous glands, and expresses the opinion that they are serous glands. Edelman regards the cardiac glands as *sui generis*, but not mucus-forming. Schaffer compares them with the pyloric gland cells and the chief cells of the fundus glands which he evidently regards as similar.

Little importance can be attached to any of these views because they are obviously not based on a clear conception of the fundamental structure of the chief cell and pyloric gland cell.

My conclusions are as follows:

1. The cardiac glands are mucous glands, because their cells contain a secretion which stains with Mayer's muchæmatein and mucicarmine and are connected with the mucigenous epithelium of the surface by a transition, the middle point of which is formed by actively dividing cells containing little mucin, which occur at the deeper constricted ends of the foveolar depressions. It is reasonable to suppose that cells which have a common origin from an element that is already differentiated as a secreting cell, are not strikingly different in nature.

2. The cardiac gland cells are fundamentally different from the chief cells of the body of the fundus glands, inasmuch as the latter give none of the staining reactions of mucin, but, on the contrary, contain two characteristic substances which are phases in the elaboration of their

secretion, namely the zymogen granules and the so-called basal filaments containing prozymogen.

3. The cardiac gland cells are closely related to the mucous chief cells of the neck of the fundus gland and to the pyloric gland cells. This conclusion is based on the facts that all three stain similarly in mucin stains, are connected by a similar transition with the surface epithelium, and are recruited from similar dividing cells at the bottoms of the foveolæ. Furthermore, if one traces the transition from the fundus zone to the pyloric zone on the one hand or the cardiac zone on the other, it is found to take place by the gradual lengthening of the neck of the gland, together with the gradual disappearance of the chief and parietal cells.

This similarity does not amount to actual identity of the several structures although such differences as exist are rather of degree than of kind. In the cardiac gland cells as a rule only the distal portion of the cell near the lumen is occupied by the mass of secretion, in the pyloric gland cells and mucous neck cells, it frequently fills the whole cell, the nucleus being compressed and flattened at the proximal end. Moreover, the mucin of the cardiac gland cells stains with less intensity in muchæmatein and mucicarmine than that of their prototypes in the other glands. The obvious explanation of these differences is that the cardiac gland cells are physiologically less active and secrete their mucin less rapidly and in a less concentrated form.

4. The peculiar grouping and branching noted by Edelman and others in the cardiac glands possess no important significance either as a characteristic of the cardiac glands or as a point of difference between them and the fundus and pyloric glands. The fact that among the human cardiac glands there occur highly complex branched tubular glands, similar in all respects to the other cardiac glands except that they are formed wholly or in part of zymogenic chief cells, indicates clearly that this branching and arrangement are determined by other factors than the phylogenetic history of the glands or the nature of the cells composing them.

5. The cardiac glands are decadent or retrogressive structures derived from fundus glands by the disappearance of their more highly specialized cellular constituents, the zymogenic chief cells and the parietal cells. This conclusion will be discussed at greater length in the next section, but in the meantime the histological arguments in its favor may be stated. These are in brief: (1) the circumstance that both parietal cells and zymogenic chief cells occur in small numbers in the human cardiac glands; (2) the feeble physiological activity of the

cells as indicated by their structure, and (3) the tardy assumption by the cells of the cardiac glands in the pig of the mucigenic function.

THE PHYLOGENETIC SIGNIFICANCE OF THE CARDIAC GLANDS
AND THE SO-CALLED ŒSOPHAGEAL SACS.

Concerning the phylogenetic significance of the cardiac glands the various writers express themselves with considerable reserve and not always with clearness. Edelmann, 89, suggests two possibilities as follows: "Phylogenetisch kann die Cardiadrüsenregion entweder als ein in die Bildung des Magens hineingezogener Abschnitt der Vorderdarmdrüsen oder als ein modificierter Teil der Schleimhaut des Mitteldarms aufgefasst werden." Between these two possibilities he does not attempt to decide. He, however, regards the cardiac glands as physiologically important structures. "Die physiologische Bedeutung der Cardiadrüsenregion beruht in der Bildung einer Art Vorraum im Magen, welcher keine Säure dagegen Fermentquellen enthält, und in dem die Verdauung der Stärke vor sich gehen kann." "Der von der Cardiadrüsenregion gebildete Vorraum für die Stärkeverdauung kann zum Teil ersetzt werden durch Œsophageale Vormägen, so dass die Cardiadrüsenregion also auch mit diesen morphologisch in einem korrespondierenden Verhältnis steht." This last sentence would seem to imply the view that both cardiac gland and Œsophageal sac have a common origin, but for the doubt expressed in the first sentence quoted as to the phylogenetic significance of the former.

Oppel, 96, suggested that the conditions described by Schäfer and Williams, 76, Cordier, 90, and others, in the kangaroo, were primitive and that the simple glands or cardiac glands of these animals were of the same nature as the simple gastric gland of lower vertebrates. This suggestion, which, indeed, the author did not seriously advance, may be dismissed with but slight discussion. In the first place, the cardiac glands are not histologically similar to the fundus glands in the lower vertebrates, and in the second place, the more primitive marsupials, such, for example, as the opossum, resemble closely in the structure of their stomachs the simplest conditions found in the placental mammals.

The universal occurrence of cardiac glands in Mammalia seems probable. It is true that their presence in the carnivorous Cetacea and in the ruminants was denied by Edelmann and in three of the suborders of Rodentia by Fleischmann. The latter author, however, did not recognize as cardiac glands the extremely narrow zone of mucous glands found around the cardiac orifice of the stomach in these forms, nor the narrow zone of similar glands found along the "Grenzfalte" in the Myomorpha.

Even if we admit that the cardiac glands occur in all mammals, it does not by any means follow that they have any palingenetic significance.

If we reject the hypothesis of Oppel that the cardiac glands of mammals correspond morphologically to the simple fundus gland of the lower vertebrate classes, the possibilities as to the origin of these peculiar structures become reduced to the following:

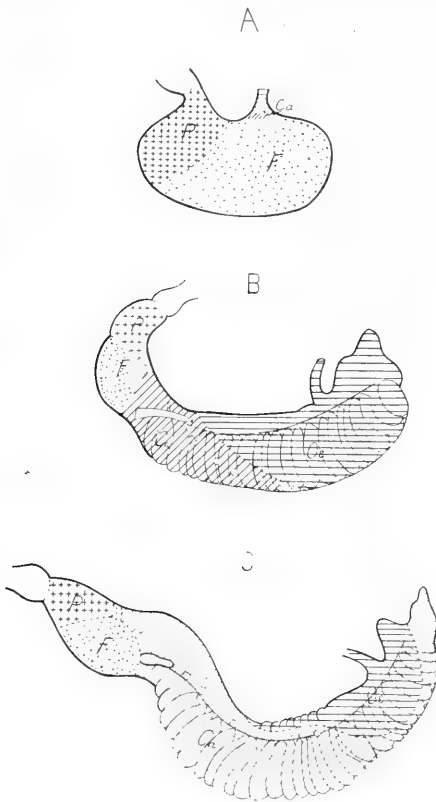
1. They are œsophageal glands and the region which they occupy is a portion of the œsophagus;
2. They are modified fundus glands;
3. They are secondary structures of physiological importance which have arisen in the Mammalia in response to a new functional demand.

The first of these hypotheses involves the discussion of the whole question of the participation of the œsophagus in forming the stomach of mammals. It is a well-known fact that in many mammals belonging to different sub-classes and orders, a considerable portion of the stomach is devoid of glands and provided with a stratified epithelium. This is more particularly the case in the Ungulata and Rodentia, but these œsophageal cardiac sacs also occur in the Cetacea, Edentata and Marsupialia and in a few individuals belonging to other orders. The natural conclusion based on the absence of glands and on the character of the epithelium would be that these sacs are produced by a dilatation of the lower end of the œsophagus, and this is the view taken by Ellenberger and Edelman, and more recently by Kingsley, 99. The latter author in his recent work on Vertebrate Zoölogy expresses his conception of the morphology of these structures as follows:

“Usually the stomach is regarded as the saccular enlargement of the alimentary canal, lying between the œsophagus and the intestine; but when histological and physiological features are taken into account, it is seen that frequently the lower end of the œsophagus expands and takes part in the formation of the gastric enlargement, and that the stomach proper begins only where the gastric glands appear.” This simple hypothesis is not, however, in accord with the results of comparative anatomy and ontogeny, both the older anatomists, as for example, Gegenbaur and Wiedersheim, and the later investigators, Toepfer, Fleischmann, Boas, Cordier and Oppel, agreeing to regard the stomach of mammals as a morphological unit of equal value throughout the group, the cardiac sacs having been produced by gradual modification of the condition found in a simple stomach, such as that of the Carnivora and Insectivora and many individuals of other orders.

Cordier, 90, whose important researches on the comparative anatomy

of the stomach of ruminants entitles his opinion to some weight; expresses himself thus: "On est donc en présence d'une cavité à son maximum de différenciation"—"Je me refuse absolument à croire, par exemple, à l'origine œsophagienne du rumen."



FIGS. 10-16. Diagrams to illustrate the regions occupied in different stomachs by the various kinds of glands.

FIG. 10. Stomachs of: A, *Didelphys*; B, *Dorcopsis*; C, *Macropus*; the two latter after Schäfer and Williams.

Abbreviations: Ca=cardiac glands; F=fundus glands; P=pyloric glands; Oe=portion of stomach without glands and lined by a stratified epithelium.

Among the marsupials two types of stomach are met with. In the opossums (Fig. 10, A) *Dasyures*, *Bandicoots* and *Phalangers* the stomach is simple, resembling closely in shape and in the arrangement of its parts those of the insectivorous and carnivorous placentals. A large fundus gland zone occupies the greater portion of the mucous surface, the rest being occupied by the pyloric glands. The cardiac gland zone is either altogether absent

The alternative hypothesis that the cardiac sacs have been derived by a gradual change in the cardiac portions of the stomach by reason of which the glands have disappeared and the epithelium has changed in character, suggests an examination of the stages, if stages there be, and of the factors that have been operative, in the production of this extraordinary transformation.

Before proceeding with the discussion of this matter, a brief survey will be made of the relations and extents of the various portions of the stomach in a number of representative species of several orders of Mammalia.

In the *Monotremata* the stomach is lined throughout by stratified squamous epithelium and is quite devoid of glands, although a well-developed group of Brunner's glands is found at the pyloric orifice.

(Phalangista) or occupies an extremely narrow area at the termination of the œsophagus (*Didelphys*, *Dasyurus*, *Perameles*). The œsophageal epithelium does not extend into the stomach.

In the kangaroos, on the other hand, a highly complex condition exists. The stomach is elongated intestiniform in shape and exhibits peculiar colon-like sacculations. The œsophageal epithelium extends some distance into the stomach and a considerable cardiac gland zone is present. As a result of these important modifications, the fundus and pyloric glands are confined to a small portion of the stomach near the pyloric cord. Particularly interesting are the figures of the stomach of *Macropus giganteus* and *Dorcopsis luctuosa*, given by Schäfer and Williams (Fig. 10, B and C). Externally the similarity between these two stomachs is remarkable. The general form, the sacculations along the greater curvature, and the distribution of the fundus and pyloric glands is the same in each, the similarity in shape extending even to the two small secondary cœca at the left extremity of the fundus sac. Some difference exists, however, in the relative extent of the portions lined by œsophageal epithelium and cardiac glands respectively. In *Macropus giganteus* the œsophageal epithelium extends only a short distance from the cardiac orifice, but in *Dorcopsis* it lines the whole of the fundus sac and extends a considerable distance to the right of the œsophagus, the cardiac gland zone being correspondingly reduced. In *Dendrologus bennetti*, according to Beddard, there is also an œsophageal division of the stomach but it occurs in the middle region between the opening of the œsophagus and the pylorus.

A similar diversity of structure exists in several of the placental orders. This has been particularly well investigated by Toepfer for the Rodentia and by Edelmann, Boas, and especially Cordier, for the Ungulata.

In the former order a simple stomach is found in the Sciuromorpha, Lagomorpha (Fig. 11, A) and Hystricomorpha. In the Myomorpha, on the other hand, there is usually a sac of considerable size lined by squamous epithelium and without glands. The simplest condition is found in *Mus* (Fig. 11, B) in which the glands extend to the œsophageal opening and in which the stomach has retained the simple form. The right and left divisions of the stomach are separated by a moderately well-defined "Grenzfalte" and along this is a narrow zone of cardiac glands. The next phase of specialization is presented by *Cricetus frumentarius* (Fig. 11, C) in which the stratified epithelium extends past the opening of the œsophagus over into the right division of the stomach. The subdivision of the stomach is now clearly indicated externally

by a constriction. The stratified epithelium is not however confined to the cardiac sac but extends in the form of two wing-like processes preceded by the "Grenzfalte" into the pyloric sac. In *Arvicola* amphibius, according to Toepfer, the stratified epithelium has encroached

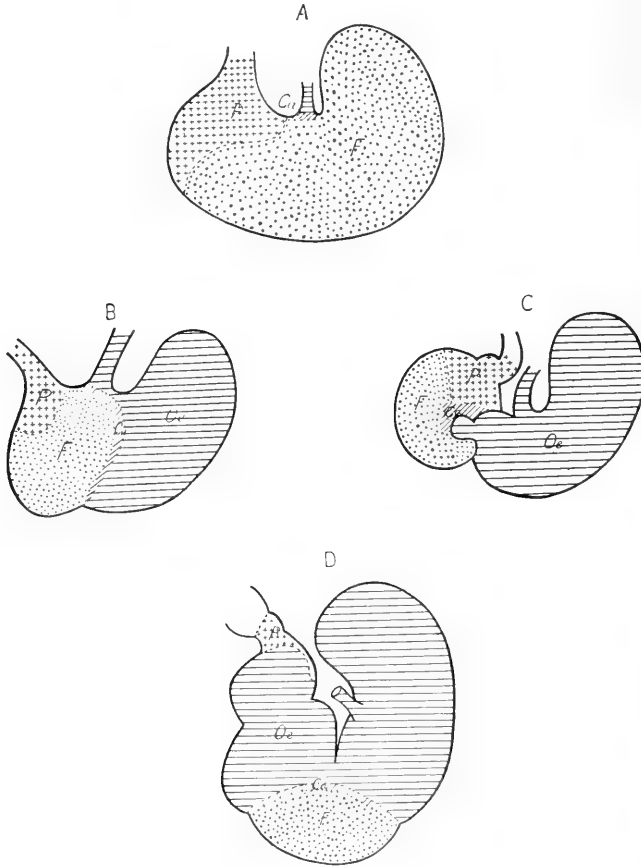


FIG. 11. Stomachs of: A, *Lepus*; B, *Mus*; C, *Cricetus*, after Toepfer; D, *Fiber*.

upon the lesser curvature and replaced a considerable portion of its glands.

In *Fiber* (Fig. 11, D) and in a number of species of *Arvicola* this specialization has reached its highest degree, the stratified epithelium extending over into the pyloric sac along the greater curvature, and replacing to a large extent the pyloric glands and the glands of the lesser curvature in such a way that the fundus glands form an islet completely

surrounded by a glandless mucous membrane covered by a stratified squamous epithelium. Around the margin of this islet of fundus glands is a narrow row of cardiac glands and a continuous "Grenzfalte."

Although the stomachs of the existing Ungulata have reached a considerable degree of complexity, anatomists have made out an interesting series of gradations culminating in the highly complex ruminant stomach. The simplest conditions are found in the Perissodactyla and in the Pigs among Artiodactyla. In the former the conditions obtaining in the Tapirs, Horses and Rhinoceroses (Fig. 12, A, B and C) are very similar. The stomach is externally undivided. In the mucous membrane four regions are to be distinguished, an œsophageal region lined by stratified squamous epithelium, a cardiac gland region of some width intervening between this and the fundus region and finally a pyloric gland region. The published descriptions are not quite satisfactory as regards the Tapirs but the evidence seems to be that the œsophageal portion is of much less extent than in the horse and rhinoceros, in both of which it forms a sac of considerable size, in the latter fully one-third of the stomach. In the Artiodactyla the simplest condition is found in the Suidæ (Fig. 12, A). Here the condition closely resembles that to be found in the Tapirs but the cardiac gland zone is more extensive.

The next stage of complexity is found in the Peccaries (Fig. 13, B), the stomach of which is divided into three sacs, a middle one lined by stratified epithelium except at the point most remote from the œsophagus where a few cardiac glands are found, a left saccule lined by cardiac glands and a right saccule containing, according to Edelman, fundus glands and pyloric glands, according to Cordier pyloric glands only. The stomach of the sheep (Fig. 14, A) is too well known to require any description. The stomachs of the Tragulidæ and Moschidæ differ from those of the better known Ruminants in the absence of a Psalterium and in the less perfectly developed œsophageal groove (Cordier). The stomach of the

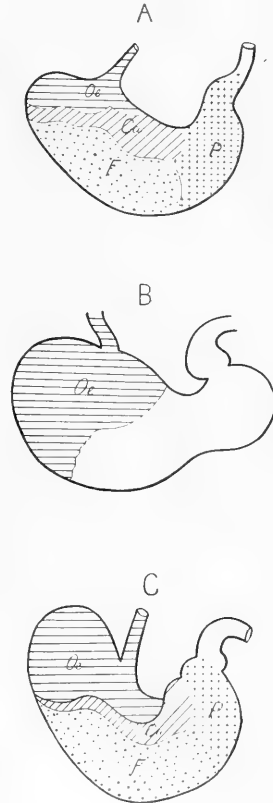


FIG. 12. Stomachs of: A, Tapir (after Edelman); B, Rhinoceros (after Owen); C, Equus (after Edelman).

camel (Fig. 14, B) has been the subject of histological and anatomical study by Pilliet, 85, Boas, 90, and Cordier, 90, whose results harmonize as regards points of fact although the two latter authors differ as to their interpretation of the homologies of the various regions: Pilliet had pointed out that the so-called water cells of the rumen of the camel were lined by a simple epithelium through which glands open. This observation is confirmed by Boas and Cordier, the former of whom

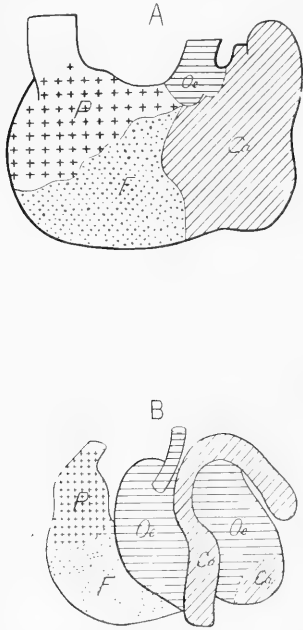


FIG. 13. Stomachs of: A, *Sus* (from Oppel, after Greenwood); B, *Dicotyles* (from Oppel, after Edelmann).

regarded them as the remains of the glands which at one time occupied all the mucous membrane of the rumen. Cordier is the most precise as to the nature of these glands which he describes as follows: "Les glandes découvertes par Brandt étudiées histologiquement par Pilliet, qui tapissent le fond et les parois latérales des poches, sont très courtes, puisque déjà cette région de la paroi est fort mince. Elles ne sont point pourvues de cellules bordantes, et nous ne savons rien sur la nature de leur sécrétion. Il est probable cependant que cette dernière est simplement muqueuse, et il convient peut-être d'assimiler ces régions glandulaires à celles apparemment de même nature, qui avoisinent l'oesophage chez beaucoup d'animaux monogastriques et étudiées dans la série des Mammifères par Edelmann." In brief, he regards the glands of the water cell in the camel as cardiac glands.

The greater portion of cylindrical glandular division of the camel's stomach appears to be occupied by cardiac glands. The mucous membrane of the region is described by Boas as exhibiting marked longitudinal folds, comparable to those of the psalterium of other ruminants. It contains close-set and extremely short gland tubules which Cordier states to be identical with the glands of water-cells. The distal one-sixth of the mucous membrane is occupied by the usual fundus and pyloric glands.

In the Edentata the stomach assumes several peculiar and interesting forms. The nearest approach to the simple form of stomach that is usual to mammals is presented by *Dasypus* (Fig. 15, A), *Myrmecephaga* and allied genera in which the stomach is lined throughout by a simple

epithelium through which ordinary fundus and pyloric glands open. The cardiac glands are restricted in distribution or absent. Specialization is however manifested in the subdivision of the stomach by an external groove into right and left sacs connected on the outside by a broad tendinous band, and in the greatly increased thickness of the wall of the right or pyloric sac. There are no intermediate stages among the Edentata between this condition and the extremely specialized stomachs of *Manis* and *Bradypus* (Fig. 15, B). In *Manis javanica* (Fig. 16), according to Weber, 91, the whole stomach is lined by stratified epithelium. The fundus glands are not, however, entirely destroyed but are confined to a small portion of the greater curvature, where large compound glands which may be interpreted as evaginations of the mucous membrane occur. The cardiac and pyloric glands are represented by highly branched glands occupying the region around the large complex fundus gland above described, the lesser curvature and a portion of the pyloric region near the intestine.

In *Bradypus* (Fig. 15, B) the stomach has an extremely bizarre form. The œsophagus opens into a large chamber subdivided into three parts called by Klinowström, 95, the cardiac stomachs (Cardiamägen), all of which are without glands. Into this opens a long-pointed sac (*b*) the mucous membrane of which is provided with cardiac glands. On the other side the organ is continued into the intestine by a narrow tube, divided into two parts. The first subdivision is occupied, though not completely, by fundus glands. Along the lesser curvature there is a groove lined by stratified epithelium and on the sides of the groove, the squamous epi-

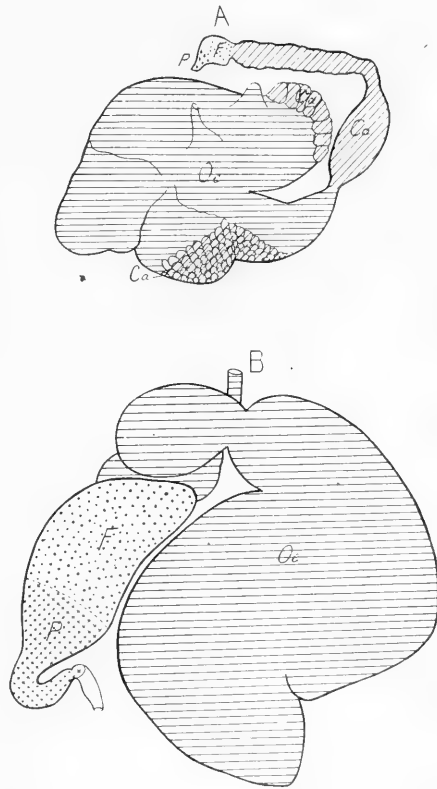


FIG. 14. Stomachs of: A, *Camelus* (modified from Cordier); B, *Sheep* (modified from Opperl).

thelium is separated from the fundus glands by a narrow row of glands called by Klinckowström, pyloric glands, but probably correctly interpreted by Oppel as cardiac glands. The final section of the stomach is lined by stratified epithelium and is without glands.

An examination of the schemes presented in the foregoing pages reveals a number of interesting facts, to some of which attention has been already directed by Oppel and others.

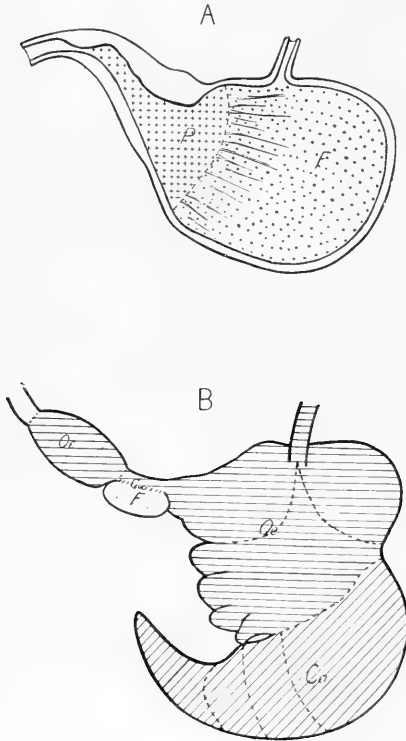


FIG. 15. Stomachs of: A, *Dasypus*; B, *Bradypus* (both modified from Klinckowström).

in an organ already highly specialized.

Moreover, in the Ungulata, no existing member of which exhibits a perfectly simple stomach, the nearest approach to this is found in those animals (the pigs in the Artiodactyla, and the tapirs in the Perissodactyla) which have been conservative in other respects, as for example, dentition and foot structure.

The obvious inference from these facts is that the specialized stomachs found in many mammals belonging to different orders, have been differentiated at a comparatively late period and entirely within the

The first fact that strikes one is that in all these orders except the Ungulata, individuals exist, the stomachs of which closely resemble in structure those of many existing Carnivora, Insectivora and Primates.

There are good reasons for supposing that these stomachs represent a persistent primitive condition. They correspond closely in the relations of the different gland areas with the stomachs of lower vertebrates. Furthermore specialization in the stomach of mammals is accompanied by suppression of existing elements (glands, etc.) as well as by increasing complexity of structure, and it is therefore unlikely that primitive conditions would be simulated in a stomach that has been derived secondarily by degenerative or retrogressive processes occurring

limits of the ordinal groups. Any similarity that may exist between various orders in the direction and nature of this differentiation, is probably simply a parallelism due to the operation of similar causes.

Turning now to the question of the origin of the œsophageal divisions of the stomach, we find that there are two possible explanations put forward of which the first is that they are formed by the dilation of the lower end of the œsophagus.

The arguments in favor of this view are in brief as follows:

In nearly all cases where the œsophageal sac is of large dimensions it is traversed from the opening of the œsophagus to the glandular division by a continuous groove called the œsophageal groove. This has been interpreted as the direct continuation of the œsophageal tube, and it has been suggested that the œsophageal sac has been produced by a hernia-like protrusion of that portion of the œsophagus. On this assumption Ellenberger, 88, and Edelmann, 89, include these œsophageal sacs and the œsophagus together in the fore-gut (Vorderdarm), the true glandular stomach, according to these two authors, forming a part of the mid-gut (Mitteldarm). The second reason is based on the supposed specificity of the epithelium, which is in all respects similar to that of the œsophagus.

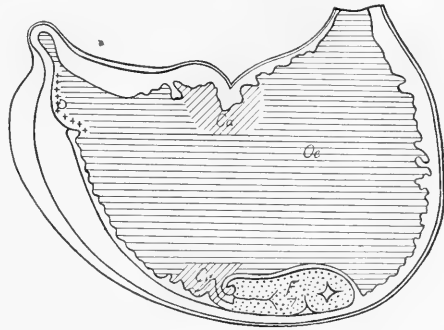


FIG. 16. Stomach of *Manis javanica* (modified from Weber).

In view of the great plasticity of epithelium of a low grade of specialization, little importance can be attached to the argument because, both pathological histology and normal histology afford many instances of the transformation of a cylindrical or a ciliated epithelium into a stratified epithelium, as a result of the operation of simple mechanical causes, such as friction. Such an instance has been noted by Haycraft and Carlier, 89-90, in the trachea of the cat. Here owing to the peculiar shape of the ring of cartilage, and the mode of insertion of the muscular layer, there is a permanent fold of the mucous membrane at the back of the trachea. As a result of the constant friction between the two layers of epithelium behind this fold the cilia are to a large extent lost and the number of layers of cells greatly increased so as to bear a great resemblance to a stratified squamous epithelium.

As regards the supposed continuation of the œsophagus by the œsophageal groove it is found on examination that the resemblance is but superficial. This has been carefully studied by Cordier, 90, who has shown that the œsophageal groove is produced by change in arrangement of the inner layer of muscle which is contrary to the rule in the œsophagus parallel to the direction of the groove. This layer becomes enormously developed at the two margins to form the lips of the groove and reduced or completely absent in the region corresponding to the bottom of the groove. The development and functional completeness of the groove is proportional to the degree of specialization of the stomach in which it occurs, not the reverse as would be the case if it were a persistent primitive structure. Apart from the inadequacy of the argument advanced in its support, the hypothesis of œsophageal origin is incapable of explaining the facts of structure as we find them.

One of the strongest arguments against this hypothesis is furnished by the stomachs of the monotremes *Ornithorhynchus* and *Echidna* which as indicated above, are lined throughout by stratified squamous epithelium and contain no glands unless indeed a portion of the extensive group of Brunners glands represent a persistent group of pyloric glands. It is only by suppression of the pre-existing glands that such a condition could be reached. That the stomach of the *Echidna* is really a stomach and not a portion of the œsophagus is indicated by the observation of Oppel, 96, that at a period of development at which the epithelium of the œsophagus has already become converted into several layers, that of the stomach is still a simple cylindrical epithelium.

Another example of the stomach which while retaining its simple external form has undergone extensive internal adaptative modifications, is that of *Manis javanica* in which the stratified squamous epithelium is found throughout the stomach although the glands are still retained in parts. By no process of simple addition from the œsophagus could such a stomach be produced.

Equally inadequate is the theory of œsophageal origin, to explain the structure of the stomachs of *Fiber* and certain of the *Arvicolidæ* where the fundus glands form an isolated group surrounded on all sides by stratified epithelium.

It is, of course, at present impossible to definitely exclude the œsophagus from any participation in the formation and development of the cardiac sacs. Until more complete histological information is available concerning the structure of the stomach in the *Cetacea*, some reservation must be made for these forms. But even here it must be remembered that in constructing his hypothetical series to show the phylogeny

of such a stomach as that of *Phocæna*, Weber started from the *a priori* assumption that the first portion was of œsophageal origin. The observation of Jungklaus, 98, that the epithelium of the first chamber of the stomach of *Phocæna* becomes stratified at a very early stage of development is not, in my opinion, sufficient evidence in itself of œsophageal origin.

In all other mammals, the evidence at present available is that the complex stomachs such as those of Ruminants, Rodents, etc., are produced from a simple stomach by progressive specialization in which the œsophagus takes no part, and in which the important phenomena are the suppression of the gastric glands and the replacement of the mucigenous epithelium by a stratified squamous epithelium. Further investigation may show the same to be true of the Cetacea.

It now remains to examine, as far as present information permits, into the cause of the transformation and the stages through which it has passed.

The changes which have taken place in the process of specialization in the stomach may be divided into two categories. To the first belong the changes of structure of the coats of the stomach more particularly of the mucous membrane; to the second, changes of form brought about by the expansion of certain portions of the stomach by the occurrence of constrictions dividing the stomach into successive chambers, or by the formation of saccular outgrowths.

In connection with the first group of changes, namely those affecting the structure of the coats of the stomach, it has been already indicated that the salient features as far as the mucous membrane is concerned are the disappearance of the gastric glands and the replacement of the simple epithelium by stratified squamous epithelium. It remains to be seen by what steps this condition has been reached and what causes have been operative in producing them.

An examination of the stomachs of *Macropus*, *Sus* and *Tapirus* in which the stratified epithelium has advanced but a short distance into the stomach, makes it extremely probable that the process of transformation has begun at the œsophageal opening, has gradually spread over the fundus sac and the left portion of the stomach, finally encroaching in the same gradual manner on the right half of the stomach. A comparison of the stomachs of *Tapirus* and *Rhinoceros*, *Macropus* and *Dorcopsis* is particularly convincing, the main difference being in the relative extent of the non-glandular division which has expanded to include the whole of the dilated fundus of the stomach in both *Rhinoceros* and *Dorcopsis*. In the *Rodentia* again, although, as far as we know,

no recent rodent presents the intermediate stage between the simple stomachs of the squirrels, rabbits and porcupines and the complex stomach of the *Myomorpha*, such a comparison as that of Toepfer shows clearly that the stomach of *Arvicola arvalis* has been produced from such a stomach as that of *Mus* by a continual encroachment of the stratified epithelium on the glandular region proceeding particularly in the sides and lesser curvature, but ultimately including the pyloric gland region. It is furthermore clear from such a series that the lines of least resistance to the encroachment have been afforded by the cardiac glands and the pyloric glands.

It is inconceivable that such an important process should take place without leaving some traces of the stages in the suppression of the glands. In the writer's opinion this intermediate stage is represented by the cardiac glands. It has already been pointed out that in certain mammals, more particularly *Bradypus*, *Dicotyles*, *Camelus*, and *Auchenia*, large areas of cardiac glands occur completely isolated from the other gastric glands and surrounded on all sides by stratified non-glandular epithelium. The supporters of the theory of œsophageal origin would doubtless regard these as œsophageal glands which have been included in the œsophageal hernia by which the sac was formed, but it must be borne in mind that in no case are they covered by œsophageal epithelium, but, on the contrary, have a simple epithelial covering. It is true that Schaffer has described such a condition in his so-called superior cardiac glands of the human œsophagus, but there is no evidence that these isolated structures which have been found in no other mammal, are primitive. The theory of œsophageal origin is inadequate to explain the persistence of these groups of glands.

On the other hand, the theory suggested by Oettel that the cardiac glands form the intermediate stage in the process of complete obliteration of the gastric glands in portions of the stomach affords a simple explanation of the occurrence of these isolated groups of cardiac glands, and is in accord with the results of histological investigation. Some suggestion of this kind apparently occurred to Edelman, but he was turned aside from the full consideration of it by his failure to find the cardiac glands in the higher ruminants.

The facts in favor of this view are briefly as follows:

1. A layer of cardiac glands is always interposed between the glandless zone with stratified epithelium and the gland-bearing zone. In the further advance of the stratified epithelium into the stomach, the first structures to suffer suppression would be these cardiac glands. As it is unlikely that new glands of a different origin would be produced at

a point where the bulk of the changes are degenerate, a new intermediate zone of cardiac glands can only be produced by the transformation *in situ* of fundus glands.

2. In some mammals, *Bradypus*, *Camelus*, etc., cardiac glands have been retained in the mucous membrane of certain saccular diverticula of the stomach which on account of their shape have not experienced the full effect of the mechanical action of the food.

3. Comparing the stomachs of *Macropus* and *Dorcopsis* a most remarkable resemblance is observed in the external form and in the relative extents of the pyloric gland and fundus gland zones respectively. In *Dorcopsis*, however, the cardiac zone region is much smaller than in *Macropus* and the oesophageal portion much larger. It is evident that this condition has been reached by the suppression of the anterior cardiac glands and their replacement by a stratified epithelium. A similar comparison may be drawn between *Sus* and *Dicotyles*.

4. In a retrogressive process affecting such a structure as the gastric gland composed of several kinds of elements, it is reasonable to suppose that the various elements would disappear in the order of their specialization, that is, by inference, in the inverse order of their power of independent reproduction. Chief cells and parietal cells rarely divide and it is difficult to decide as to their degree of relative specialization. The whole question of the nature of the parietal cells has been reopened by Schaffer's discovery, recently confirmed by Hewlett, 01, of their occurrence in the glands of the mucous membrane (obere Cardialdrüse) of the upper portion of the human oesophagus. It is possible that we shall be forced presently to admit that we know nothing of their nature or function and include them in a common category with those other little understood elements, the crescent cells of mucous glands. Both chief and parietal cells are clearly more highly specialized than the mucous neck cells for the latter sometimes undergo division. In the histological part of the paper attention has been directed to a number of facts which point to the conclusion that the cardiac glands have been so derived from the fundus glands by the disappearance first of the chief cells and second of the parietal cells.

An analysis of the causes that have been operative in producing these changes is beset with unusual difficulties. In his discussion of the results of the research of his pupil, Toepfer, on the stomach of *Rodentia*, Fleischmann, 91, utters a warning against the too hasty conclusion that the specialization which has taken place in such stomachs as those of the *Ruminants* and *Myomorpha* is due to an herbivorous diet. He points out that in three out of the four main subdivisions of the *Roden-*

tia, composed of animals that are as distinctly herbivorous as the *Myomorpha*, no such specialization has taken place. On the other hand, the fact that in the purely herbivorous Kangaroos, in the leaf-eating sloths, and in the graminivorous and herbivorous Rodents and Ungulates, similar differentiations of the stomach have arisen independently, is surely worthy of serious consideration. Another factor which is discussed by Fleischmann is a possible correlation between dental evolution and gastric structure. He found, however, that in various species of *Arvicola* there was no relation between the complexity of the molar pattern and the structure of the stomach. In any case in the writer's opinion the principle of correlation would not explain, except in a general way, the increasing complexity of the stomach. The direct effect must be exerted through the food. The occurrence of similar specializations in certain Anteaters and in the Cetacea, which subsist on food which is in a sense the chemical antithesis of that of the herbivores renders it necessary to seek the causes of this specialization in conditions which are common to all the animals which possess it. If we conclude that the object of the complex structure of the ruminant stomach is simply to provide increased storage capacity or an antechamber to the stomach in which carbohydrate digestion can go on, then we must seek for wholly different causes in the Cetacea and Anteaters. It seems more probable that similar causes have operated in all the various instances and that chemical composition has been important only inasmuch as it determined the bulk and consistence of the food masses in the stomach. Any discussion of the methods by which these changes have been effected must for the present be largely speculative, and the final solution of the question must rest with the experimental physiologist. There are, however, a number of facts which indicate that the causes have been of a physical, mainly mechanical, nature.

I have already pointed out that in all these stomachs it is probable that the change began at the cardiac orifice and proceeded gradually into the stomach, encroaching more and more upon the normal glandular mucous membrane. This is exactly paralleled according to the experimental researches of Ellenberger, *90*, by the course of the food. According to this investigator, the food does not "circulate" in the stomach of the horse, but accumulates as it is swallowed in the left extremity of the stomach in the fundus sac. When food is again taken that previously swallowed is displaced *en masse* in the direction of the pylorus by the new food which is in turn similarly displaced by the next meal. There is thus a gradual progression of the food from cardia to pylorus. During this process the food is undergoing various changes.

It is being softened by the action of the saliva and of the secretion of the cardiac glands, subjected to the action of bacterial enzymes, and, after it has passed the cardiac zone, to the digestive action of the gastric juice; it is being converted into a softer and more plastic mass. In view of these changes, the fact to which Oppel has called attention that the distribution of the food masses in Ellenberger's diagram corresponds almost exactly with the areal subdivision of the mucous membrane, is not without significance.

The newly-swallowed food is contained in the portion of the stomach which is lined by stratified epithelium, the cardiac gland region is occupied by food which has already undergone some maceration and softening, and the fundus and pyloric gland zone contains food in which the softening process has reached its highest degree. I can see no other explanation for these circumstances than that the changes have been primarily due to the mechanical action of the food on the mucous membrane, and that the rapidity of their production in any region bears a direct relation to the consistency of the food that is contained in that region. This mechanical effect would be in part due to friction owing to the unusual consistence of the food, but doubtless other factors play an equally important part. Among these, over-distention of the stomach, owing to the greatly increased bulk of the food as compared with that of animals such as carnivora which subsist on a more concentrated diet, is of the first importance. This distention is in placental mammals most prominently displayed in the fundus sac, the portion where histological changes first appear. Another factor of importance is the prolonged stay of the food in the stomach owing to the increased bulk, unfavorable consistence and reduced digestibility. A fourth factor which may possibly play a considerable rôle in aquatic animals with a reduced dentition, is the reduction of the temperature in the mucous membrane due to the rapid ingestion of considerable masses of food of lower temperature than the body.

That such conditions may be the cause of profound changes in the mucous membrane of the stomach is indicated by the recent study by Cade, *op. cit.*, of the histological changes in the mucous membrane of the cat's stomach due to a gastro-enterostomy. In this experiment the cat's stomach was divided completely into two portions, one containing the fundus zone and the other the pyloric zone, and the cut ends closed by suture. An anastomosis was then effected between the greater curvature and a loop of the ileum. After a lapse of six months the animal was killed and the stomach examined, with the result that the mucous membrane was found to have undergone changes in the neighborhood of

the new outlet of such a nature that the parietal and chief cells had disappeared from the glands and their places had been taken by muciparous elements similar to but not identical with those normally found in the neck of the gland. It might of course be urged that these changes had been of inflammatory origin due to the surgical injury inflicted but it seems more reasonable to suppose that they have been due to the fact that a new focus for the motor activities of the stomach has been set up and that this coincides with the opening into the intestine. If such change can be produced in the life of a single individual by surgical interference, it is not difficult to believe that just such simple causes acting through many generations and assisted by the processes of natural selection have produced the changes which we see in so many herbivores belonging to both the placental and marsupial series.

As to the precise way in which the factors enumerated above have acted, very little can be said because there is as yet no experimental evidence on which to base conclusions. Possibly limitation of the blood supply to the mucous membrane owing to the pressure exerted by the great bulk of food, and exhaustion of the glands from continued over-secretion may be of importance, while actual friction will explain the change in the surface epithelium.

A further argument in favor of the view that the changes in the stomachs of herbivorous mammals owe their origin to mechanical causes aided by natural selection, is afforded by the occurrence in the sloth, in the camel and the llama and in the peccary of saccular diverticula lined by cardiac glands. If the hypothesis that the cardiac glands are the intermediate stage in the disappearance of the glands, be correct, it is easy to understand why they have been retained in these animals. Suppose, for example, that an animal is undergoing a change of habit of such a nature that it is passing from an omnivorous to an herbivorous diet. The effect of this would be, if the above hypothesis is correct, to cause the transformation of the fundus glands in the neighborhood of the cardiac orifice into cardiac glands and finally the disappearance of the latter and the conversion of the epithelium into stratified epithelium. If, however, in the portions of the stomach where these changes were taking place, sacculation occurred, the mucous membrane of such a saccule would be less exposed to the disadvantageous action of the prolonged presence in the stomach of a food mass of firm consistence or of the friction caused by the movement of the latter over the surface of the mucous membrane. It would be less likely to come into contact with the freshly-swallowed food or to be subjected to sudden changes of temperature. The result would be that the degenerative

processes would be delayed in the mucous membrane of such a saccule, and that its mucosa would still contain fundus glands long after those of the adjacent portion of the stomach had been converted into cardiac glands. Individuals possessing such saccular diverticula would have a higher digestive potential, and thus a greater chance of survival and of propagation than others less favored.

There would thus be for a time a tendency to preserve and perfect by natural selection these saccules. Ultimately, however, the degenerative processes would extend even to the mucous membrane of the saccule and their glands would be first converted into cardiac glands and finally disappear.

We are thus furnished with a means of explaining the retention of cardiac glands in the large pointed sac of *Bradypus*, in the first chamber of the stomach of the peccary, and in the water cells of the camel and llama, while they have disappeared from the rumen, reticulum, and omasum, of the higher ruminants. The cells of the reticulum do not contain cardiac glands because they are not primary diverticula of the rumen. Cordier has produced evidence to show that the partition walls between the cells of the reticulum are produced by fusion of rows of vascular papillæ, such as occur in the rumen.

In the anteaters, *Manis*, and *Echidna* and the duck-bill, the mechanical factor has been introduced in all probability by the admixture of small stones, grains of sand, etc., with the food.

The interpretation of the glands of the water-cells of the camel's stomach and of the pointed sac of the stomach of *Bradypus* as cardiac glands which have been retained long after the glands in the walls of the main cavity of the stomach have disappeared, because of the fact that they have been somewhat removed from the direct action, friction, pressure, etc., of the food, suggests a very interesting field of speculation as to the mode of production of the division into chambers of the stomach of ruminants and some allied changes in form of the stomachs of other mammals. The purpose of specialization of this character is usually conceded to be the provision of storage chambers of sufficient capacity to accommodate the greatly increased bulk of food of reduced nutritive value, and in which the preponderating carbohydrate element may be subjected for a longer period to the amylolytic action of the saliva. That the first of these considerations is of the greatest importance in determining the progressive specialization of the herbivorous stomach there can be little doubt. The precise way in which it acts however is extremely obscure. Moreover, leaving out of consideration the question of the prolonging of carbohydrate digestion, it is not clear

what advantage from the mere standpoint of the storage function a chambered stomach possesses over one in which this purpose is subserved by a mere increase in size of the stomach. On this basis alone, it is difficult to understand the occurrence of a highly specialized chambered stomach in forms like *Cricetus* in which there are supplementary storage chambers in the form of capacious cheek pouches. It is possible, on the other hand, that the division of the stomach into two or more successive chambers has been an indirect effect of the increase in bulk of the food and its altered consistence and has been in reality a conservative effort on the part of the organism designed to check the further advance of the degenerative process in the mucous membrane. The evidence seems to indicate that the natural sequence of changes in the stomachs of herbivorous mammals and of certain other forms which subsist on a peculiar form of food, results in the suppression of the gastric glands beginning at the œsophageal orifice and gradually proceeding from left to right, involving more and more of the mucous membrane. Ultimately, if no conservative process intervenes, this would result in the complete suppression of the gastric glands, as has occurred in *Echidna* and *Ornithorhynchus*.

The subdivision of the stomach by constriction into two or more chambers might be interpreted as such a conservative effort, the object of which is to check the advance of the degenerative process and so provide sufficient storage capacity to meet the needs of the animal with the minimum reduction of digestive potential. If it is true that the disappearance of the glands is due to the mechanical action of a food mass of unusual consistence, it is easy to understand how such a constriction would be of use to the animal by confining the food to the first chamber until it had undergone such a change in consistence from maceration and the action of salivary and bacterial enzymes that it was no longer a source of danger to the mucous membrane. If the constriction rapidly reached such a degree that food could only pass over into the second chamber after a considerable degree of softening had been reached, it would prove an effective barrier to the advance of the degenerative process. This appears to have been the case in the *Tragulidæ*. In many cases, however, the constriction has been insufficient to check completely the degenerative process and merely retards it, as in the stomachs of *Arvicola*, *Fiber*, etc. An interesting example of this condition is afforded by *Camelus* and *Auchenia* in which notwithstanding the constriction, the degenerative process has invaded the distal segment of the stomach and converted the glands of a considerable portion into cardiac glands. This doubtless represents, as Boas, 90,

suggests, an earlier condition, common to the Camelidæ and the ancestral forms of the other Ruminants. In the latter the condition has been effectively met by the occurrence of a second constriction marking off the omasum, but in the Camelidæ the degenerative process has advanced until only an extremely narrow zone of fundus glands remains. A similar explanation is suggested for the peculiar tæniated colon-like stomach of the kangaroos, in which the sacculation may have for its object the retarding of the passage of the food mass from left to right in order to give greater time for the change in consistence referred to above.

A difficulty in the way of accepting this explanation of the origin of sacculation in the stomach is presented by the peculiar stomach of *Myoxus* in which a division into two chambers has taken place in the absence of degenerative changes of any kind whatever, and the peculiar tæniated stomachs of certain Primates, *Semnopithecus*, etc., in which there is an œsophageal division, but a very slight development of cardiac glands. It is possible that an investigation of the latter by more discriminative cytological methods may reveal changes in the proximal fundus glands which would justify their interpretation as cardiac glands. Pilliet's researches only indicate that the glands in question contain parietal cells, they do not give any information as to whether the chief cells which accompany these are pepsin-forming or mucin-forming.

In conclusion, it may be remarked that if the hypothesis of Oppel, which is supported in the foregoing pages, that the cardiac glands are modified fundus glands is correct, it will be necessary to substitute a definition of the cardiac glands based on phylogenetic grounds, for the definition given by Edelman. In the case of the human stomach in the cardiac glands of which both parietal cells and ferment-forming chief cells are present in small numbers, the distinction between cardiac glands and fundus glands might be dispensed with altogether. In the interests of comparative anatomy and particularly on account of the great extent of these glands in the pig, camel, peccary, etc., it seems desirable to retain the present classification and to define the cardiac glands as modified fundus glands occurring at the cardiac orifice of the stomach, or at the junction of the glandular and non-glandular divisions of the stomach, or in special sacs, differing from the usual fundus glands in the reduction in numbers, or complete absence of the parietal or ferment-forming chief cells, or both, and by the increased number of mucous chief cells.

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PRESENT PROBLEMS OF MYOLOGICAL RESEARCH AND THE
SIGNIFICANCE AND CLASSIFICATION OF
MUSCULAR VARIATIONS.¹

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WITH 7 COLORED PLATES.

The study of comparative myology and of myological variations impresses three facts of cardinal importance on the observer:

1. Forms, which according to the zoological system commonly accepted are widely separated from each other in the series, present in some details of their myological structure identical or very closely allied characters.

2. Human muscular variations and supernumerary muscles are frequently homologous with muscles normally occurring in species apparently very far removed from man in the zoological scale.

3. Within the confines of a more limited group, as a single mammalian order, the smaller subdivisions of family and species are at times sharply differentiated from each other in some detail of their structure, which distinguishes the form possessing it from the remaining divisions of the group, no matter how close in other respects their morphological congruence may be.

The concurrence of a structural character, or its occasional recurrence by variation, in species which in other respects have little in common, necessitates a very careful revision of its development, derivation and functional significance in order to avoid erroneous conclusions respecting the phylogeny of the species in question.

The further the study of comparative myology is carried, and the more complete our knowledge of this science and of human muscular variations becomes, the clearer does the fact appear that, with few exceptions, the living mammalia present in their muscular system very complicated conditions. These are, in many forms, the result of

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specialization and differentiation carried to the fullest possible degree—masking antecedent conditions, or combining them with other elements which make the determination of homologies a matter of difficulty.

In the light of more extended knowledge the commonly accepted relative phylogenetic position of many forms requires careful revision. Especially does the view which regards the Primates as a comparatively late and structurally higher derivative from the mammalian stem meet with reversal at the hand of the morphological facts. In some respects man and the other Primates offer simpler morphological conditions than are found in other mammalian orders, and conversely many of the so-called “lower animals” are, in respect to certain structural specializations, far in advance of the stage occupied by the Primate homologues. Deductions, to be of phylogenetic value, must be drawn with the knowledge and appreciation of two facts:

a. The impulse to perpetuate muscular structure along primitive ancestral lines is a strong and influential factor in determining normal myological conditions for any given species, and in the production of muscular variants. This factor is active, notwithstanding the well known tendency of muscular structures to adapt themselves extensively by migration, concrescence, metamorphosis and fibrous regression to skeletal modifications and to changes in their functional application. In dealing with muscular homologies it is of the greatest importance to reckon with these changes, to differentiate between the secondary acquired characters and the primitive fundamental elements. Especial care must be exercised in assigning the correct morphological value to the skeletal connections, and here again the variability of the area of *origin* requires particular consideration.

b. Under altered functional requirements *rehabilitation* may take place of muscles which practically at one period in the evolution of the species had become rudimentary, but which under the stimulus of a new physiological application, resume an active place in the organism, combining at times with adjacent muscles to form compounds of a puzzling myological character.

Modern investigations of the muscular system should meet the following demands:

Accurate determination, for the muscle or muscular group in question, of the norm and of the range of variation, with full consideration of the nerve supply, as the decisive factor in establishing homologies. These data should be based on the examination of an adequate number of individuals of the species under consideration.

Full and detailed comparison, on the same lines, with the correspond-

ing structures in the allied genera and species of the same zoological order.

Determination, by reconstruction from these data, of the *common plan* of the muscle or muscle group underlying the specialized differentiations encountered in the individual forms; in other words the reconstruction of the primal antecedent *myo-type* of the order.

Comparison, as extensive as possible or desirable, with the homologous structures in *other mammalian orders*. This is of especial importance where myological characters appear confined to limited groups within an order, not occurring in the remaining genera and species of the same order, but found again more or less widely distributed throughout other mammalian orders.

Based on the preceding comparative study the attempt should be made to define the relation of the muscle or muscular variant to the common ancestral myological stem of the mammalian *class*.

Conclusions respecting the phylogenetic value of the muscle or muscular group.

The study of muscular variations, based on the data supplied by comparative anatomy, shows that departures from the normal type of myological development in any given form may be grouped, in reference to their derivation and significance, under one of the following three heads:

1. Fortuitous variations. 2. Progressive variations. 3. Reversional variations.

Fortuitous Variations.—A very small percentage of the muscular anomalies can, at least provisionally, be placed in this class. Congenital deficiencies of muscles or muscular groups, in part or in whole; malformations depending upon accidental errors in development, either by themselves or associated with cognate errors in the development of other structures; finally a small number of supernumerary muscles and muscular slips.

The arrangement of the Pectoral muscles shown in Pl. I, Fig. 1, may be taken as an example of this group of accidental or fortuitous variations.

The sheet of the Pectoralis major appears deficient in the portion of the sterno-costal segment corresponding to the third and fourth chondrosternal junction. The muscular fibres which should fill the cleft are united to form an intermediate pectoral slip (Pectoralis minimus, var., tensor semivaginae articulationis humero-scapularis, Gruber), which crosses laterad between the Pectoralis major and minor to reach an expanded fascial insertion beneath the Deltoid close to the upper extremity of the humerus.

We are evidently dealing here with an accidental displacement of a portion of the otherwise normal Pectoralis major, which has, in consequence of an error in the differentiation of the muscle, resulted in the formation of an accessory intermediate pectoral slip. This slip has followed the lead of the Pectoralis minor in gaining a more proximal insertion, while its origin shows it clearly to be the missing portion of the Pectoralis major.

The case speaks for the original common derivation of both Pectoral muscles, but the error in differentiation is an accidental and fortuitous occurrence without special reversional significance.

Progressive Variations.—A still more limited number of muscular abnormalities may be placed in the division of *Progressive variations*, as departures from the normal type possessing the significance of indicating evolutionary processes which will eventually lead to permanent pronounced structural modifications of existing muscles, or to the acquisition, as normal constituents of the organism, of new muscular integers.

This class of variations is illustrated by the cases in which the Peroneus tertius defaults, and is replaced by a short extensor of the 5th toe added to the Extensor Brevis Digitorum.

Reversional Variations.—In number and diversity—as well as in frequency of occurrence—the variations belonging to this subdivision far exceed all the others. They offer reversional indications of the stages through which, in the phylogenetic history of the muscular apparatus, the specific myological types of to-day have obtained their individual structural character.

The most complicated and specialized muscles of living forms owe their present high degree of development and individuality to progressive modifications of a primitive ancestral muscular system, presenting the typical metameric arrangement still preserved in the lowest living vertebrates and in the ontogeny of the higher forms.

Closely dependent upon the further elaboration of the skeleton, and directly associated with the same as an integral part of the locomotory apparatus, the muscle-groups and individual muscles appear as derivatives from this common stem, varying in their degree of separation from, or combination with adjacent muscular groups, and capable of further numerical augmentation and specialization by cleavage and division (Pl. II, Fig. 2.)

In following the evolution of any given muscular group a point will be reached at which the definition of the special type characteristic of the great *vertebrate classes* begins. From the antecedent *common ver-*

tebrate stem main branches are derived representing the complete muscular group or the individual muscle in e. g. Reptiles, Birds and Mammals (Pl. II, Fig. 2), to confine the consideration, for the sake of simplicity, to the higher vertebrate types. Take, for example, the *common mammalian myological stem*. It contains primarily elements possessing a *potential* evolutionary force, capable of *progressive* development. It can, by differentiation, cleavage and subdivision, acquire greater *complexity*, and the resulting new muscular organs can become highly specialized, changing their skeletal relations by migration, acquiring new functional applications and entering in varying degrees into combination with adjacent muscles.

On the other hand the common mammalian muscular prototype carries within it the possibility of *regression* and *metamorphosis* into fibrous and ligamentous tissue, or of complete *default*, according to the conditions surrounding and influencing its development in the specific types. New lines of *adaptation* to the evolutionary demands of the specialized *mammalian orders* are thus derived from the *common antecedent* stem of the complete mammalian muscle, which latter includes *potentially* the development of all the diverse forms assumed by the muscle in the various mammalian orders, genera and species. Thus the same muscle in Man, in a Carnivore, and in a Rodent, may pursue widely divergent developmental paths. It may practically retain the primitive arrangement in one of these forms, while in another the origin and insertion shift by migration, or in the third the organ changes its original functional character and becomes partially converted into fibrous tissue by metamorphosis and degeneration. Yet inherently in all these diverse types the muscle corresponds to the fundamental mammalian *class-stem* from which the special differentiations are derived by adaptation to skeletal conditions and functional requirements.

Within the limit of a single mammalian order a muscle or muscular group may present a number of congruent structural characters which lead back to the type *common to the entire order*. From this common ancestral form of the muscle the adaptations characterizing the genera and species of the order are derived.

If, for example, we consider any given muscular group in reference to its origin from the common mammalian myological stem along the line of *Primate adaptation*, the type thus presented must include *potentially* the capacity of developing into the diverse forms which the muscle assumes in the individual families and species composing the order. This primate ancestral type of any muscle or muscular group may be reconstructed from the data furnished by the various forms assumed in

living representatives of the order, and must contain within its structural plan the elements which, by successive modifications, lead to the differentiation of the diverse extant types.

Thus the detailed examination of the Pectoral muscular group in the Primates will show the existence of three main types, phylogenetically related to each other, which can be illustrated by the following selected forms:

I. PRIMITIVE TYPE.

1st Example: *Hapale jacchus*, Common Marmoset, Columbia University Museum, No. 427 (Pl. III, Fig. 3). The Pectoral mass in this animal is composed of two main layers.

The Superficial Layer (Ectopectoralis, Wilder) is again distinctly divisible into two segments:

A. CEPHALIC PORTION.—A thick triangular muscle, arising by its base from the entire ventral surface of the sternum along the ventral midline, and inserted by its truncated apex into the lateral ridge of the humerus. This muscle corresponds to the main portion of the sternocostal division of the human Pectoralis major.

B. CAUDAL PORTION.—This forms an extensive thin sheet of paler muscular fibres, prolonging the level of the superficial portion caudad of the sternum. It arises from the ventral abdominal aponeurosis, passing superficially to the Rectus abdominis, as far as the umbilicus. It is inserted, under cover of the cephalic portion, in combination with the deeper layer, into the lateral tubercle of the humerus, cephalad of the insertion of the cephalic portion (Pectoralis major).

This segment is the homologue of the reduced abdominal pectoralis slip of the human subject.

The Deep Layer, corresponding to the human Pectoralis minor (*Entopectoralis, Wilder*), arises from the ventral surface of the sternum in its entire extent, under cover of the sternal or cephalic portion of the superficial layer. Cephalad this layer is almost directly continuous with the broad origin of the subclavius muscle; caudad, beyond the lower margin of the superficial sternal portion, it is directly continuous with the thin abdominal sheet of the superficial layer. It would, therefore, be quite correct to describe the Pectoral muscles of *Hapale* as forming two layers in the entire extent of their sternal attachment—a superficial layer or Pectoralis major, and a deep layer or Pectoralis minor; the Pectoralis major ceases at the lower border of the sternum, and allows the caudal

portion of the deeper layer (*Pectoralis minor*) to come to the surface as the thin abdominal sheet. The latter, in the superficial dissection (Pl. III, Fig. 3 right side), appears to continue the layer of the *Pectoralis major* caudad beyond the sternum. But after reflection of the divided *Pectoralis major* it is seen that the abdominal portion is really directly continuous with the deeper sternal division of the muscular mass (*Pectoralis minor*), the entire sheet having a common humeral insertion under cover of the superficial layers of the *Pectoralis major* into the lateral surface of the shaft of the humerus.

The *Pectoralis* mass has no attachment to the clavicle. The clavicular portion of the Deltoid, extending mesad to the sterno-cleido-mastoid muscle, is separated from the cephalic border of the Pectoral by a cleft filled with loose cellular connective tissue.

In none of the Marmosets examined was a distinct axillary arch encountered. The panniculus in these animals appears very slightly developed in the thoraco-humeral segment, and not recognizable as a distinct layer.

2nd Example: *Nycticebus tardigradus*, The Slow Lemur, Columbia University Museum, No. 1068 (Pl. III, Fig. 4). Compared with *Hapale* the Pectoral muscle of this lemur presents:

1. A less complete differentiation of ecto- and ento-pectoral layers.
2. A greater independent pannicular development and, as a segment of this sheet, a distinct axillary arch.
3. A marked reduction of the abdominal portion of the *Pectoralis*.

The *Pectoralis* arises from the entire extent of the ventral midline of the sternum, passing at the caudal extremity of the bone laterad to the eighth costal cartilage, and by a thin aponeurotic lamella to the ninth costal cartilage. The converging fibres of the superficial portion of the muscle form a triangular sheet which is inserted into the lateral surface of the shaft of the humerus, closely united with the adjacent margin of the Deltoid. The latter muscle, in its ventral segment, arises from the outer third of the ventral surface of the clavicle, leaving a broad triangular interval between its ventral margin and the cephalic border of the *Pectoralis*, in which the broad and well-developed *Subclavius* appears after removal of the superficial fatty and connective tissue filling in the fossa.

Division of the superficial layer of the *Pectoralis* (Pl. III, Fig. 4, left side) reveals the existence of a deeper, entopectoral layer, separated from the ectopectoral layer in the cephalic and middle portions, but directly continuous with and inseparable from it at the caudal extremity of the entire Pectoral mass. This rudimentary representative of the human

Pectoralis minor arises from the ventral surface of the sternum, under cover of the superficial layer, from the level of the 2nd chondro-sternal junction caudad to the fusion of both layers in the terminal portion of the common origin. This deeper sheet, receiving all the muscular fibres from the caudal common origin corresponding to the cartilages of the last two sternal ribs, proceeds, under cover of the superficial layer, intersecting the course of the fibres of the same at an acute angle, across the ventral axillary wall to expand into a broad tendinous lamina which, after receiving the well developed axillary arch along its caudal margin, expands under cover of the Deltoid to be inserted into the lateral tubercle of the humerus and the adjacent portion of the lateral surface of the shaft.

The axillary arch appears as a derivative of the well developed ventro-lateral thoracic panniculus. It crosses the axillary border of the Latis-simus, but has no direct connection with that muscle.

COMPARISON OF PECTORAL GROUP IN *Hapale* and *Nycticebus*.

Both these forms, selected as representative examples of the primitive Pectoralis type in existing Primates, show a comparatively early stage in the differentiation of the two main component elements, Pectoralis major and minor. In *Nycticebus* the differentiation is still incomplete in the caudal segment of the Pectoral mass. In *Hapale* the cleavage is complete—and with this the ectopectoral layer has gained a distinct caudal limit and presents a thick well marked border extending from the caudal end of the sternal origin to the humeral insertion. On the other hand the entopectoral layer, occupying the same extent of sternal origin at this point, is left to become directly continuous with the thin abdominal extension of the Pectoralis. In *Hapale* a fairly distinct *intermediate* entopectoral muscular slip (Pl. III, Fig. 3, left side) effects the junction between the caudal margin of that portion of the deeper layer which arises under cover of the ectopectoral entirely from the sternum, and the thin expanded caudal sheet arising from the abdominal aponeurosis. This intermediate entopectoral slip arises by an aponeurotic lamella over the cartilages of the lower sternal ribs, and proceeding laterad, fuses with the main entopectoral plane before the same unites with the abdominal portion near the common insertion into the lateral surface of the humerus. Comparison with *Nycticebus* shows this slip to correspond to the distal united portion of both pectoral planes, arising from the 8th and 9th costal cartilages, while the abdominal Pectoralis in *Nycticebus* has not yet differentiated from the general pannicular plane.

Careful examination of the two forms indicates very clearly the value

of the *fixed sternal line* of origin in the differentiation of the muscles. This process, in passing from the stage illustrated by *Nycticebus* to that obtained in *Hapale*, may be regarded as presenting the following steps:

1. The advantage of the fixed sternal origin leads to the complete differentiation of the ectopectoral from the entopectoral as seen in *Hapale*—compared with the incomplete segmentation observed in *Nycticebus* in the caudal common portion of both planes. With this complete differentiation the volume of the ectopectoral increases and the muscle obtains a distinct caudal limit.

2. The entopectoral likewise begins to differentiate as a stronger cephalic portion with sternal origin, leaving the interval seen in *Hapale* between its own caudal margin and the slip arising by an aponeurotic lamella over the costal cartilages of the lower true ribs.

3. The abdominal pectoral appears to be a derivative of the pannicular muscle. In *Nycticebus*, where the pannicular plane is well developed and independent, the abdominal pectoralis is wanting. On the other hand in *Hapale*, which animal presents a marked reduction of the cuticular thoraco-humeral muscle, the abdominal pectoral is fully developed. Comparison of the two types produces the strong impression that the abdominal portion develops in the lead of the axillary arch. As seen in *Nycticebus* this connection of the pannicular muscle with the Pectoral system is well developed. Mesal extension of the same would lead to the development of the abdominal pectoral as a secondary derivative of the pannicular layer. It is quite possible that, when once established, this connection with the main pectoral system would continue to favor the more independent development of the abdominal pectoral and cause its more complete differentiation from the rest of the lateral thoracic panniculus, which in the floor of the axillary space metamorphoses into fascial layers, while the original point of connection between the cuticular system and the Pectoralis remains as the apparently isolated axillary arch. In this way the condition encountered in the majority of the lower monkeys (Pl. IV and V, Figs. 6-8) would be explained, where, with a well developed and distinct abdominal pectoral and axillary arch, the intervening fascial floor of the axillary space is devoid of muscular fibres. Many of the human muscular variations, as the different types of union between a Pectoralis quartus and the axillary arch, and a number of axillary supernumerary muscular slips, lead back to this same hypothetical primate condition. An example of these variations occurring in one of the lower Primates is offered by the abnormal arrangement of the Pectoral muscles in the specimen of *Macacus cynomolgus* shown in Pl. IV, Fig 5 (Columbia University Museum, No. 1132^a).

Two supernumerary slips, one derived from the junction of Pectoralis minor and abdominalis, the other from the latter muscle nearer the insertion, cross the axillary space and insert into a fibrous lamella, the caudal slip fusing with the axillary arch. The absence of a distinct axillary arch in *Hapale* must, I think, be taken as a specific character without special significance, for the structure reappears so uniformly in the remaining Primates up to the anthropoid apes and Man, and is such a common variation in the latter, that its position as a distinct myological character of the Primate order may well be recognized.

II. INTERMEDIATE TYPE.

1st Example: *Cynocephalus anubis*, Olive Baboon, Columbia University Museum, No. 1243 (Pl. IV, Fig. 6). In this form, while the general arrangement of the pectoral mass corresponds to that found in *Hapale* and the *Lemur*, individual differentiation of the component muscles has proceeded further. The Pectoralis minor has segmented as a distinct muscle, both from the Subclavius cephalad, and from the abdominal Pectoral caudad. The cleft separating the minor from the latter muscle extends nearly to the insertion. The same is, however, still common to both muscles into the lateral tubercle and the adjacent proximal portion of the shaft of the humerus under cover of the Pectoralis major and Deltoid. The axillary arch is more closely adherent to the underlying margin of the Latissimus and is combined at the insertion with the abdominal pectoral muscle. The Pectoralis minor still arises largely from the ventral surface and lateral margin of the sternum, but some of the deeper fibres of the cephalic portion have obtained an attachment further laterad to the upper costal cartilages. There is no clavicular Pectoralis.

Cynocephalus is a very representative generalized form of the intermediate type of the Primate Pectoral group, which obtains with only slight species modifications in all the lower monkeys of both hemispheres. The following characters are to be noted, in comparison with the primitive type illustrated by *Nycticebus* and *Hapale*.

1. The complete differentiation of Pectoralis major and minor and the sharply defined individuality of the muscles.

2. This character is accentuated in *Cynocephalus* by the cranial shifting of the attachment of the Pectoralis minor along the sternal origin, developing a wide and well marked interval between this muscle and the abdominal Pectoralis.

In some of the other Cynomorpha the more primitive extensive

thoracic origin of the Pectoralis minor is retained, as in the Macaques (Pls. IV and V, Figs. 5 and 7).

3. It will be noted, however, that in these latter forms the muscle has begun to shift its origin laterad, from the sternum to the adjacent costal cartilages. This is particularly the case in the specimen of *Macacus melanotus*, Gray—shown in Fig. 7, Pl. V (Columbia University Museum, No. 1871).

4. In some forms belonging to this intermediate type, the Pectoralis minor presents both the cephalic and lateral migration of the origin, which is carried to its full development in the secondary type found in Man and the Anthropoid Apes.

Pl. V, Fig. 8, shows this character of the muscle in a specimen of *Semnopithecus entellus* (Columbia University Museum, No. 1251).

III. SECONDARY TYPE.

This is presented by the arrangement found in Man and in the closely corresponding disposition of the Pectoralis in the Anthropoid Apes. It is characterized by—

1. Further differentiation of the individual muscles composing the group.

2. Extension of the Pectoralis major to the clavicle and consequent relative reduction of the clavicular portion of the Deltoid.

3. Migration cephalad of the insertion of Pectoralis minor from humerus to the coracoid process of the pectoral girdle.

4. Complete separation, consequent upon this shifting, of Pectoralis minor and abdominalis, at their insertion.

5. The secondary assignment of the latter muscle, in its greatly reduced form, as a component of the Pectoralis major, forming the abdominal slip of the latter muscle, arising from the external oblique aponeurosis and inserting into the deep layer of the Pectoralis major tendon.

6. Reduction of the Pectoralis minor and migration laterad of the origin of this muscle from sternum to the ribs, obtaining the consequent digitate attachment to a varying number of the upper ribs, below the first.

7. The freeing of the sternum by the lateral recession of the minor affords the increased area of sternal attachment for the Pectoralis major, which muscle, in addition, occupies in its deeper portion some points of attachment to the costal cartilages.

8. Reduction of the thoracic panniculus in the axillary region and the disappearance, in Man and the Anthropoid Apes, of the axillary arch as a normal muscular integer, while the same is still observed as a frequent individual variation.

Figs. 9 and 10 represent the superficial and deep pectoral muscles in a fresh dissection of an adult male orang—*Simia satyrus*.

RECONSTRUCTION OF THE COMMON PRIMATE PECTORAL GROUP.

In view of the disposition found in *Nycticebus* we may assume that the ancestral common Primate type of the Pectoral group presented a very slightly differentiated ventro-appendicular muscular sheet, connected at the insertion with an extensive thoraco-humeral pannicular muscle.

The skeletal relations of this primitive muscle at the origin give us the indications of the lines along which subsequent differentiation took place.

The pre- and mesosternum evidently afforded the most advantageous line for the mesal attachment of the muscle, and consequently we see in *Nycticebus*, and still more in *Hapale*, that both the superficial and the deep segment of the Pectoral plane in the sternal portion is strongly developed and in contrast, as a massive condensed muscular mass, with the thin expanded abdominal sheet.

It is not difficult to recognize in the latter a derivative of the pannicular layer which has obtained a secondary line of attachment to the abdominal aponeurosis, but which, lacking the advantage of the firm connection afforded by the sternum, has failed to develop in a corresponding degree. For the original pannicular derivation of the abdominal pectoral we have evidence in the connection of this muscle at the insertion both in *Nycticebus* and *Cynocephalus* with the axillary arch, which appears as a distinct pannicular element in *Nycticebus*, and only begins to obtain its secondary connection with the Latissimus in *Cynocephalus*.

Of course the question of the original derivation of the entire Pectoral mass, as a differentiated product of the deeper layers of a primitive extensive tegumentary muscular sheet demands consideration at this point. We may assume, however, that in the common Primate type the skeletal attachment to the sternum had already sufficed to produce the differentiation of the cephalic portion as a distinct muscular integer. Probably, in this segment, the further differentiation into Ecto- and Entopectoral (Pect. major and minor) had likewise begun in the common ancestral prototype.

On the other hand very probably the abdominal portion was still incorporated in the general thoraco-humeral pannicular sheet, closing the floor of the axilla without definite mesal attachment, but beginning to join laterally the intrinsic appendicular muscles, along the lines indicated by the abdominal pectoral and axillary arch in *Nycticebus* at the

connection with the tendon of insertion of that portion of the deeper plane, which in *Cynocephalus* has differentiated distinctly as the Pectoralis minor.

From this hypothetical common ancestral type of the Primate Pectoral group the further evolution along the lines illustrated by the representative examples above indicated may be summed up in the following manner:

1. *Lemurs and Marmosets*.—1. The influence of the sternum, as affording a fixed line of origin, determines the differentiation of the main ectopectoral layer as Pectoralis major.

2. The same influence extends to the deeper plane of the Pectoral mass in the sternal region and leads to the beginning differentiation of the Pectoralis minor, which muscle is, however, still entirely sternal in origin.

3. Pectoralis major and the segment of the deeper plane corresponding to Pectoralis minor have completely differentiated from each other in the Marmosets, while in *Nycticebus* the caudal portion still forms a continuous mass common to both planes at the origin, but differentiated toward the insertion.

4. In *Hapale* the Pectoralis minor is still nearly directly continuous with the Subclavius cephalad, and with the Pectoralis abdominalis caudad.

5. In the same animal this latter muscle forms an extensive thin superficial muscular sheet investing the abdominal region and retaining characters pointing to its derivation from the pannicular sheet of the trunk.

6. In *Nycticebus* the abdominal Pectoralis of *Hapale* still appears as part of the general pannicular plane whose only connection with the Pectoral system appears in the well developed axillary arch.

7. The axillary arch of *Nycticebus* is still entirely pannicular in character and has not contracted the secondary attachment to the axillary margin of the Latissimus dorsi. In *Hapale*, as a specific character the axillary arch seems to default.

8. The Pectoralis major is folded at the insertion into the lateral humeral ridge and occupies the position which it retains in the more completely differentiated higher types.

9. The continuity of the Pectoralis minor and abdominalis is preserved at the insertion into the lateral and surface of the shaft of the humerus under cover of the Pectoralis major and Deltoid.

10. The caudal margin of this deeper plane of the Pectoral insertion receives the insertion of the axillary arch.

11. There is no clavicular portion of the Pectoralis major—a corresponding mesal development of the clavo-humeral Deltoid occupying the situation of the human clavicular portion in *Hapale* while in *Nycticebus* the Delto-pectoral interval develops into an extensive subclavicular fossa.

II. *Lower Monkeys*.—1. The same general arrangement of the ecto-pectoral layer, with a distinct sternal Pectoralis major is observed.

2. In the entopectoral plane the Pectoralis minor has differentiated completely from both Subclavius and abdominal pectoral.

3. The Pectoralis minor is still almost entirely sternal in origin, but migration laterad to the costal cartilages has begun in the cephalic segment of the muscle.

4. The insertion of both ecto- and entopectoral planes corresponds still to the earlier type but has moved further cephalad upon the humerus to the lateral tuberosity.

5. The axillary arch is relatively reduced and indirectly connected with the Latissimus.

6. There is no clavicular portion of the Pectoralis major.

7. More extensive migration of the Pectoralis minor origin, both cephalad and laterad from sternum to costal cartilages, is observed in some forms transitional between the intermediate and secondary types of the muscle.

III. *Man and the Anthropoid Apes*.—1. Complete differentiation of Pectoralis major and minor.

2. Migration laterad of origin of latter muscle from sternum to ribs.

3. Lateral extension in deeper parts of origin of Pectoralis major to costal cartilages.

4. Migration cephalad of insertion of Pectoralis minor from lateral tubercle of humerus to coracoid process of scapula.

5. Reduction of Pectoralis abdominalis and secondary addition of same to Pectoralis major, joining the deep layer of the tendon of insertion as the “abdominal slip.”

6. Development of clavicular portion of the Pectoralis major, and corresponding reduction of the clavo-humeral Deltoid. The secondary character of this addition to the primitive sternal Pectoral in man is still attested by—

(a) Cellular interval between it and sterno-costal division.

(b) Variations in the nerve supply (ant. thoracic, circumflex).

(c) Range of independent physiological action of the two portions.

7. Default of axillary arch, the last remnant of the thoraco-humeral

panniculus or of the primitive continuous plane of Pectoralis and Latissimus across the axillary space, as a normal structure in man, although occurring in him as a frequent variation.

In utilizing the results of extensive comparisons for the determination of the phylogenetic value and significance of variations three facts are found to have an important bearing on these problems:

1. Within a single mammalian order certain groups are frequently sharply differentiated by the uniform development of a structural character which is as consistently wanting in other genera and species composing the order. This is true not only of muscles, but also of morphological details in other organic systems.

2. Such isolated characters, while absent in other species of the order, may appear more or less widely distributed in other mammalian orders, or even in other vertebrate classes.

3. Further, they may appear, as variations, in individuals of a species which does not normally possess them.

Thus, for example, among the Primates certain groups, like the Lemurs and the Cebidæ, are characterized by the uniform development of the supracondyloid foramen, with the corresponding arrangement of the artery, median nerve and Pronator radii teres muscle, while in Man, the Anthropoids and in general in the monkeys of the Old World the humerus does not normally carry the foramen.

Now this collection of anatomical details, confined among the Primates to certain groups and normally absent in the other genera, although observed in them occasionally in individual instances as a variation, possesses a very definite structural character and identity, and appears widely distributed in other Mammalian orders, such as the Insectivora, except *Erinaceus*, the Edentates, Marsupials, Monotremes, the Felidæ among Carnivora, etc. In judging of the phylogenetic value of this condition in its more isolated appearance in certain specialized primate groups, the following considerations suggest themselves:

The prevalence of this arrangement in other mammalian orders, not to speak of reptilian homologies, indicates clearly that it belongs to the *common mammalian prototype*. In all probability it leads back beyond the class distinction into the *common vertebrate stem* (Pl. VII, Fig. 11).

As regards its persistence in certain primate groups, as the Lemurs and the Cebidæ, and its default in other genera of the same order, two possibilities may be considered:

1. These structural characters were transmitted from the common mammalian stem through the line of *Primate adaptation* to the common primate ancestral type.

The Lemurs and the Cebidae continue to perpetuate this type which has become modified in Man, the Anthropoids and the Old World monkeys generally by the suppression of the supracondylar process and foramen with the consequent alteration in the position of the artery and the median nerve, although in these latter forms the primitive arrangement may reappear as an individual variation. (*Ataval variation, vide infra, p. 174.*)

2. The ancestral primate type, in deviating from the common mammalian stem, had already modified the arrangement of these structures, by loss of the supracondyloid foramen. It would then be necessary to assume that in their derivation from the primate stem the ancestors of the living Cebidae had *reverted* in this structural detail to the *common mammalian* type and had preserved and transmitted such reversion as their descendants further specialized to form the Cebus group. (*Progonal reversion, vide infra, p. 174.*)

The first hypothesis appears the better founded of the two. Observation teaches us that structural differentiation within a limited group is usually progressive. When once carried to the point of morphological independence further special modifications may take place, but *return* to the primitive condition for an entire group of individuals composing the species or genus is the less warrantable supposition. Examples are encountered in which a partially degenerate and rudimentary structure has *revived* under the influence of a new functional adaptation. Moreover, under adequate physiological stimulus, an organ may even be evolved *de novo*, along the same paths and following the same developmental lines which far back in the phylogenetic history of the species led to the production of its prototype, which has, in course of the intervening evolutionary period, become rudimentary or adapted to other functional purposes. Thus in the Teleost families of the *Ophiocephalidae* and *Labyrinthici* the pharyngeal mucous membrane is in the process of evolving the vascular area, serving purposes of respiration, which we must regard as the phylogenetic point of departure for the evolution of the swim-bladder, an organ, present in both of these Teleost groups, which has long lost its primary respiratory character and has been adapted to other uses. Yet under the same stimulus of physiological environment, furnished by the shallow and muddy waters of the habitat of these forms, the same evolutionary structural development is beginning over again. Such conditions are, however, exceptional and depend upon special physiological demands. It is more in conformity with the results of our observations to consider, in the example in hand, the supracondylar foramen as a character

transmitted from the common mammalian stem to the Primatè ancestral line, just as it has been transmitted to the branches of other mammalian orders. The Lemurs, Cebidæ and allied genera among living Primates have retained this structural character. It has disappeared in the Old World forms of the order, as a normal occurrence, but appears as a reversional variation in individuals, indicating their derivation from the common primate ancestral type possessing it.

It will be appreciated that in many instances close scrutiny is required in order to correctly determine the phylogenetic value of any given structure. To illustrate, for a moment, by another example taken from the same group. The Cebidæ are uniformly distinguished by a partly convoluted cæcum of comparatively narrow lumen, placed laterad to the continuous line of the ileo-colic junction, differing markedly from the form and position of the cæcal pouch in all other Primates, except the Marmosets, which somewhat resemble the Cebidæ in the arrangement and structure of the cæcum. Moreover, the Cebidæ in this particular respect resemble only one other group among Mammalia in general, namely the Cynoid carnivora. Here we are evidently dealing with secondary modifications and adaptations of a preceding common mammalian, or even generalized vertebrate type, which in the Cebidæ and Cynoidea have taken parallel lines of development and have led independently of each other to the production of the coiled lateral pouch characteristic of these forms. More complete and detailed knowledge of comparative anatomy will unquestionably furnish important indications as to the relative point of derivation of the individual genera and species from the common *order-stem*.

To return to the subject of muscular homologies we may assume that the common prototype of the order will in general present simpler structural conditions, with less complete segmentation of the entire mass into smaller subdivisions or individual muscles, and with fewer and more generalized points of skeletal attachment.

Reversional muscular variations may be grouped in accordance with their probable phylogenetic significance, in reference to their point of derivation from the stem, which has led by gradual differentiation to the development of the specific form of the muscle or muscle-group normal for the type in question. (Pl. II, Fig. 2.)

ARCHEAL REVERSIONAL VARIATIONS.²—A limited number of muscular variations repeat conditions which are not normally encountered in

²'Αρχή = beginning, origin.

any mammalian type, but which appear homologous with normal muscles in the lower vertebrate classes. They indicate a return in the development of the individual muscle to a phylogenetic point antedating the *class-distinctions*, a reversion to the common antecedent vertebrate myo-type. They illustrate the persistence of structural conditions which have not been carried normally into the mammalian stem, but which appear in the Sauropsid derivatives of the common vertebrate trunk.

PROGONAL REVERSIONAL VARIATIONS.³—A muscular variation not represented by a homologous muscle normally present in any species of the order indicates a reversion to a phylogenetic point *preceding* the derivation of the ancestral *order-line*, namely to the common antecedent mammalian *class-stem*.

I have in a former publication⁴ defined these reversions as “*myo-typical*,” with the desire to emphasize their relation to the “*myo-type*” of the entire mammalian stem. But it appears preferable to co-ordinate the terminology, and I therefore propose to designate these variations as “*progonal*.”

ATAVAL REVERSIONAL VARIATIONS.⁵—Under this head are to be grouped variations reproducing myological characters which are abnormal for the species in question, but which appear normally in other allied species of the same *order*. They revert to the common ancestral myo-type of the *order*, from which by successive differentiations the generic and specific forms included in the order are derived.

It is of course possible that certain of these ataval variations should at the same time be progonal in character, i. e., that the homologous muscles should normally appear also in other mammalian orders.

Careful determination will be required in any given case to assign the true phylogenetic value of such variants.

EXPLANATION OF FIGURES ON PLATES I TO VII.

FIG. 1. *Adult human subject.* Pectoralis major with deficiency of sternocostal portion, and resulting production of an atypical displaced intermediate Pectoral muscle (Tensor semivaginae articulationis humero-scapularis, Gruber, Pectoralis minimus). From a fresh dissection.

³ *πρόγονος* = earlier born, hence an ancestor, used of a god as father of a race, as *Ζεῦ πρόγονε* (Euripides).

⁴ “The Significance of Muscular Variations, Illustrated by Reversions of the Antibrachial Flexor Group.” *Trans. N. Y. Acad. Sci.*, Vol. XIV, 1895, pp. 231-259.

⁵ *Atavus* = grandfather of a grandfather; hence ancestor in the wider sense.

FIG. 2. Phylogenetic Schema of muscular variation.

FIG. 3. *Hapale jacchus*. Common Marmoset. Dissection of Pectoral muscles. Columbia University Museum, No. 427.

FIG. 4. *Nycticebus tardigradus*. Slow Lemur. Dissection of Pectoral muscles. Columbia University Museum, No. 1068.

FIG. 5. *Macacus cynomolgus*. Kra monkey. Dissection of Pectoral muscles with variant supernumerary axillary slips. Columbia University Museum, No. 1132a.

FIG. 6. *Cynocephalus anubis*. Olive Baboon. Dissection of the Pectoral muscles. Columbia University Museum, No. 1243.

FIG. 7. *Macacus melanotus*. Dissection of Pectoral muscles. Columbia University Museum, No. 1871.

FIG. 8. *Semnopithecus entellus*. Dissection of Pectoral muscles. Columbia University Museum, No. 1251.

FIG. 9. *Simia satyrus*, Orang. Superficial dissection of right pectoral region. From a fresh specimen.

FIG. 10. *Simia satyrus*, Orang. Deep dissection of right pectoral region. From a fresh specimen.

FIG. 11. Diagram illustrating the phylogeny of the supracondyloid foramen in vertebrates, the red line indicating its distribution in the series.

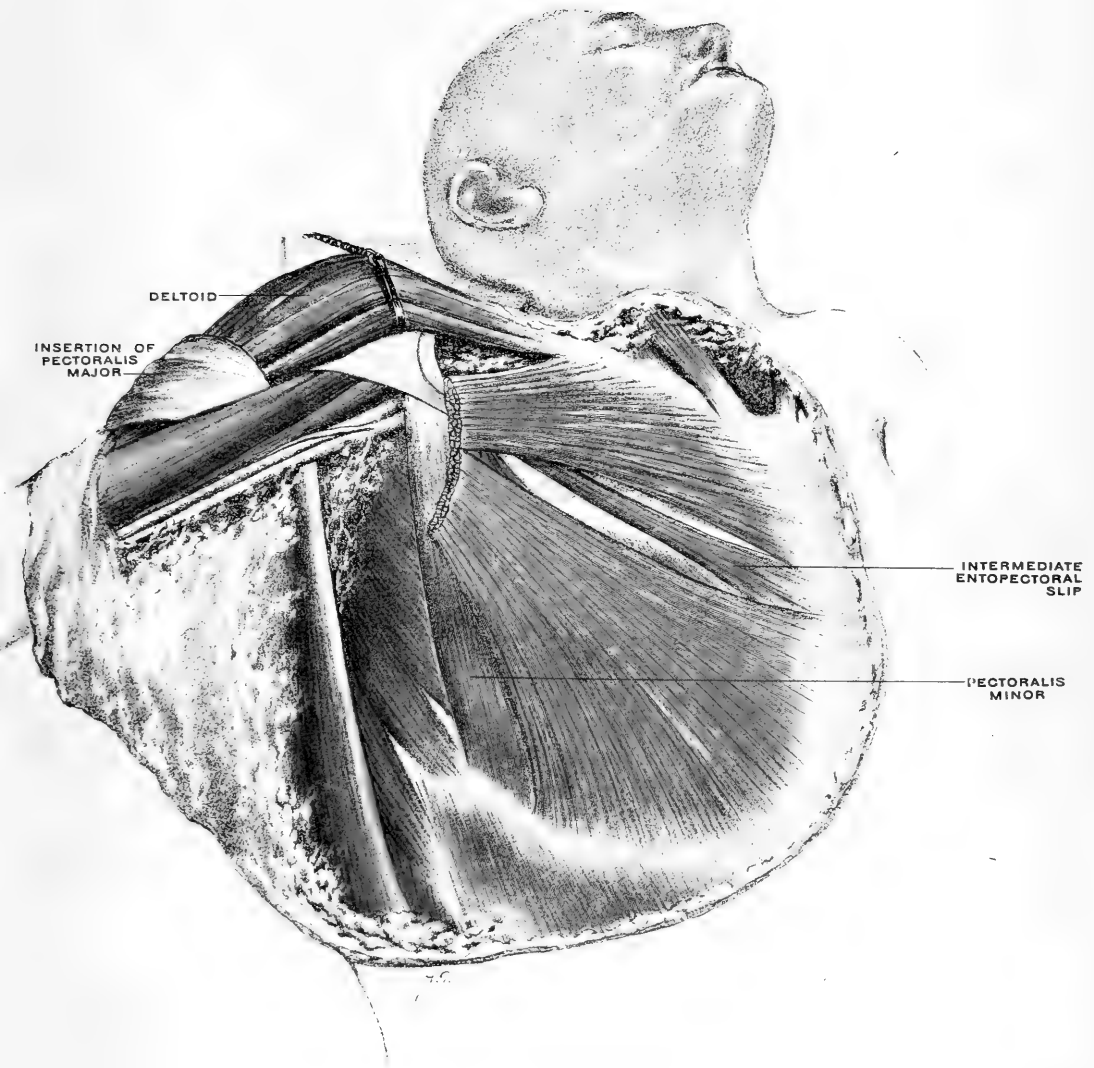


FIG. 1--MAN

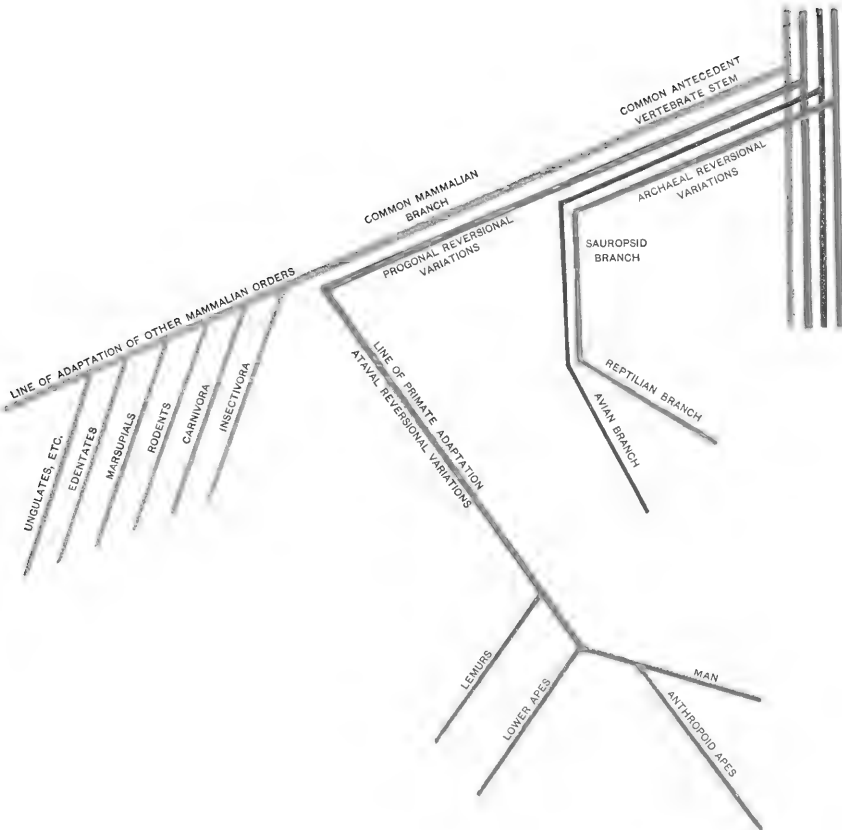


FIG. 2--PHYLOGENETIC SCHEMA OF MUSCULAR VARIATIONS

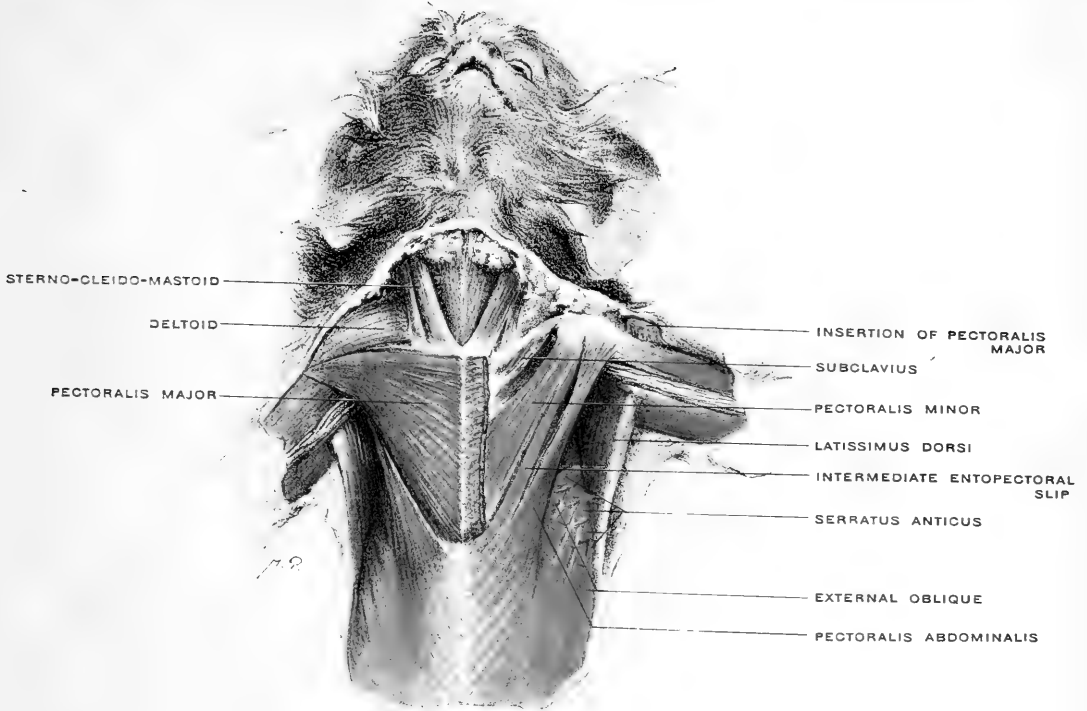


FIG. 3--HAPALE JACCHUS

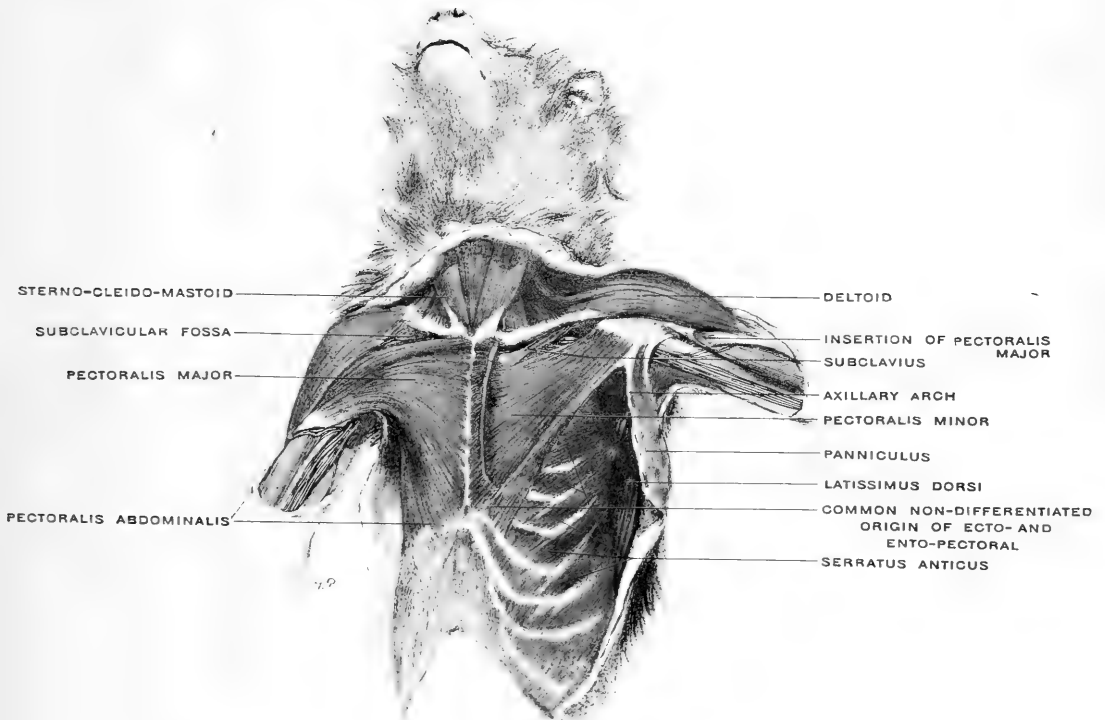


FIG. 4--NYCTICEBUS TARDIGRADUS

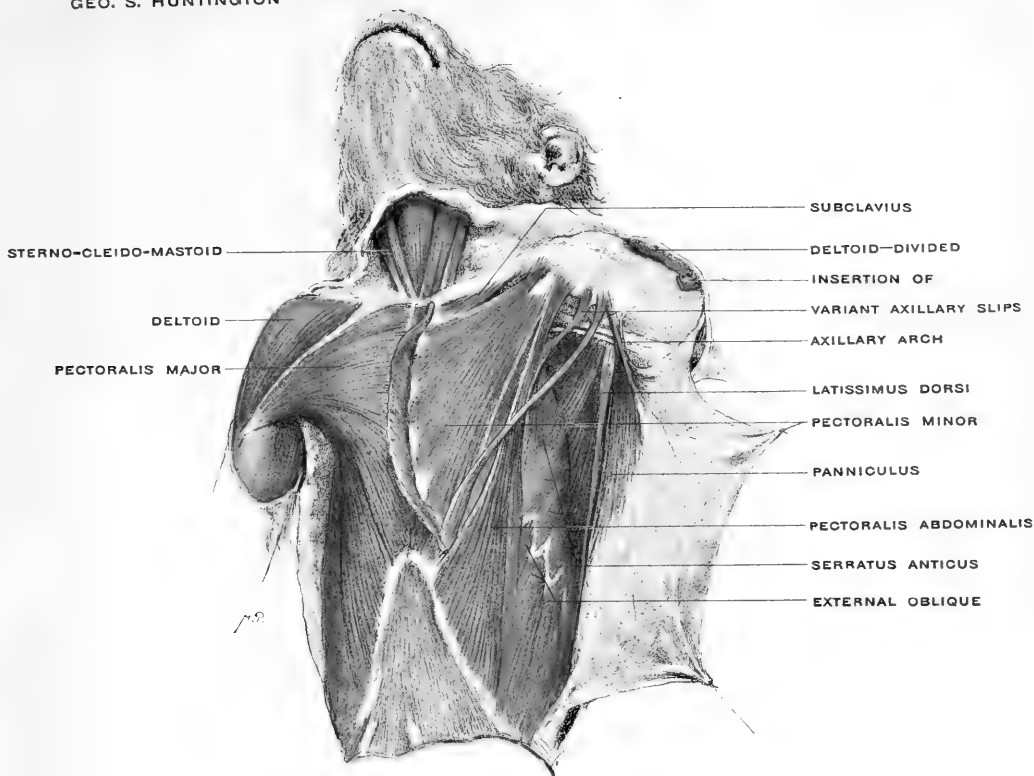


FIG. 5--MACACUS CYNOMOLGUS

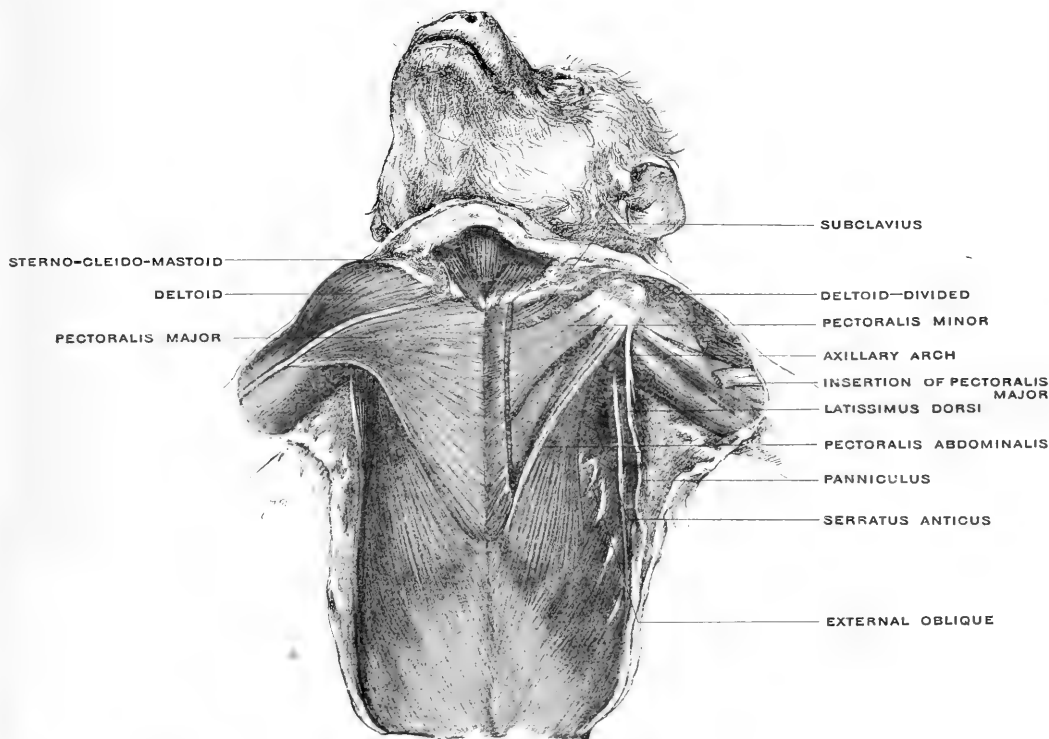
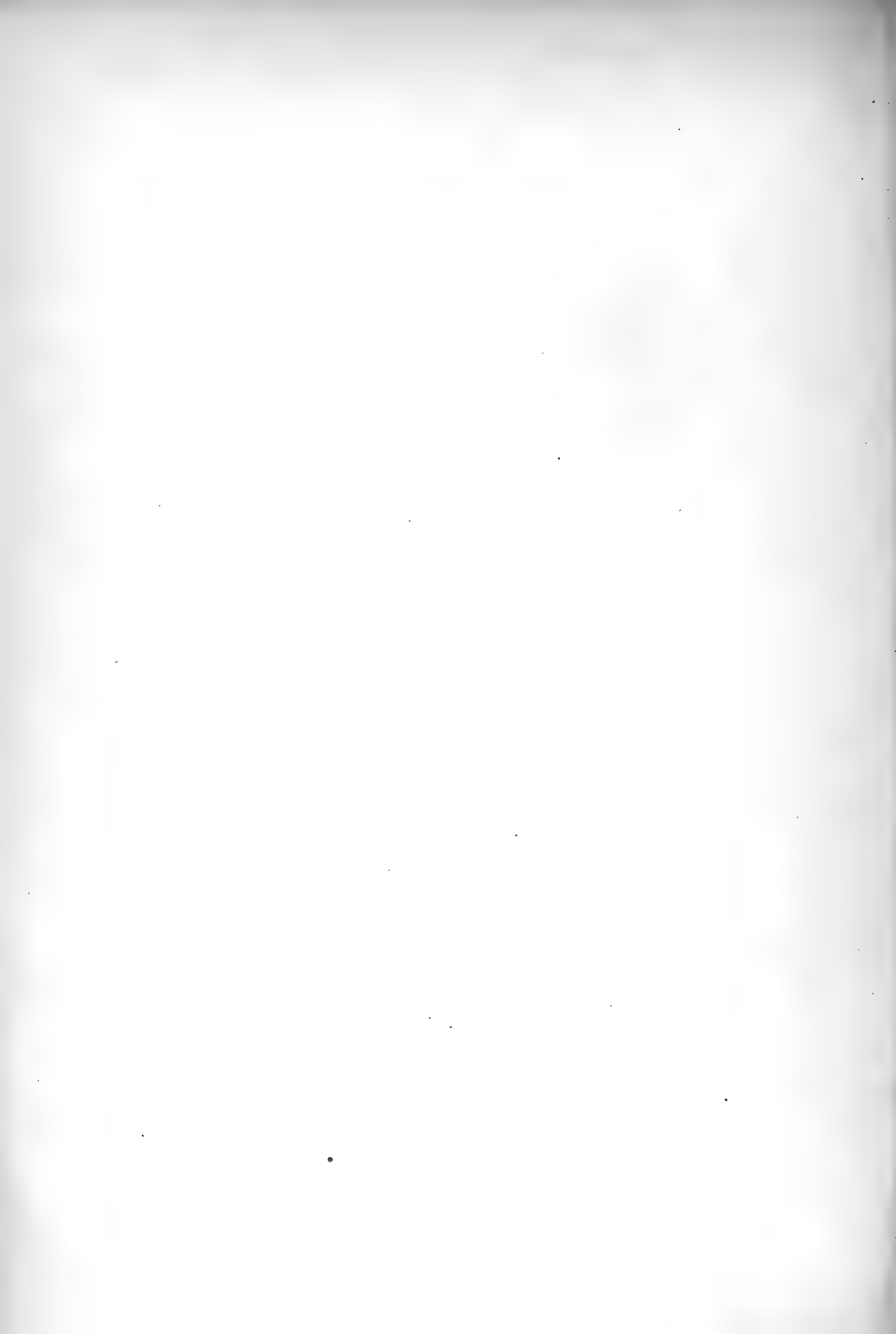


FIG. 6--CYNOCEPHALUS ANUBIS



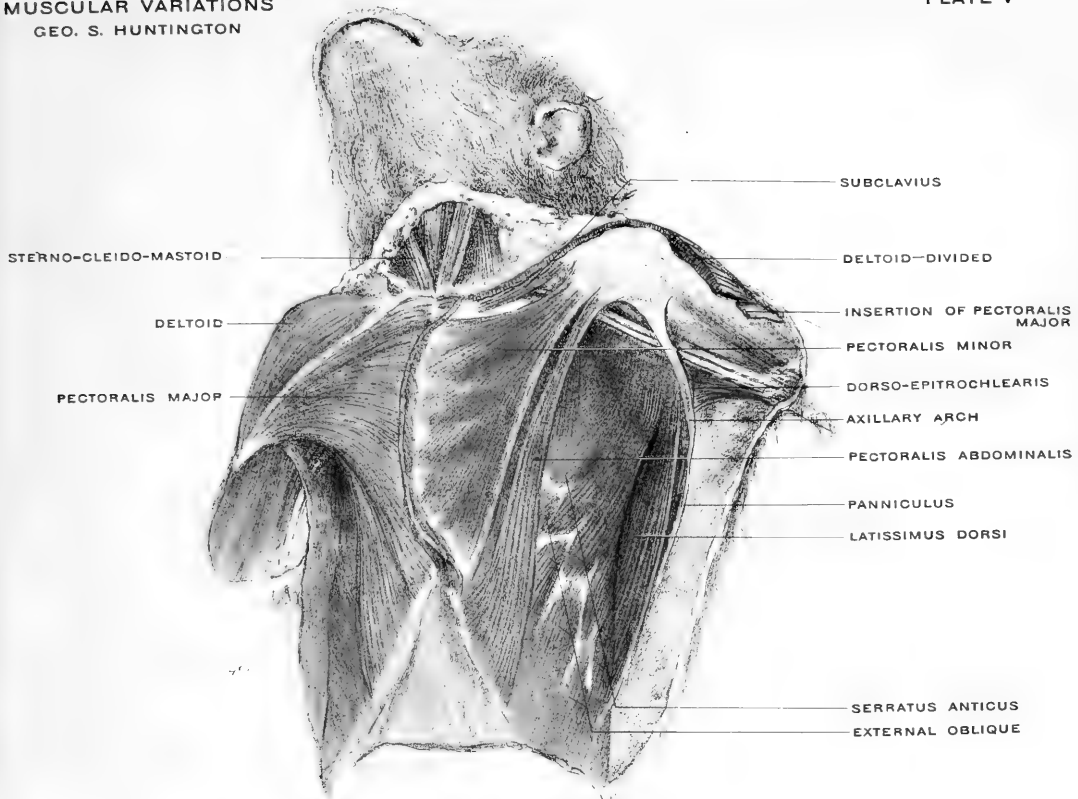


FIG. 7--MACACUS MELANOTUS

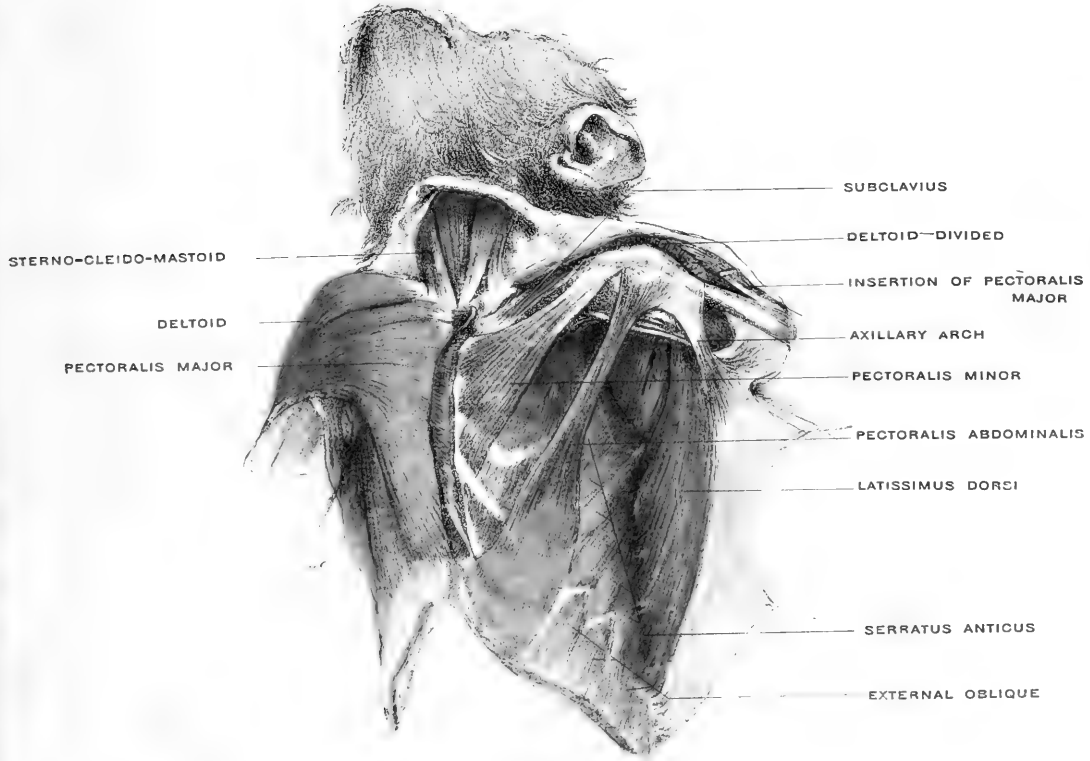


FIG. 8--SEMNOPITHECUS ENTELLUS

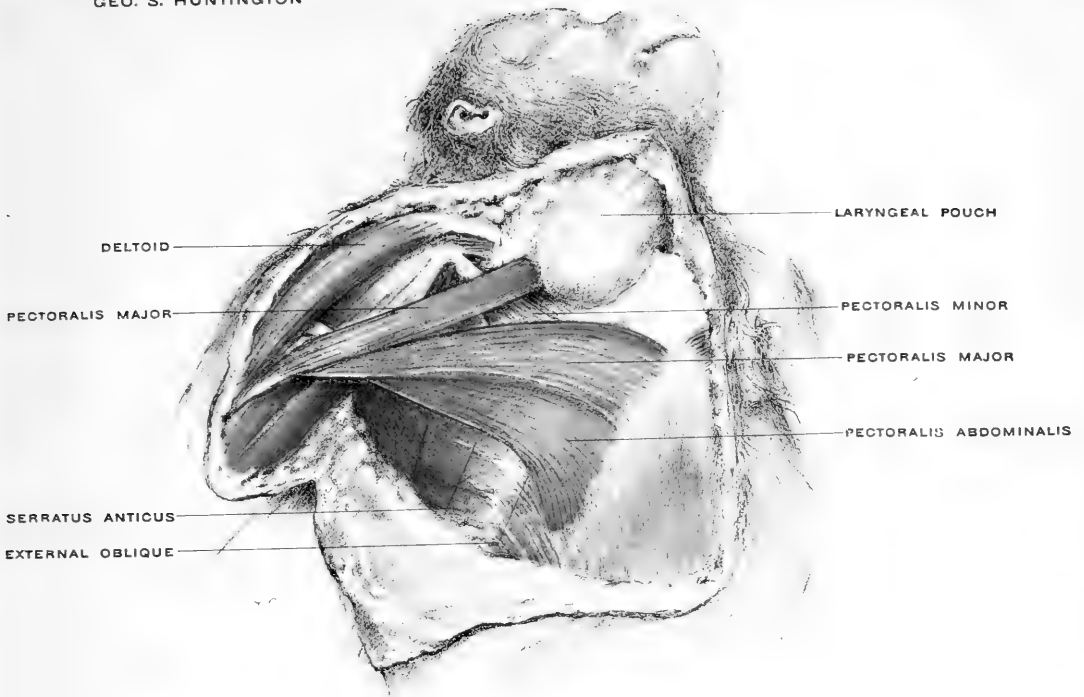


FIG. 9--SIMIA SATYRUS

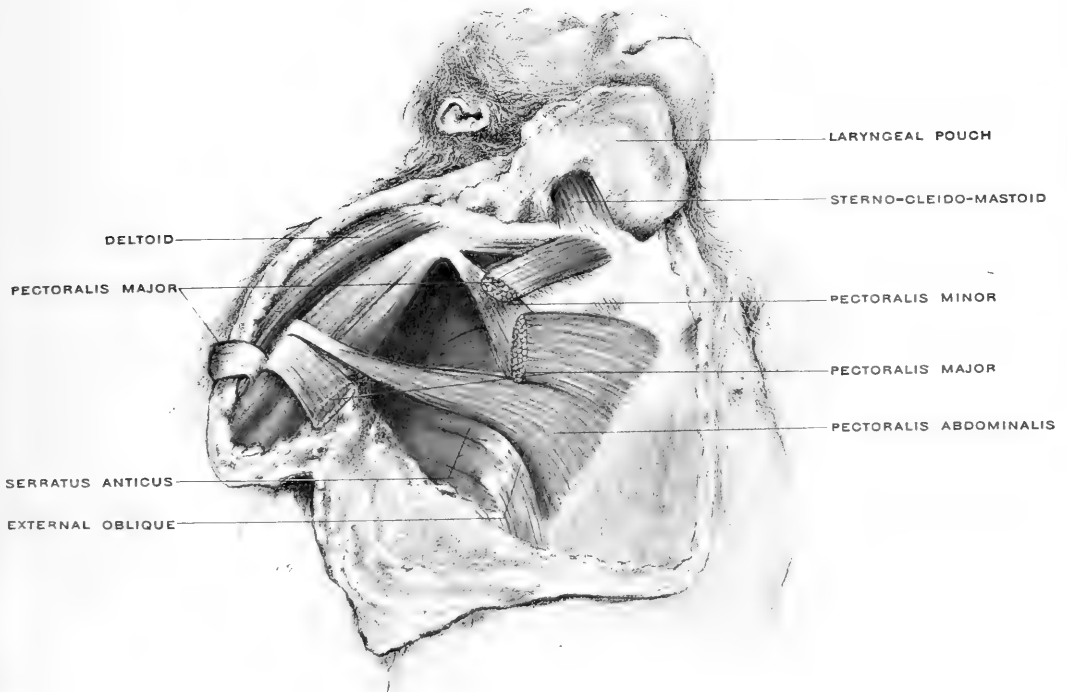


FIG. 10--SIMIA SATYRUS

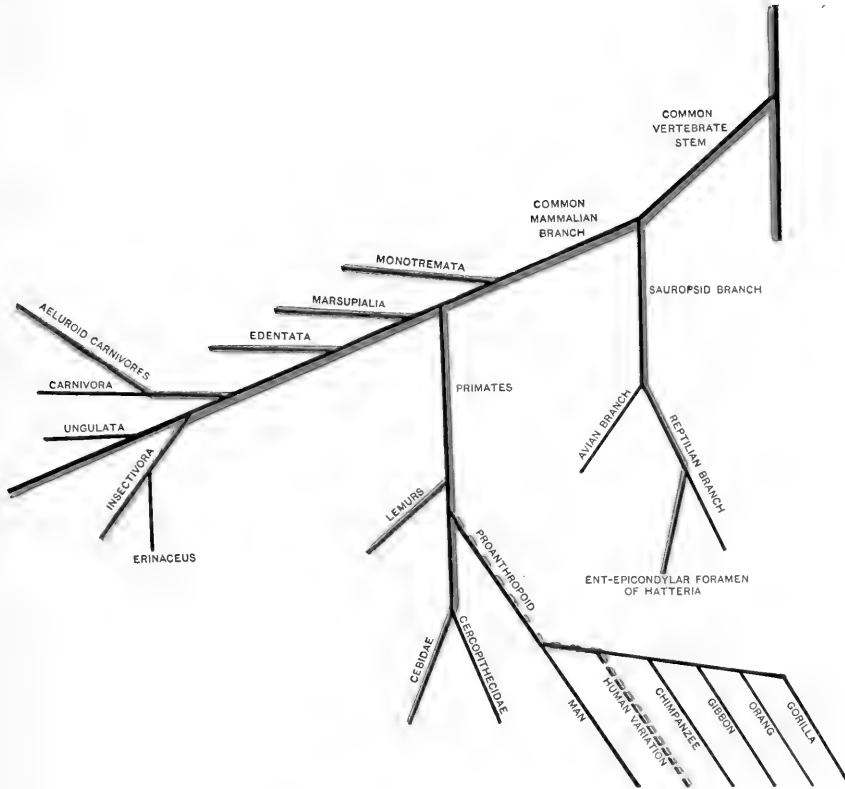


FIG. 11--THE PHYLOGENY OF THE SUPRACONDYLAR FORAMEN



THE PHYLOGENY OF THE FOREARM FLEXORS.

BY

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From the Anatomical Laboratory of the University of Michigan.

WITH 13 TEXT FIGURES.

Notwithstanding the voluminous literature of descriptive myology, comparatively little has been accomplished toward the determination of the exact homologies of the limb muscles throughout the vertebrate phylum. Something has been done in the way of elucidating a fundamental plan for the mammalian muscles, especially through the efforts of Ruge, Cunningham, Windle, Leche and von Bardeleben, to mention only some of the more recent authors, but even with regard to this group there are still gaps to be filled out and the earlier stages in the phylogeny still require study, notwithstanding Eisler's very important contribution to that side of the story. That author (1895) has made a careful study of the limb muscles of the urodelous amphibia, taking *Menopoma* as a type, and has attempted to reduce the mammalian condition to a modification of what obtains in that group. Having omitted to consider the reptilia, however, Eisler has missed some important points bearing on the question, and I propose in the following pages to give the results of observations made on both amphibia and reptilia and hope to demonstrate a detailed homology of the arm muscles in these groups and then to extend the homologies to the mammalian muscles.

My attention was primarily directed to the subject through some study which I had made of the perforated flexors of the hand and foot. It has been a general custom to regard these muscles as equivalent and to assume that the primary condition, so far as mammalia are concerned, is represented in the arm and that there has been a secondary recession of the muscle into the foot in the lower limb (cf. Wiedersheim, 1893). On looking into the matter it seemed that the evidence which could be brought forward in support of such a theory was decidedly scant, and I determined to test it by a phylogenetic study, beginning with an attempt to trace the evolution of the flexor sublimis of the arm. This muscle, as a distinct element, being, however, confined to the mammalia, it was evident that in order to obtain a correct appreciation of its significance

and a basis for its comparison with the flexor brevis of the foot, it would be necessary to discover what structures, if any, represented the sublimis in the lower vertebrates. Thus the investigation broadened to include a determination of the phylogeny of the entire flexor-pronator mass of the forearm and it is to the results of this portion of the problem that the present paper will be devoted. I hope to consider at some future date the muscles of the leg in a similar manner and so return to the question of the equivalency of the muscles in the two limbs.

A few words are necessary regarding the forms studied and the methods employed. My first intention was to approach the question from the embryological side, and to study the development of the forearm muscles in embryos of *Amblystoma tigrinum*, *Anolis sagrei*,¹ the rabbit and man. I soon discovered, however, that this method would not yield the desired results, for in the mammalian embryos the forearm muscles, when first distinctly recognizable, have practically the adult arrangement. The same result has been obtained by Lewis (1902) in his admirable study of the development of the arm in man, and it would seem that there is a very extensive condensation in the ontogenetic development of the limb muscles in the mammalia. It is probable that the entire phylogenetic history of the forearm muscles of man, for instance, is condensed into the stages during which the muscles are represented by an undifferentiated mesodermic blastema and that, therefore, anomalies of reversion are referable to the possibilities, dependent on past history, latent in this blastema.

The embryological method being then excluded, it was necessary to have recourse to comparative anatomy. Careful dissection revealed much that was of importance, but far more valuable results were obtained from the study of serial sections. From these the topographic relations of the various muscles and their nerve supply could be determined with certainty, and the pictures presented were so much more perfect and striking that I finally relied on the sections rather than on dissections, employing the latter mainly for confirmation.

As types of the urodelous amphibia I studied by both dissections and sections *Amblystoma tigrinum* and by sections only *Plethodon erythronotum*. Of the reptilia I studied *Phrynosoma cornutum*, *Liolepisma laterale*, *Callisaurus draconoides* and *Chrysemys picta*, and of mammalia I examined *Didelphys virginiana* (the material of which I owe to the kindness of Dr. C. F. W. McClure, of Princeton University), the cat,

¹ For material of this form I am indebted to the kindness of my friend, Dr. Henry Orr, of Tulane University.

the mouse and man, employing for my serial sections advanced embryos of these forms instead of adult individuals, simply as a matter of convenience in preparation. I made use of von Ebner's decalcifying solution, embedded in paraffin, cut to a thickness of $20\ \mu$ and stained on the slide either with picrolithium carmine or with Delafield's hæmatoxylin followed by van Gieson's picrofuchsin, this latter method giving excellent differentiation of the various tissues.

I. THE FOREARM FLEXORS OF THE URODELOUS AMPHIBIA AND LACERTILIA.

It is well known that the flexor muscles of the forearm of the urodele amphibia may be regarded as consisting of three layers. The most superficial layer consists of muscles arising from the internal condyle of the humerus and extending longitudinally to be inserted either into the carpus or into a strong palmar aponeurosis; the middle layer is made up for the most part of oblique muscles arising from the ulna and passing distally and radially to be inserted into the palmar aponeurosis, one muscle only, the *ulno-carpalis*, having an almost longitudinal direction and being inserted into the carpus; while the third layer consists of a sheet extending obliquely across between the ulna and radius.

The superficial layer is divided into three or four muscles; (1) the *palmaris superficialis* (Fig. 1, PS), which occupies the median portion of the layer and inserts into the palmar aponeurosis, (2) the *flexor carpi ulnaris* (F. C. U.), (3) the *flexor antibrachii ulnaris* (*epitrochleo-anconeus*), Eisler, which inserts into the ulna and is more or less perfectly differentiated in different forms, and (4) the *flexor carpi radialis* (F. C. R.).

The oblique muscles of the middle layer are divided by the *ulno-carpalis* into an ulnar and a radial portion, the latter being again more or less distinctly divided into two portions, so that altogether the layer is composed of four muscles. The most ulnar of these and therefore the most superficial may be termed the *palmaris profundus* III (Eisler) (P. P. III); it arises from the ventral surface of the lower part of the ulna and is inserted into the under (dorsal) surface of the palmar aponeurosis. To the radial side of it and separating it at its origin from the *palmaris profundus* II is the *ulno-carpalis* (U. C.), which, arising from the ulna, descends almost longitudinally to be inserted into the distal row of carpal bones. More radially lies the *palmaris profundus* II (P. P. II) which resembles closely the *palmaris profun-*

dus III, arising from the radial side of the lower part of the ulna and inserting into the dorsal surface of the palmar aponeurosis toward its radial edge; and, finally, most radial of all, is the *palmaris profundus* I (P. P. I), which arises from the lower part of the ulna and also from the carpus and may be traced distally and radially to an insertion into the aponeurosis and the base of metacarpale II. As has been already stated the distinction between portions I and II is not always quite evident and there is also a close relationship between I and the muscle of the third layer, the *pronator quadratus* (P. Q.), both being supplied

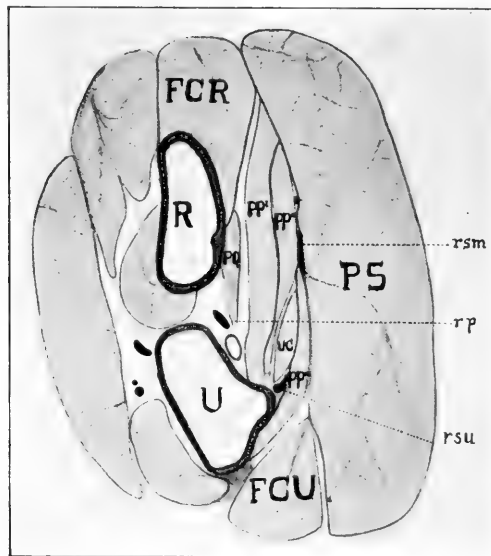


FIG. 1. Transverse section through the lower half of the forearm of *Amblystoma tigrinum*. F. C. R., flexor carpi radialis; F. C. U., flexor carpi ulnaris; PP'-PP''', first to third portions of palmaris profundus; PQ, pronator quadratus; PS, palmaris superficialis; R, radius; rp, ramus profundus; rsm, ramus superficialis medialis; rsu, ramus superficialis ulnaris; U, ulna; UC, ulno-carpalis.

by the same nerve; portion II has, however, a different nerve supply, receiving branches from the same stem which supplies portion III.

The relations of these muscles as seen in sections may be perceived from Fig. 1, which represents a transverse section through the lower half of the antibrachium of *Amblystoma tigrinum*.

Turning now to the lacertilia one finds a condition which seems at first sight far removed from that obtaining in the amphibia. There is a greater amount of longitudinal division of the muscle layers and a

diminution in the amount of the oblique musculature in the middle layer, as well as a tendency for it to associate itself more or less closely with the superficial layer.

Taking the condition found in *Phrynosoma cornutum* as typical, the arrangement of the muscles at about the middle of the forearm is as shown in Fig. 2. Starting from the ulnar side there is first the flexor carpi ulnaris (F. C. U. and F. C. U.), consisting of two distinct slips; traced distally these fuse to form a single tendon which inserts into the ulnar side of the carpus, while proximally they separate more

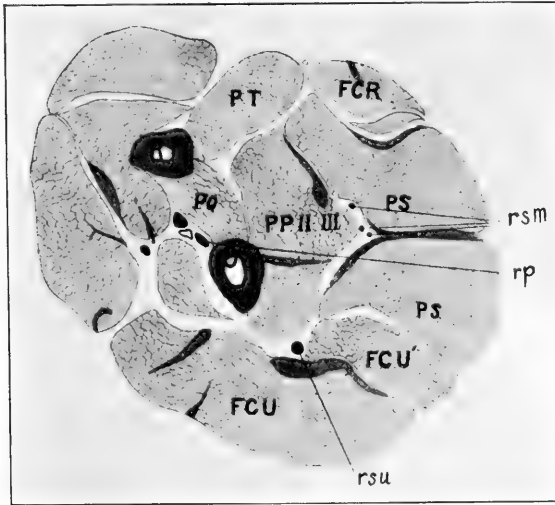


FIG. 2. Transverse section through the middle of the forearm of *Phrynosoma cornutum*. F. C. R., flexor carpi radialis; F. C. U. and F. C. U', lateral and medial portions of the flexor carpi ulnaris; PP II, III, deep portions of the palmaris communis; PQ, pronator quadratus; PS, superficial portions of the palmaris communis; P.T., pronator teres; R, radius; *rp*, ramus profundus; *rsm*, ramus superficialis medialis; *rsu*, ramus superficialis ulnaris; U, ulna.

and more, their origins from the internal condyle being separated by the epitrochleo-anconeus, whose insertion into the ulna lies above the level of the section figured.

The median portion of the arm is occupied by a strong mass which forms the *flexor digitorum profundus* (auct.), although it would be better to use the term flexor communis digitorum employed by Stan-
nius, or, better still, palmaris communis if we are to regard it as a single muscle. In reality it consists of five distinct portions, only four of which are seen in Fig. 2. Two of these four (P. S.) are superficial,

occupying the interval between the more median head of the flexor carpi ulnaris and the flexor carpi radialis (F. C. R.), and the other two (P. P. II and III) are deeper, one resting immediately upon the ventral surface of the ulna, while the other lies ventral to the pronator quadratus (P. Q.) and the radius. The fifth portion (Fig. 3, P. P. I) is short and is an oblique muscle arising from the ventral surface of the ulnar side of the carpus. All five portions insert distally into the palmar aponeurosis, which, in the majority of the forms studied, contains a strong volar cartilage.

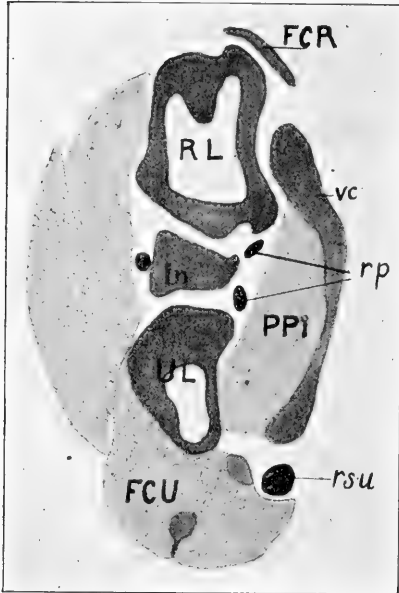


FIG. 3. Transverse section through the wrist of *Liolepisma laterale*. F. C. R., flexor carpi radialis; F. C. U., flexor carpi ulnaris; In, intermedium; PP I, first part of deep portion of the palmaris communis; RL, radiale; pp, ramus profundus; rsu, ramus superficialis ulnaris; UL, ulnar; vc, volar cartilage.

Proximally the superficial portions take origin from the internal condyle, while the deeper portions arise from the ulna or, in the case of the fifth portion, from the ulnar side of the carpus.

On the radial side of the arm are two muscles, a more superficial flexor carpi radialis (F. C. R.) and a deeper *pronator radii teres* (P. T.) both of which arise from the internal condyle of the humerus, the former having its insertion into the radial side of the carpus and into the base of metacarpale I, while the latter inserts into the lower part of the radial side of the radius.

Finally, constituting the deepest layer, there is a pronator quadratus (P. Q.), extending between the radius and ulna, and in the proximal

part of the arm a *pronator accessorius* (Mivart), which arises from the internal condyle and is inserted into the radius.

Before proceeding to a comparison of the individual muscles of the amphibia and reptilia a description of the nerves of the forearm in the two groups will be necessary. For they present a remarkable similarity in their arrangement and will serve as guides in the determination of some of the more obscure homologies.

In the amphibia the flexor muscles of the forearm are supplied by a large trunk which enters from the brachium towards the radial side and constitutes what has been termed the *N. brachialis longus inferior*.

It passes obliquely inwards between the flexor carpi radialis and the radius and soon divides into a superficial and a deep branch. The *ramus profundus* (Fig. 1, *rp*) passes behind the pronator quadratus, which it supplies, and descends the arm in that position to the lower edge of the muscle, where it comes to lie immediately below, *i. e.* dorsal to the palmaris profundus I to which it sends fibres.

The superficial branch passes toward the median line of the arm ventral to the pronator quadratus, and divides into two branches after giving a twig to the flexor carpi ulnaris and to the epitrochleo-anconeus. The two branches may be termed the *ramus ulnaris* (*rsu*) and the *r. medialis* (*rsm*). The former gives off a second branch to the flexor carpi ulnaris and passes obliquely across the ventral surface of the ulno-carpalis, which it supplies, and then descends the arm upon the ulnar side of that muscle. In *Amblystoma* it lies in the lower part of the forearm between the ulno-carpalis and the palmaris profundus III, and, as it nears the carpus, it bends ulnarwards between the latter muscle and the ulna and comes to lie superficially upon the ulnar side of the arm. In *Plethodon*, however, in which the origin of the palmaris profundus III does not extend so high upon the arm, the nerve begins to bend ulnarward before it reaches the origin of the muscle and consequently possesses somewhat different relations to it than it does in *Amblystoma*.

The medial ramus breaks up into a number of branches which ramify in the substance of the palmaris superficialis, one, however, descending a short distance to give off a branch to the palmaris profundus II and also to the palmaris profundus III.

The supply of the various amphibian muscles may be tabulated, then, as follows:

Epitrochleo-anconeus	}	R. superficialis ulnaris.
Flexor carpi ulnaris		
Ulna-carpalis		
Palmaris superficialis	}	R. superficialis medialis.
Palmaris profundus II		
Palmaris profundus III		
Palmaris profundus I	}	R. profundus.
Pronator quadratus		
Flexor carpi radialis		

In the reptilia the main nerve stem for the flexor muscles of the forearm enters from above upon the radial side and, as in the amphibia, may be termed the N. brachialis longus inferior. It early divides into two stems, a *ramus profundus* and a *R. superficialis*, whose general relations are practically identical with those found in the amphibia.

The *R. profundus* (Fig. 2, *rp*) bends mesially and dorsally, curving around the radius, and comes to lie dorsal to the pronator quadratus, in which position it descends the arm. It supplies the pronator quadratus and also the pronator accessorius and the flexor carpi radialis, and at the lower border of the quadratus it passes ventrally so as to lie upon the ventral surface of the carpus (Fig. 3, *rp*), giving off a branch to the oblique portion of the palmaris communis.

The *R. superficialis* divides, as in the amphibia, into a *R. medialis* (Fig. 2, *rsm*) and a *R. ulnaris* (*rsu*). The latter passes obliquely across the arm between the superficial and deep layers of the palmaris communis, reaching the ulna at the lower edge of the insertion of the epitrochleo-anconeus, which muscle it supplies, also sending twigs to the lateral head of the flexor carpi ulnaris. It then continues down the arm, lying to the ulnar side of the deep portions of the palmaris communis and so passes into the manus.

The *R. medialis* follows at first the course of the ulnaris until it reaches approximately the median line of the arm, when it gives off branches to the more median head of the flexor carpi ulnaris. Early in its course it gives a branch to the pronator radii teres. It passes down the arm between the superficial and deep portions of the palmaris communis, both of which it supplies and in which it is finally lost.

Tabulating the muscles according to their nerve supply the arrangement is as follows:

Epitrochleo-anconeus	}	<i>R. superficialis ulnaris.</i>
Flexor carpi ulnaris (lateral head)		
Palmaris communis (superficial portions)	}	<i>R. superficialis medialis.</i>
Palmaris communis (deep portions II & III)		
Flexor carpi ulnaris (median head)		
Pronator radii teres		
Palmaris communis (oblique portion)	}	<i>R. profundus.</i>
Pronator quadratus		
Pronator accessorius		
Flexor carpi radialis		

We are now in a position to make a comparison of the individual amphibian and reptilian muscles. On the ulnar side the epitrochleo-anconeus has become more distinctly separated from the flexor carpi ulnaris in the reptilia, and with the latter muscle a portion of the palmaris superficialis has associated itself to form the medial head, while the rest of the palmaris superficialis, represented by the superficial portions of the palmaris communis, shows a tendency to divide into two portions.

The palmares profundi II and III are represented by the deep por-

tions of the palmaris communis shown in Fig. 2. They have, however, undergone a very important modification by the extension of their origin proximally upon the bones of the forearm, so that they have acquired a more longitudinal direction, a condition which is associated with a reduction of the width of the volar cartilage into which they are inserted as compared with the amphibian palmar aponeurosis. The proximal extension has occurred chiefly in connection with portion II of the muscle and with it there has been a certain amount of extension of its origin radialwards. The palmaris profundus I has retained its original oblique direction and also its primary origin from the lower end of the ulna and the ulnar carpal bones, and has thereby been brought into somewhat different relations to the other portions of the profundus than obtained in the amphibia. In a section through the distal part of the forearm of *Amblystoma* the profundus I appears as the most radial of the profundus muscles, while in the reptilia it seems to be the most ulnar. The identification of the muscle in the two groups rests mainly on its nerve supply and, if this be accepted as a sufficient criterion, an explanation is to be sought for the apparent difference in its position. I believe that this can be found in the change in the direction of the second and third portions of the profundus and the migration of their origins proximally, the profundus I being thereby permitted to occupy exclusively the lower part of the ulna and the ulnar side of the carpus, and since its insertion in the reptilia is into the dorsal surface of the volar cartilage, while the other portions of the profundus insert into its proximal border, there is no obstacle in the way of a conversion of the arrangement seen in the amphibia into what occurs in the reptilia.

One muscle of the amphibian forearm I have not been able to recognize in the reptilia. This is the ulno-carpalis. The ramus ulnaris of the superficial branch of the inferior brachial nerve passes across the ventral surface of this muscle and descends the arm upon its ulnar surface and in the reptilia the corresponding nerve has the same relations to the second part of the palmaris profundus, using that designation for the portion of the palmaris communis which has been identified with the amphibian profundus II. Arguing from this topographic relation, it seems possible that the muscle has been incorporated in the reptilian profundus II. Such a condition would, however, necessitate a decided alteration of the insertion of the ulno-carpalis, which must have shifted from the carpus to the palmar aponeurosis and, furthermore, I find no branches of the ramus ulnaris, which supplies the amphibian muscle, entering the substance of the reptilian palmaris profundus. While I hesitate to express a conviction that the muscle

is unrepresented in the reptilia, the weight of evidence seems to me to point that way.

The flexor carpi radialis seems to be equivalent in the two groups, while the pronator radii teres seems to correspond to the radial portion of the amphibian palmaris superficialis. In *Liolepisma* the nerve which passes to the flexor carpi radialis arises from the N. brachialis inferior longus before its division into the deep and superficial rami, but it is more nearly associated with that portion of the nerve which becomes the R. profundus and I have therefore associated it with that ramus. The branch to the pronator teres, on the other hand, was the first branch from the R. superficialis medialis and there is, accordingly, good reason for believing that the pronator teres and the flexor carpi ulnaris are quite distinct structures.

The reptilian pronator accessorius is supplied, like the pronator quadratus, from the R. profundus and I see no reason for doubting the conclusion of Fürbringer (1870), that it represents the upper portion of the amphibian quadratus.

The homologies of the amphibian and reptilian muscles as described above may be tabulated thus:

Amphibia.	Reptilia.
Ulno-carpalis	?
Epitrochleo-anconeus	Epitrochleo-anconeus
Flexor carpi ulnaris	Flexor carpi ulnaris (lateral head)
Palmaris superficialis	{ Flexor carpi ulnaris (medial head) Palmaris communis (superficial portions) Pronator radii teres
Palmaris profundus III	{ Palmaris communis (longitudinal deep portions)
Palmaris profundus II	
Palmaris profundus I	{ Palmaris communis (oblique deep portions)
Pronator quadratus	{ Pronator quadratus Pronator accessorius
Flexor carpi radialis	Flexor carpi radialis

II. THE FOREARM FLEXORS OF THE MAMMALIA.

In the amphibia and reptilia it is evident that the forearm muscles proper end at the wrist joint, their action upon the digits being through their insertion into the palmar aponeurosis, from which the palmar muscles arise. In the mammalia it is customary to regard the long digital flexors as extending from their antibrachial origins to the phalanges, and in comparing them on this basis with the corresponding muscles of the lower groups, it is necessary to assume that there has been either an extension of the origin of certain palmar muscles proxi-

mally, or a shifting of the insertion of antibrachial muscles distally, or, perhaps, a combination of both these processes. My results show that such a way of regarding the long flexors is erroneous and that if we are to obtain correct homologies we must compare only the antibrachial portions of the mammalian flexors with antibrachial muscles of the amphibia and reptilia, the palmar portions being comparable to palmar structures, tendons or muscles. My reason for this conclusion will be given in a subsequent section of this paper, but in what follows here attention will be directed solely to the strictly antibrachial portions of the mammalian flexors.

I regret greatly that I have not been able to include a monotreme in the material studied, for, to judge from the descriptions to which I have access, they present most interesting resemblances to the conditions obtaining in the reptilia. The tendency toward an indistinctness in the separation of the superficial and deep layers of the forearm flexors seen in the reptilia is apparently carried further in the monotremes, there being recognizable in them, as distinct muscles, only a flexor carpi radialis, a pronator radii teres, a flexor communis digitorum, an epitrochleo-anconeus and a flexor carpi ulnaris, the last in *Echidna* being united with the flexor communis to about the middle of the forearm. Dissections have failed so far to reveal any division of the flexor communis into constituent elements such as may be recognized in other mammals, and it would be interesting to determine whether or not such a division could be recognized in sections. Lacking information on this important point I must perforce take, as my starting point for a consideration of the mammalian muscles, a condition in which a differentiation of the flexor communis has occurred, a condition a little in advance of what is found in the monotremes and yet a little below what is found in such a mammal as the opossum, in that it fails to show any differentiation of the antibrachial portion of the flexor sublimis. I take such a condition for comparison with the lower forms rather than one in which the forearm portion of the sublimis is differentiated, because this muscle is peculiar to the mammalian series and possesses within that series a somewhat complicated development which may more conveniently be considered later on.

The arrangement of the muscles in the somewhat hypothetical condition may be supposed to be as follows. Superficially upon the ulnar side of the forearm is the flexor carpi ulnaris (Fig. 4, F. C. U.) arising by two heads, one from the internal condyle of the humerus and the other from the olecranon process, and inserting below into the ulnar side of the carpus. In close proximity to this muscle is the epitrochleo-

anconeus, also arising from the condyle of the humerus and inserting into the olecranon process.

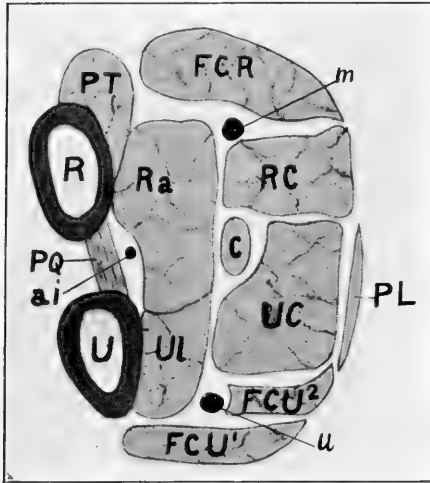


FIG. 4. Transverse section through the forearm of an hypothetical mammal. *ai*, anterior interosseus nerve; *C*, centralis; *F. C. R.*, flexor carpi radialis; *F. C. U.*¹ and *F. C. U.*², lateral and medial portions of the flexor carpi ulnaris; *m*, median nerve; *PL*, palmaris longus; *PQ*, pronator quadratus; *PT*, pronator teres; *R*, radius; *Ra*, radialis; *RC*, condylo-radialis; *U*, ulna; *u*, ulna nerve; *UC*, condylo-ulnaris; *U*¹, ulnaris.

Upon the radial side there is a flexor carpi radialis (*F. C. R.*), extending from the internal condyle to the base of one or more of the radial metacarpals, and a pronator radii teres, again from the condyle and inserting a varying distance down the outer surface of the radius.

The median portion of the arm is occupied by (1) a palmaris longus (*P. L.*), extending from the internal condyle to the palmar aponeurosis, and (2) a large mass, composed of several more or less distinct portions and which may be termed the flexor communis digitorum. The constitution of this muscle has been admirably elucidated by Windle (1890), and I propose to follow closely his description of it, based

as it is upon a profound and critical analysis of its various components. My observations have confirmed his for the most part, the only modification which I shall make being the omission for the present of a sublimis component. I do this because, as I hope to show later, the sublimis is far from being an equivalent muscle throughout the mammalian series, a view which differs fundamentally from that apparently held by Windle.

Omitting the sublimis, then, as a distinct component, there are recognizable in the flexor communis digitorum five components. Three of these, named by Windle, the *condylo-radialis* (Fig. 4, *R. C.*), the *condylo-ulnaris* (*U. C.*) and the *centralis* (*C.*), have their origin from the internal condyle of the humerus; the fourth and fifth components, the *radialis* (*Ra*) and the *ulnaris* (*U*), on the other hand arise from the bones from which they derive their names. All the five components unite in a common tendon.

Finally, as one of the mammalian muscles there is to be mentioned the pronator quadratus, which extends across between the distal two-

thirds of the radius and ulna, its upper border occasionally, however, reaching almost the proximal ends of the bones.

If, now, we attempt to employ the nerve supply of these muscles as a guide to their homologies in the lower vertebrates, we are at once met with the difficulty that the arrangement of the nerves in the mammalia is very different from what was characteristic for the lower forms. In place of the single *nervus brachialis inferior longus* entering the forearm to supply all its flexor muscles, there are two such nerves, the ulnar and the median. In a general way the ulnar corresponds to the *R. superficialis ulnaris* of the lower forms and the median to both the *R. Profundus* and the *R. superficialis radialis*, but the homology cannot be carried into detail. Indeed, from what I have observed in the forms I have studied, I am inclined to believe that the median and ulnar nerves are not perfectly equivalent throughout the mammalian series, the ulnar, for instance, in one case containing fibres which in another case are included in the median. That such may be the case has already been pointed out by von Bardeleben (1891), who finds in the mammalia a plexus formation between the median and ulnar in the proximal part of the forearm, and Kohlbrugge (1897),² arguing from the differences he finds in the nerve-supply of apparently homologous forearm muscles in different mammals, goes so far as to maintain that the median and ulnar nerves are not to be regarded as definite and invariably equivalent nerves, but merely as paths which may conduct elements of different origins.

I may say that in the arm of the human embryo I employed in the present study, a strong branch was given off from the median at the level of the branching of the brachial artery and, following the course of the ulnar artery, it passed obliquely inward between the *sublimis* and *profundus* muscles to join and become completely incorporated in the ulnar nerve. Krause and Telgmann (1868) mentioned this condition as of occasional occurrence in man and state that it is almost constant in apes.

But while we cannot employ the nerve supply as a certain basis for the homologies of the mammalian muscles, yet it may yield accessory evidence if we can determine the general plan of the rearrangement of the nerve fibres, which has taken place. I believe the rearrangement may be pictured as being along the following lines:

² I regret that I have not been able to consult this paper. The statement made concerning it is based on the review of the paper by von Bardeleben in the *Ergebnisse für Anatomie und Entwicklungsgeschichte*, Bd. IX, 1899.

The separation of the *N. brachialis inferior longus* into its forearm branches has, in the intermediate forms between the reptilia (or amphibia) and mammalia, receded up the arm until in the mammalia it occurs practically at the brachial plexus. During the recession a very considerable change in the relative position of the *R. profundus* has occurred, since it has left its deep situation and come forward to join the greater part of the *R. superficialis radialis*, forming a stem, the median, which lies ventral to the deeper muscles and has on the whole a radial position.

That portion of the original profundus, however, which supplies forearm muscles remains more or less distinct from the median and forms the anterior interosseous nerve which passes to its destination anterior to the pronator quadratus.

The ramus superficialis medialis, which, even in the lower forms, splits into numerous branches soon after its entrance into the forearm, probably associates itself partly with the *R. profundus* to form the median and partly joins the *R. superficialis ulnaris* to form the ulnar, and it is in the relative amounts of it which enters into the composition of each of these nerves that variation occurs in the mammalia.

Bearing in mind, then, that we probably have in the mammalian anterior interosseous nerve the representative of the portion of the *R. profundus* which is supplied to the forearm, the portion of that nerve destined for the hand being included in the main stem of the median, and considering also the topographic relations of the deep portions of the flexor communis digitorum supplied by it, it seems that we are justified in identifying these portions of the communis with the portion of the reptilian palmaris profundus which is supplied by the *R. profundus*; in other words the radialis and ulnaris portions of the flexor communis are together almost equivalent to portion I of the palmaris profundus. But not entirely so, since as a rule the ulnar portion of the ulnaris also receives some twigs from the ulnar nerve, and the portions of the muscle so supplied probably represent another portion of the deep muscles of the lower forms, but exactly which, it is difficult to state with certainty. There seem to be two possibilities worthy of consideration; either (1) the twigs for the ulnar nerve, which enter the muscle, represent a portion of the *R. ulnaris*, in which case it is necessary to turn to the amphibia to find a homologue for the muscle fibres in the ulno-carpalis, or (2) the twigs represent a portion of the *R. superficialis medialis* which has associated itself with the *R. ulnaris*, and in this case the muscle fibres would represent either the second or third portion or both these portions of the palmaris profundus. I am not prepared to say

which of these possibilities is correct, although I am much more inclined to favor the second than the first.

However that may be, I feel confident that in the radialis and ulnaris portions of the flexor communis digitorum we have the representatives of the palmaris profundus and that these muscles are the only representatives of the profundus. The remaining portions of the flexor communis, together with the palmaris longus, represent the palmaris superficialis, and it is interesting to note that the mammalian muscles have the same relations to the elbow joint, so far as their general origin is concerned, as those of their reptilian prototypes; there has been, in other words no skipping across the joint of the profundus group of muscles.

For the remaining muscles the homologies are less complicated. The flexor carpi radialis is equivalent throughout all the forms under consideration; the pronator radii teres, which in the majority of mammals lacks the coronoid head, seems undoubtedly equivalent to the reptilian muscle of the same name; this is also true for the epitrochleo-anconeus, which, it may be remarked, is, as Leche (1898) has suggested, a member of the flexor group and not one of the extensor series with which it has usually been classified. The flexor carpi ulnaris presents a slight difficulty, it being a question whether it represents the compound muscle so named in the reptilia, or merely the lateral head of that muscle. The double origin of the mammalian muscle, which is usual, seems to indicate that it is the equivalent of the entire reptilian muscle, in which case we have further evidence that a portion of the R. superficialis medialis is included in the mammalian ulnar nerve.

Tabulating the homologies stated above we get the following results:

Amphibia.	Reptilia.	Mammalia
Ulnocarpalis	?	?
Epitrochleo-anconeus	Epitrochleo-anconeus	Epitrochleo-anconeus
Flexor carpi ulnaris	Flexor carpi ulnaris (lateral head)	Flexor carpi ulnaris (lateral head)
	{ Flexor carpi ulnaris, (medial head)	Flexor carpi ulnaris (medial head)
Palmaris superficialis	{ Palmaris superficialis	{ Palmaris longus Portio condylo-radialis Portio condylo-ulnaris Portio centralis
Palmaris profundus III } Palmaris profundus II } Palmaris profundus I }	{ Pronator radii teres Palmaris profundus II, III } Palmaris profundus I }	{ Pronator radii teres Portio ulnaris Portio radialis
Pronator quadratus	{ Pronator quadratus Pronator accessorius	{ Pronator quadratus
Flexor carpi radialis	Flexor carpi radialis	Flexor carpi radialis

The results which I have recorded above differ materially from those obtained by Eisler (1895) from the comparison of the mammalian mus-

cles with those of an amphibian. His homologies may be stated briefly as follows: The superficial palmar of the amphibia is represented by the palmaris longus, having become very much reduced in size correlatively with a marked increase in the size of the deep palmars. Of these the palmaris profundus II, gradually extending its origin proximally and radially, becomes transformed into the flexores digitorum profundus and longus pollicis; the palmaris profundus III similarly migrates proximally upon the ulna and eventually, passing over the elbow joint, reaches the internal condyle of the humerus and becomes the flexor digitorum sublimis; while the profundus I is normally unrepresented in the mammalian forearm, but occasionally appears as the anomalous radio-carpeus of Fano (the flexor carpi radialis brevis seu profundus of Wood).

It seems to me that these results are open to criticism along three general lines. In the first place the omission of all consideration of the reptilia has placed Eisler at a disadvantage in having no bridge over the enormous gap which undoubtedly exists between the urodelous amphibia and the mammalia. Even if we accept an amphibian ancestry for the mammalia, it seems probable that the ancestors were much more reptilian in character than are any of the existing urodeles and, furthermore, not only must the mammalian musculature be referred back to the amphibian but so must the reptilian. Accordingly we may expect to find in the reptilian muscles, if not direct evidence of the phylogeny of the mammalian conditions, at all events indications of the lines along which it proceeded and, it seems to me, this expectation has been fully borne out by the results described in the preceding pages. There is certainly much more general similarity in the arrangement of the reptilian and mammalian forearm musculature than in that of the amphibia and mammalia.

In the second place Eisler has failed to take into consideration the evidence derived from the nerve supply of the amphibian musculature. It may not be possible as yet to institute a certain homology between the amphibian and mammalian forearm nerves, but I believe that I have shown a sufficient general equivalency to warrant the acceptance of the nerve supply as important corroborative evidence. The identification, therefore, of the palmaris profundus II with its nerve supply from the R. superficialis medialis with the mammalian flexor profundus supplied by fibres which represent the R. profundus, seems very doubtful, unless the evidence from other sources is more than ordinarily convincing, and that it is so has not, I believe, been demonstrated.

Thirdly, the homologies proposed by Eisler demand a very consider-

able modification in the topographic relationship of the muscles. A muscle, the profundus III for example, which is clearly a portion of the deep layer in the amphibia, becomes, in the mammalia, the superficial flexor sublimis, altering its topographic relations to the principal nerves of the arm. Such an alteration is of course possible, but its probability is greatly diminished if an homology can be found which does not demand it, and I have shown that there is such an homology. Indeed, the superficial and deep layers of the amphibian forearm musculature are clearly recognizable in both the reptilia and the mammalia, and there seems no reason for manufacturing homologies which require their confusion. Furthermore, it seems to me that an homology which demands an extensive migration of muscle masses across joints should be viewed with suspicion, and such a migration is demanded by Eisler's identification of the palmaris profundus III with the flexor sublimis. With the enormous reduction which he supposes to have occurred in the palmaris superficialis, room is afforded upon the internal condyle for such a migration, but as has just been indicated and as will be shown later there is evidence to show that this reduction has not occurred. Hence, independently of the *a priori* objections to a migration of a profundus muscle across a joint, there is, in the present case, an additional objection on the ground that the muscle would have found the territory for which it was striving already preëmpted.

Finally, a word concerning the identification of the palmaris profundus I with the anomalous flexor radialis brevis. I have had an opportunity for studying this muscle in a subject dissected last winter in the Anatomical Laboratory of this University, and from its general relations I should be strongly inclined to regard it as a portion of the flexor carpi radialis, though I cannot exclude the possibility of its derivation from the pronator quadratus. In either event, however, I agree fully with Le Double (1897) in assigning it to the group of progressive anomalies: "Il est la conséquence du morcellement plus complet de la masse flexo-pronatrice, et non un 'remnant' de cette masse, pour me servir d'une expression du professeur Humphry."

III. THE ANTIBRACHIAL FLEXORS IN MAN AND THE EVOLUTION OF THE FLEXOR SUBLIMIS.

The flexor muscles of the forearm in man present certain departures from the condition which has been considered fundamental for the mammalia, the more important of these departures concerning the pronator radii teres and the flexor communis digitorum. The peculiarity in the pro-

nator consists in its possession of a coronoid head in addition to the condylar one, the median nerve passing into the forearm between the two heads. This condition, so far as I am aware, occurs only in man and in the anthropoid apes, and in these forms it is associated with a marked reduction in the size of the pronator quadratus. There seems to be no doubt but that Macalister (1868) was right in regarding the deep head as something quite distinct from the pronator teres proper, and I believe we may go further than Macalister when he says in his earlier paper that it is to be regarded as "the germ of a superior transverse muscle, the upper equivalent and co-ordinate of the pronator quadratus below." In its highest degree of development in the mammalia this latter muscle occupies the entire length of the forearm, and in *Perameles* and some species of *Halmaturus*, in the dog and the hyæna, its proximal portions are united with the pronator teres (Leche). In man and the anthropoids, as Macalister points out in his later paper (1869), we seem to have other instances of a similar fusion, in association with which there has been, however, a degeneration of a considerable portion of the quadratus, only its proximal and distal portions persisting.

In the case of the flexor digitorum communis the modifications are much more complicated. The most striking peculiarity of the human flexor is its separation into a large flexor sublimis seu perforatus and a flexor profundus seu perforans, and, furthermore, the separation of the profundus into the profundus of anthropotomy and the flexor longus pollicis.

That the occurrence of a flexor longus pollicis is due to a differentiation of a portion of the profundus, to be more precise of a portion or all of the portio radialis, seems beyond question. It is a muscle which has not infrequently been described as absent in the lower forms, or in other cases, its absence has been accounted for by a fusion with the profundus. To my mind neither of these expressions fits the case; the latter one implies that it is an independent typical constituent of the mammalian flexors which in certain cases has disappeared by fusion with the neighboring muscle, while the former implies that it is unrepresented. The occurrence of the muscle in a comparatively small number of the mammalia, *e. g.* in certain carnivores, *Hylobates* and man, indicates by no means indistinctly its secondary nature, and it certainly seems improbable that it could appear sporadically, as it does, without having some representative in the arms of forms nearly allied to those which possess it. If it be a separated portion of the profundus, then it has a representative throughout the entire mammalian series, probably even in forms which lack a pollex, for the relation of the profundus is not primarily to the individ-

ual digits but to a common tendon, a point which will be elucidated in the succeeding part of this paper.

Independently of the decided difference in the views of Eisler and myself as to the homologue of this muscle in the amphibia, it seems to me that Eisler is wide of the mark in attempting to discover an indication of its independent existence in the lower forms, as he does in the partial separation of the profundus II into two portions. Its independence from the mammalian profundus is too recent phylogenetically to warrant a hope of an absolute identification of it in the amphibia. Its separation occurs only within the mammalian phylum and, indeed, only in certain of the more highly specialized members of that phylum. I can see no reason for supposing that the occurrence of the muscle in the dog and the hyæna has any phylogenetic relation to its occurrence in man; it seems rather to have been developed, i. e. separated from the profundus independently in the two cases.

The palmaris longus is a muscle which may well be regarded as typical of the mammalia, though its absence in the monotremes, that is to say its lack of separation from the flexor communis implies that its differentiation has occurred within the limits of the phylum. The available evidence seems to point to its having been the first separation from the common flexor, and its distinctness from the other components does not seem to be equal in different forms. In other words it is doubtful if the muscle is an absolutely equivalent structure throughout the mammalian series, but this, as well as the question as to the nature of the palmar fascia to which it is attached, can be more satisfactorily discussed later.

The sublimis, like the palmaris longus, has been differentiated from the flexor communis digitorum within the limits of the mammalian phylum and is not an equivalent muscle throughout the group, since it contains a greater portion of the flexor communis in man and the higher forms than it does in the lower. It is hardly necessary to remark that the identification of the sublimis with the flexor brevis digitorum (perforatus) of the reptilia, which has so frequently been made, is incorrect.

The comparison of the sublimis in different mammals must rest upon the recognition of its relations to Windle's five portions of the flexor communis and these relations are as yet unknown in the majority of the mammalia. I shall, accordingly, first describe what I have found in the forms which I have studied, namely in the opossum, the cat, the mouse and man, and employ the table contained in Windle's paper only after I have established the probable line of differentiation.

In a section through the upper part of the arm of an opossum (Fig. 5) the five portions of the flexor communis are clearly recognizable, the con-

dylo-ulnaris (C. U.), lying beneath the medial head of the flexor carpi ulnaris (F. C. U.²) and the palmaris longus (PL) and ventral to the ulnaris (UL), the condylo-radialis (CR) lying to the radial side of the palmaris and the condylo-ulnaris, while between it and the radialis is the slender centralis (C), which corresponds to the "slender little spindle of muscle, quite distinct from the rest," described by Coues (1872), whose identification of it with the flexor longus pollicis is manifestly erroneous. Tracing the various portions down the arm, it is found that

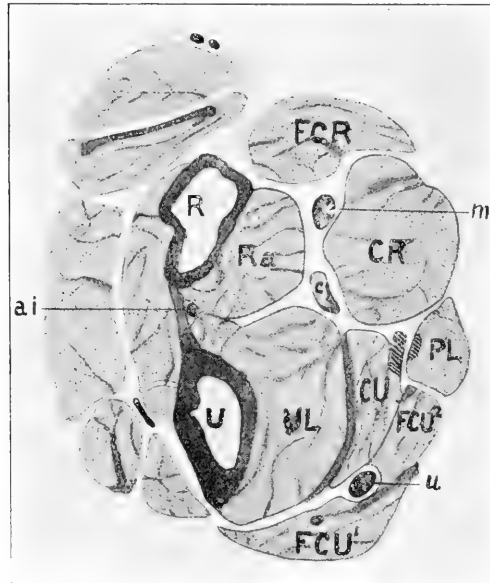


FIG. 5. Transverse section through the forearm of the Opossum. *ai*, anterior interosseus nerve; C, centralis; CR, condylo-radialis; CU, condylo-ulnaris; F. C. R., flexor carpi radialis; F. C. U.¹ and F. C. U.², lateral and medial portions of the flexor carpi ulnaris; *m*, median nerve; PL, palmaris longus; R, radius; Ra, radialis; U, ulna; *u*, ulnar nerve; UL, ulnaris. The shaded areas represent the flexor sublimis digitorum.

the condylo-ulnaris decreases in size rather rapidly, its fibres passing into a flat tendon which lies on the surface of the muscle in contact with the ulnaris. A portion of the muscle, represented approximately by the portion which is shaded in Fig. 5, may, however, be traced onward to the wrist where it passes into a tendon lying to the ulnar side of and superficial to the large tendon which is formed by the fusion of the main condylo-ulnar tendon with the other four portions of the flexor communis. Later the superficial condylo-ulnar tendon divides into three

slips, which pass to the second, third and fourth digits and are three of the tendons of the flexor digitorum sublimis.

On tracing the palmaris longus distally it is found to develop upon its deep surface a slender tendon, represented by the shaded portion in Fig. 5, and toward the wrist the rest of the muscle passes into a flat tendon which is lost in the palmar fascia. The slender tendon can be traced onward into the hand below, *i. e.* dorsal to the flat tendon and the palmar

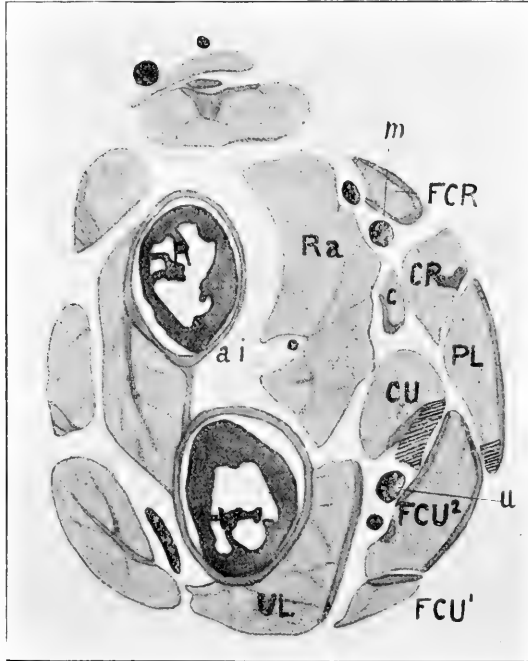


FIG. 6. Transverse section through the forearm of an embryo cat of 7 cm. Lettering the same as in the preceding figure.

fascia, and, verging toward the ulnar side of the hand, it becomes the sublimis tendon to the minimus. This origin of a portion of the sublimis from the palmaris differs from the account given by Coues, the only description of the myology of the opossum I have been able to consult; this author, as well as Windle, derives all four tendons from the condylo-ulnaris. The origin of the minimal tendon from the palmaris was found both in my sections and dissection and, as will be seen, is in harmony with what occurs in other forms in which the sublimis is in a low state of differentiation.

In the cat the condylo-ulnaris is not distinctly separated from the ulnaris in the upper part of the arm and it contains a tendon imbedded in its substance which is continuous with a tendon on the ventral surface of the ulnaris. Apparently a portion of the condylo-ulnaris inserts into the ulnaris tendon and this unites with the other four portions to form the profundus tendons as in the opossum, but the rest of the muscle, the shaded portion in Fig. 6, can be clearly seen to divide near the wrist into a smaller radial and a larger ulnar portion which remain distinct from the ulnaris and in each of which a tendon develops. The

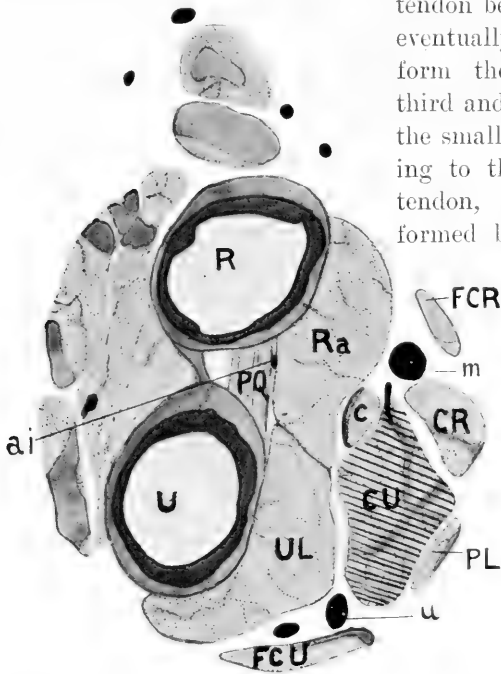


FIG. 7. Transverse section through the forearm of a new-born mouse. Lettering as in Fig. 5.

the ulnaris, radialis, centralis and condylo-radialis all unite together to form a profundus tendon. But the condylo-ulnaris remains quite separate from the rest and at the wrist divides into three portions which, becoming tendons, pass as the perforated tendons to the second, third and fourth digits, there being in this form, or at all events in the single individual I studied, no sublimis tendon to the fifth digit and hence no contribution to the sublimis from the palmaris longus.

These three forms afford a very definite clue to the relations of the sublimis to the flexor communis. It is principally associated with the

tendon belonging to the larger portion eventually divides into two slips which form the sublimis tendons for the third and fourth digits, the tendon for the smaller portion of the muscle passing to the second digit. The fourth tendon, that for the fifth digit, is formed by a slip from the palmaris longus, the relations of the sublimis being very similar to what obtained in the opossum, though the amount contributed to it by the condylo-ulnaris is somewhat greater in the cat.

In the mouse the conditions are somewhat different, however. As usual the five portions of the flexor mass and the palmaris longus can be recognized

(Fig. 7) and tracing them

downward it can be seen that

the ulnaris, radialis, centralis and condylo-radialis all unite together to

form a profundus tendon. But the condylo-ulnaris remains quite separate

from the rest and at the wrist divides into three portions which, becoming

tendons, pass as the perforated tendons to the second, third and fourth

digits, there being in this form, or at all events in the single individual

I studied, no sublimis tendon to the fifth digit and hence no contribu-

tion to the sublimis from the palmaris longus.

condylo-ulnaris, the portion to the fifth digit, however, being derived from the palmaris longus. In the opossum but a small portion of the condylo-ulnaris is devoted to the formation of the sublimis, the contribution is distinctly greater in the cat and the entire muscle is taken up into it in the mouse.

Having then some indication of the line which the differentiation of the sublimis follows, we may now turn to the table given by Windle (1890) and inquire whether it reveals any further differentiation along the same line. And first of all we may consider his account of the arrangement in the rat. The condylo-ulnaris is stated to be absent in this form, while the other four portions of the flexor mass are recognizable, and the sublimis is indicated as being an independent muscle. This may with propriety be interpreted, on the basis of what I have found in the mouse, that the condylo-ulnaris has been completely taken up into the sublimis, and, applying the same interpretation to other forms tabulated by Windle, we find that the same condition obtains in the majority of the rodentia. Proceeding to higher forms we find that in *Cebus capucinus* the condylo-ulnaris is again wanting and that, furthermore, the sublimis is closely associated with the condylo-radialis, that is to say, the sublimis not only includes the whole of the condylo-ulnaris but also receives a contribution from the condylo-radialis. The same condition occurs also in *Cynocephalus maimon*, with the addition that in this form the centralis has also disappeared, having, I imagine, been taken up into the sublimis. This disappearance of the centralis is also noted for several other monkeys, although in these no mention is made of any association of the condylo-radialis with the sublimis, and, finally, in the orang, it is stated that not only are the condylo-ulnaris and centralis wanting, but this is also the case with the condylo-radialis, the sublimis at the same time having a radial origin.

The condition in the orang is essentially the same as in man and we may now see what a study of sections of a human arm reveals, my preparations being made from an embryo of 4.5 cm. Instead of being absent in part all the five portions of the flexor mass can be readily distinguished (Fig. 8), and on tracing them downward it is found that the condylo-ulnaris, the condylo-radialis and the centralis unite together to form the flexor sublimis; the ulnaris is the flexor profundus and the radialis the flexor longus pollicis. In other words instead of the three condylar portions of the flexor communis being absent or only occasionally present as anomalies in man, they are always present and are incorporated in the flexor sublimis. Windle maintains that the condylo-radialis is represented by the second or ulnar head of the flexor longus pollicis; this I

doubt. There is no question but that, in the arm I studied, the entire mass of the condylo-radialis passed into the flexor sublimis, and the ulnar head of the radialis, *i. e.* the longus pollicis, is readily accounted for by the fact that that portion not infrequently takes its origin from the ulna as well as from the radius.

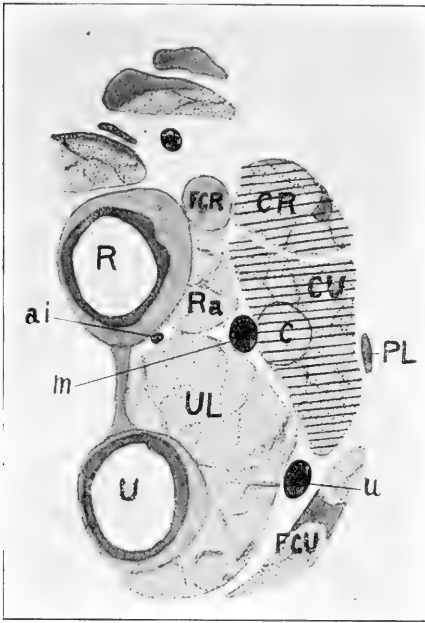


FIG. 8. Transverse section through the forearm of a human embryo of 4.5 cm. Lettering as in Fig. 5.

The various portions of the sublimis possess an interesting relation to the digits. The tendons for the two ulnar fingers come from the condylo-ulnaris; that for the medius is formed entirely from the condylo-radialis and in the arm lies to the radial side of the tendon for the index, crossing obliquely over that tendon upon its palmar surface at the wrist; the index tendon is formed mainly from the centralis, though I could not be certain that it did not also include some portions of the condylo-ulnaris.

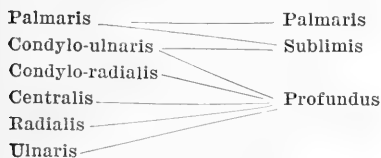
The history of the sublimis, then, seems to be as follows: In the mammalian prototypes the arrangement of the forearm flexors was somewhat as is now found in the monotremes, there being a single flexor mass without any marked differentiation of a superficial and a deep portion. The single tendon formed from this mass divided at the wrist into a superficial set of sublimis tendons and a deep set representing the profundus, but the muscle mass of the forearm showed no such separation. Its first differentiation consisted in the separation of a palmaris longus, which became attached to the minimal sublimis tendon as well as to the palmar fascia, and a portion of the condylo-ulnaris separated and became continuous with the other three sublimis tendons. Later the entire condylo-ulnaris was brought into connection with the sublimis and the portion of the palmaris which joined the ulnar tendon separated from that muscle and became incorporated in the condylo-ulnaris. In higher forms the centralis also united with the sublimis tendons as well as a portion of the condylo-radialis and, finally, in the anthropoids and in man, all the superficial or condylar portions of the

original flexor communis separated to join the sublimis tendons, leaving only the ulnaris and radialis attached to the profundus tendon. In brief, starting with a condition in which there is no definite distinction between a superficial and a deep layer of antibrachial flexors, there has been a gradually increasing separation of the superficial layer, until, finally, we have in the flexor sublimis *plus* the palmaris longus the exact homologue of the palmaris superficialis of the reptilia.

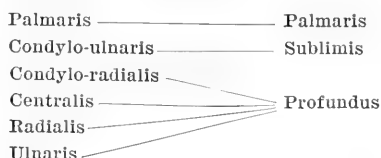
After what has been already said it is perhaps hardly necessary to point out that my views as to the significance of such anomalies as the occurrence of a distinct centralis in man are quite different from those expressed by Windle. For I do not believe its occurrence is the appearance of a muscle usually absent, but, on the contrary, the muscle is always present as a constituent of the sublimis and its recognition as a distinct structure is due to its failure to unite with the other components of that muscle. Indeed, it seems highly probable, that we are in error in stating, as is usually done, that the palmaris longus is not infrequently absent in man; we should rather say that in many cases it becomes completely incorporated with the sublimis, just as a portion of it, as represented in the lower forms, does normally.

The progressive development of the sublimis in the mammalia, together with the homologies of the flexor muscles in various forms, may be shown as follows:

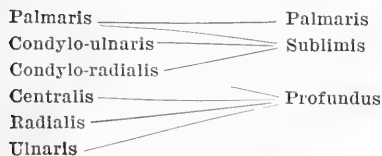
OPOSSUM AND CAT.



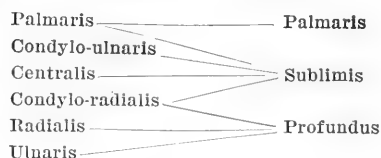
MOUSE.



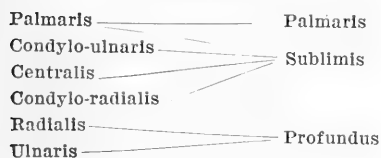
CEBUS CAPUCINUS.



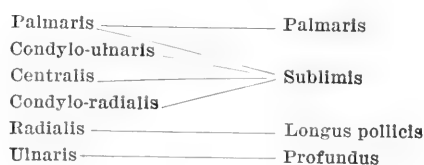
CYNOCEPHALUS MAIMON.



ORANG-OUTANG.



MAN.



IV. THE EXTENSION OF THE LONG FLEXORS INTO THE HAND.

We come now to the concluding chapter in the history of the flexors of the forearm. It has been shown that they are primarily confined to the forearm, acting on the digits only by the intervention of the palmar aponeurosis and the palmar muscles which arise from it, and it remains to be seen how the direct connection with the digits which they possess in the mammalia has been brought about.

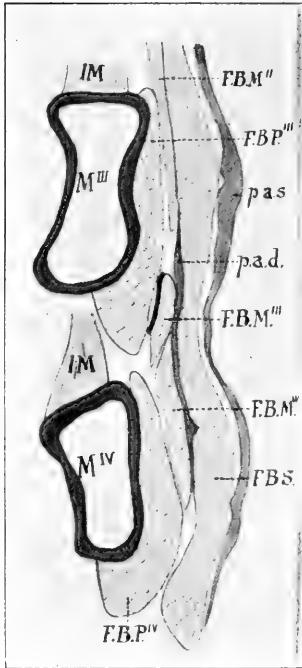


FIG. 9.

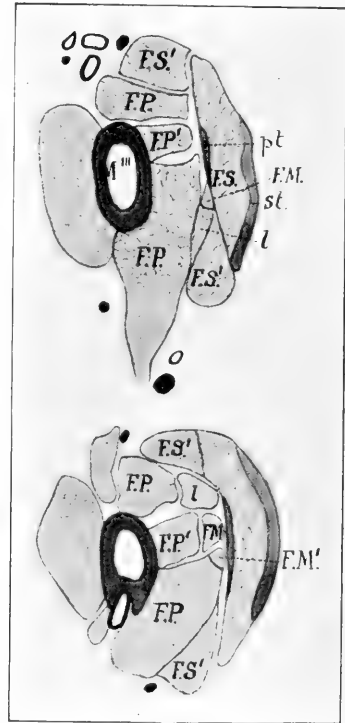


FIG. 10.

FIG. 9. Transverse section through the third and fourth metacarpals of *Amblystoma tigrinum*. F. B. P., flexor brevis digitorum profundus; F. B. M., flexor brevis medius; F. B. S., flexor brevis superficialis; I. M., intermeta-carpalis; M^{III} and M^{IV}, third and fourth metacarpals; *p. a. s.*, and *p. a. d.*, superficial and deep layers of the palmar aponeurosis.

FIG. 10. Transverse section through the second and third digits of *Amblystoma tigrinum*. F. P., and F. P', flexor brevis digitorum profundus; F. M., median portion of flexor brevis medius; F. M', portion of flexor brevis medius which unites with the flexor profundus; F. S., median portion of flexor brevis superficialis; F. S', portions of the flexor superficialis which unites with the flexor profundus; *l*, lumbricalis; *i. e.*, lateral portion of the flexor medius; *pt*, profundus tendon; *st*, superficial tendon.

To do this it is necessary to return to the amphibia and consider the relations of the palmar and forearm muscles to the palmar aponeurosis.

In *Amblystoma*, for example, as a series of sections is traced distally, one finds some distance above the wrist a layer of fascia making its appearance upon the palmar surface of the palmaris superficialis. This is the palmar aponeurosis, and it is into the deep (i.e. the dorsal) surface of this that the superficialis inserts. More distally the aponeurosis receives the insertion of the palmares profundi, also upon its deep surface, and immediately distal to this insertion one finds some muscle bundles making their appearance in the substance, as it were, of the aponeurosis. These bundles represent the proximal portion of the origin of the *flexores digitorum breves superficiales* (Eisler), and in more distal section they increase in number and form a continuous sheet (Fig. 9, F. B. S.), which divides the palmar aponeurosis into two layers, a more superficial one (*p. a. s.*) lying ventral to the flexores and a deeper one (*p. a. d.*) dorsal to them. The muscle sheet soon divides longitudinally into three portions, the more lateral parts, destined for the second and fifth digits, separating for a median part destined for the third and fourth fingers. On account of the divergence of the second and fifth digits from the median line a series of sections transverse to the axis of the forearm will, when continued into the hand, cut these digits obliquely, so that the relations of their muscles cannot be as readily perceived as those of the third and fourth digits; for the present, therefore, attention will be directed solely to the arrangement of the muscles and aponeuroses belonging to these latter digits.

Immediately beneath the deep layer of the palmar aponeurosis and arising from its deep surface are the *flexores digitorum breves medii* (Eisler) (F. B. M.), while below these again and resting directly upon the palmar surfaces of the metacarpal bones from which they arise are the *flexores digitorum breves profundi* (F. B. P.). Finally, stretching across between the metacarpals are the *intermetacarpales* (I. M.). The *flexores superficiales* and *medii* are the muscles which especially interest us just now and they may be briefly described as follows, so far as the portions which pass to the third and fourth digits are concerned. At the junction of the proximal and distal halves of the metacarpals the superficialis sheet divides into two portions corresponding to the two digits, and at about the same time a longitudinal division of the superficial layer of the palmar aponeurosis occurs, a strong slip of it being contained distally upon the palmar surface of each superficialis slip (Fig. 10), while beneath each superficialis slip a thickening appears in the deep layer of the aponeurosis. More distally the lateral portions of each superficialis slip separate (Fig. 16, F. S.) and pass dorsally to fuse with the corresponding flexor brevis profundus (F. P.), while the remaining median

portion later on divides into slips, which may be traced distally to their insertion into either side of a strong fibro-cartilaginous nodule occurring at the metacarpo-phalangeal joint.

In the meantime the deep layer of the palmar aponeurosis has divided longitudinally into slips or tendons, which are the continuations of the thickenings already mentioned as occurring in it, and one of these tendons lies immediately below the median portion of each flexor superficialis slip passing to the digits under consideration (Fig. 10, *pt*). When the final division of the muscle slips occurs, the tendons derived from the deep layer of the aponeurosis pass ventrally between the two terminal slips of the muscle and unite with the superficial tendons, passing on with them to be inserted into the base of the terminal phalanges.

The flexores medii, compared with the superficiales, are small muscles. As they are traced distally that for the fourth digit (Fig. 9, F. B. M.^{IV}) lies over the palmar surface of the fourth metacarpal, being separated from it by the corresponding flexor profundus (F. B. P.^{IV}), while that for the third digit (F. B. M.^{III}), much smaller than the other, lies rather to the ulnar side of its metacarpal. The muscle of the fourth digit divides longitudinally into three slips (Fig. 10, F. M., F. M.^I and *l*), that upon the ulnar side uniting with the subjacent flexor profundus IV, while the median and radial slips insert into the metacarpo-phalangeal fibro-cartilage, the median one entering into close relationship with the underlying median portion of the flexor profundus (F. P.^I). The muscle of the third digit, owing to its more ulnar position with reference to the axis of the digit, lacks a radial slip, dividing into only two portions (F. M. and *l*), the more radial of which corresponds to the median part of the fourth muscle and like it unites somewhat closely with the underlying portion of the flexor profundus, while the ulnar portion inserts independently into the ulnar side of the metacarpo-phalangeal fibro-cartilage.

The points to which attention needs to be especially directed for our present purpose are (1) the splitting of the palmar aponeurosis into two layers by the origin of the flexores breves superficiales, (2) the formation of tendons by the deep layer of the aponeurosis, which, after the division of the flexores superficiales into their terminal slips, pass up between them to join the tendons from the superficial layer of the aponeurosis, and (3) the origin of the flexores breves medii from the under surface of the deep layer of the aponeurosis.

Turning now to the reptilia one is at once struck by the fact that there is no strong aponeurotic layer covering the surface of the flexor brevis superficialis (flexor sublimis seu perforatus Auct.) (Fig. 11, F. B. S.).

On the other hand a very strong aponeurosis (*vc*), frequently partly transformed into cartilage, is present *beneath* the flexor superficialis, giving origin to this muscle from its palmar surface and receiving the insertion of the forearm muscles as described on a preceding page.

We may for convenience confine our attention mainly to the muscles associated with the three middle digits, for the same reason that led us to disregard the lateral digits in the amphibia.

Traced distally the central portion of the superficialis sheet divides into three portions (Fig. 11, F. B. S.), which pass to the three digits we are considering, and underneath each portion there is a strong tendon which is a distal continuation of the volar cartilage. Shortly before reaching the metacarpo-phalangeal joint each portion of the superficialis splits into two slips, which separate so as to lie one on each side of the strong tendon just mentioned and gradually fade out into the fascia covering that tendon.

The muscles which correspond to the amphibian flexores breves medii reach a much greater development than in the lower group and are arranged in two distinct layers, the superficial one (Fig. 11, *l*) lying immediately beneath the volar cartilage, from which it takes origin, while the deeper one (*pi*) is in relation with the underlying metacarpal bones.

This latter layer does not concern us at present and will be left for consideration on another occasion. The superficial layer when traced distally divides into four portions which pass to the II-V digits, there being no portion for the pollex. Each portion lies beneath the corresponding portion of the flexor superficialis, being separated from it by the strong tendon derived from the volar cartilage. More distally each of the portions corresponding to digits II-IV divides into two slips which come to lie on either side of the corresponding strong tendon and are finally inserted into opposite sides of the base of the metacarpo-phalangeal fibrocartilage of the digit to which they belong.

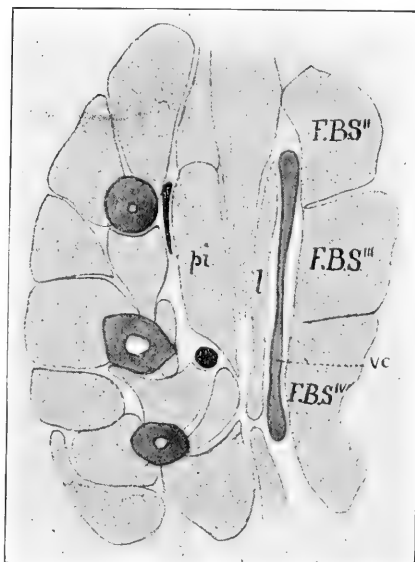


FIG. 11. Transverse section through the palm of *Liolepisma laterale*. F. B. S., flexor brevis digitorum superficialis; *l*, lumbricalis; *i. e.*, superficial layer of the flexor brevis medius; *pi*, palmar adductors; *i. e.*, deep layer of the flexor brevis medius; *vc*, volar cartilage.

In the case of the fifth digit the conditions are slightly different, in that the superficial sheet of the flexor medius does not extend laterally beyond its radial border, and hence, when the division of the sheet into separate slips takes place, that for the minimus lies upon the radial side

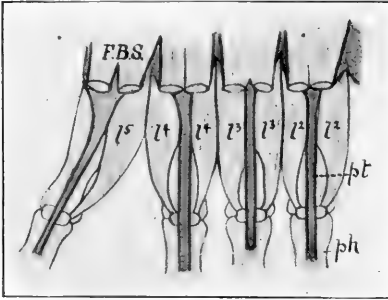


FIG. 12. Partly diagrammatic representation of the arrangement of the lumbricales (*l*), in *Liolepisma laterale*. F. B. S., flexor brevis superficialis; *ph*, phalanx; *pt*, profundus tendon.

of its digit and does not divide into two terminal slips as do the others, but inserts entirely into the radial side of the arthrodial fibrocartilage. The arrangement of these muscle-slips is shown diagrammatically in Fig. 12.

If now we proceed to compare these arrangements with those seen in the amphibia we arrive at the following conclusions. The portion of the superficial layer of the amphibian palmar aponeurosis, which covers the flexor brevis super-



FIG. 13. Diagram showing the mode of formation of the profundus tendon. F. B. S., flexor brevis superficialis; F. B. M., flexor brevis medius; P. A., palmar aponeurosis. The stippled portion of the aponeurosis disappears in the reptilia.

facialis, has disappeared in the reptilia or is represented in the flexor, if one prefers to state it that way. The more proximal portions of the aponeurosis, however, are represented by the volar cartilage, and the strong tendons which are continued distally toward the fingers from the volar cartilage are, in their proximal portions, the representatives of the tendons formed from the deep layer of the amphibian aponeurosis. Beyond the point of the bifurcation of the slips of the flexor superficialis these tendons in the amphibia fuse with the tendons

from the superficial layer of the aponeurosis, and it is probable that in the reptilia the tendons from the same point are equivalent to those of the amphibia. The annexed diagram (Fig. 13) will give, I trust, a sufficiently clear idea of the arrangement in the two groups, the portion of the amphibian aponeurosis which has disappeared in the reptilia being indicated by the stippling.

From the reptilian arrangement as interpreted above to the mammalian the passage is easy. The tendons which are continued distally from the volar cartilage to the digits clearly correspond to the mammalian

profundus tendons and the superficial layer of the flexor brevis medius is, I believe, equivalent to the mammalian *lumbricales*. The deep layer of the medius, however, entering as it does into relation with the flexores breves profundi and the metacarpals, is probably represented in the mammalia by the palmar adductors, an homology which I hope to consider in detail in a later paper. It is interesting to compare the arrangement of the lumbricales in *Echidna* as described by Westling (1889)³ with that which I have found in the superficial layer of the flexor brevis medius of the reptilia.

The reptilian equivalents of the sublimis tendons are indicated, I believe, by the condition found in the monotremes and in certain marsupials. In *Ornithorhynchus* a muscle has been described as the flexor digitorum sublimis (Smith, Westling), which has essentially the same relations as the flexor brevis superficialis of the reptilia, and in *Thylacinus* and *Phascogale* (Cunningham, 1882), this muscle is represented by four minute tendons which arise from the strong tendon of the flexor communis digitorum. The communis tendon I take to be practically the homologue of the reptilian aponeurosis in which the volar cartilage is developed and the small tendons which arise from its surface are therefore equivalent to four of the slips of the flexor brevis superficialis of the reptilia, which have undergone, as so frequently happens, transformation into connective tissue (see von Bardeleben and Bland Sutton).

The identification of the tendon of the flexor communis with the reptilian palmar aponeurosis is not, however, quite exact, for there exists in the mammalia a palmar fascia which covers the sublimis tendons and receives the insertion of the palmaris longus. This muscle is a portion of the condylar flexor mass of the forearm and is, as has already been seen, closely related to the sublimis, containing, in the lower mammals, elements which in higher forms are included in that muscle. This being the case it must be supposed that the original insertion of the palmaris was with the rest of the flexor mass into the palmar aponeurosis, and that with the separation of the palmaris there has also been a separation of a palmar layer of the aponeurosis to form the mammalian palmar fascia. The relations of the superficial thenar and hypothenar muscles to the fascia support this view of its origin, since these muscles are persisting portions of the flexor brevis digitorum superficialis. The correct equivalent, accordingly, of the reptilian palmar aponeurosis in the mammalia is the tendon of the flexor communis *plus* the palmar fascia, but it should be pointed out that there is a strong probability, that the distal

³ I have not been able to consult this paper, but the figure which bears on this point is reproduced by Leche in the *Mammalia of Bronn's Thierreich*.

portions of the mammalian fascia may represent the portion of the amphibian palmar aponeurosis which has disappeared in the reptilia I have studied.

The phylogenetic history of the mammalian long flexors, which has been traced in the preceding pages, may be briefly stated as follows: In the primary condition the entire flexor mass of the forearm terminates at the wrist, a certain portion of it inserting into the bones of the forearm and carpus and the rest into a strong palmar aponeurosis. From the latter two sets of muscles take origin, (1) from its substance the flexores breves superficiales, and (2) from its deep surface the flexores breves medii. By the mode of origin of the first of these the palmar aponeurosis is divided distally into two layers, a more superficial one which is prolonged distally into strong tendons which insert into the bones of the terminal phalanges, and a deep one also prolonged into tendons which pass between the terminal steps of the flexores superficiales to unite with the superficial tendons. This is the amphibian stage.

In the second or reptilian stage the portion of the superficial layer of the palmar aponeurosis which covers the flexores breves superficiales disappears and the action of the forearm flexors which insert into the aponeurosis is distributed to the digits entirely through the tendons of the deep layer, which, together with the persisting terminal portions of the superficial tendons, may be recognized as the equivalent of the mammalian profundus tendons. The portions of the two layers of the forearm flexors which act on the aponeurosis fuse more or less completely, the flexores breves superficiales retain their amphibian relations, while the flexores medii divide into two layers, the more superficial of which represents the lumbrical muscles of the mammalia.

In the last or mammalian stage the flexores breves superficiales become transformed more or less completely into the tendons of the flexor sublimis, and as the scale is ascended, a gradually increasing amount of the superficial portion of the flexor communis separates to become continuous with these tendons, until, in man, the entire condylar portion of the muscle, except so much as is represented by the palmaris longus, is taken up into the flexor sublimis.

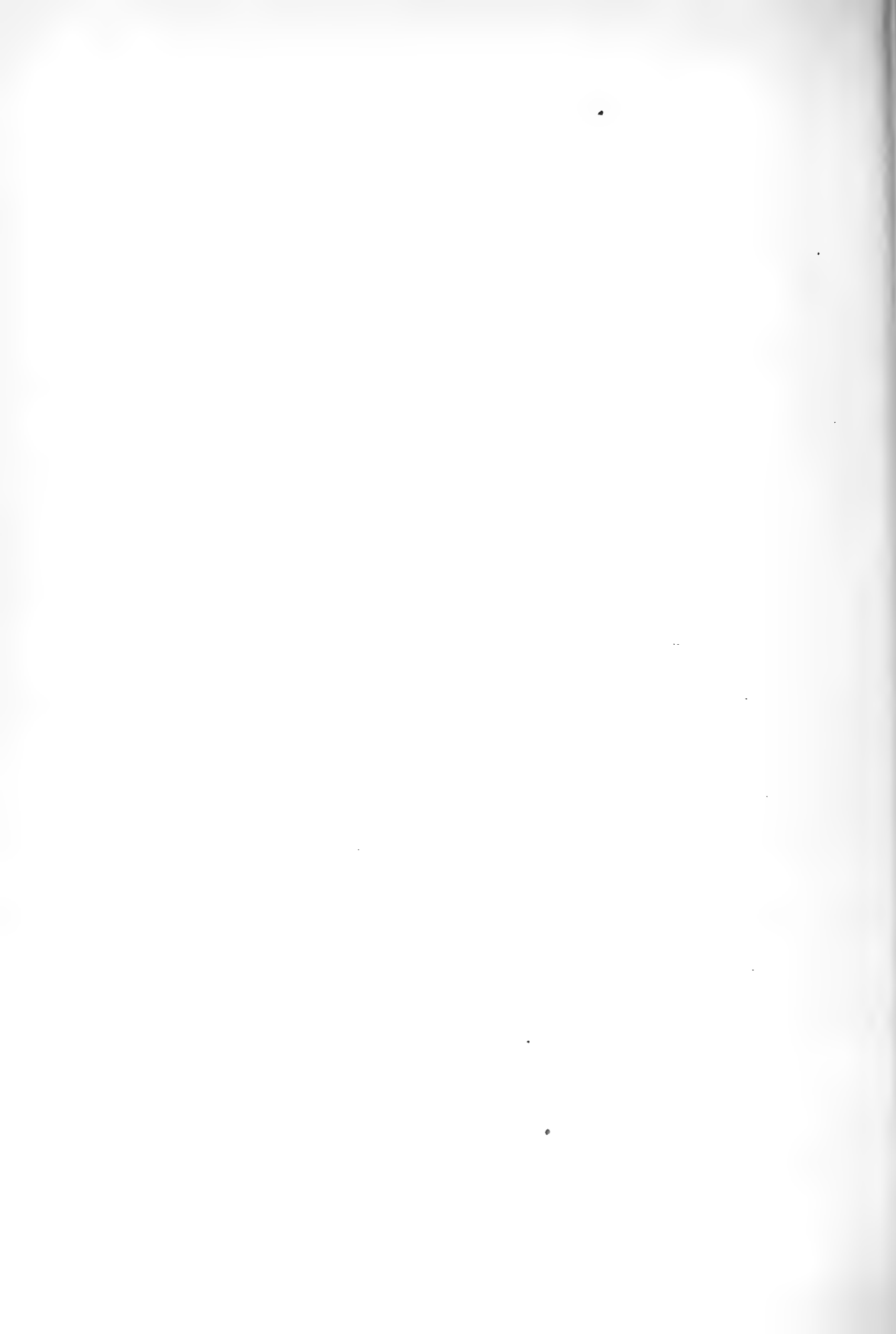
In the cases of the first and fifth digits some departures from the processes outlined above occur, but these may be more conveniently discussed in connection with the history of the other hand muscles in a later paper.

The results recorded above as to the relations of the sublimis tendons to the forearm muscles agree in general with those arrived at by Eisler, but I have succeeded, I believe, in tracing with greater exactness the processes by which the final arrangement has been acquired. Eisler has

failed to perceive the true relations of the profundus tendons to the amphibian palmar aponeurosis, relations which it would be difficult to discover without the aid of sections. He has, however, recognized the relations of the flexores breves superficiales to the sublimis and the probable end to end union of the two muscles, an arrangement which, as he points out, throws clear light on many of the anomalies occurring in connection with the human sublimis.

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THE GROSS ANATOMY OF A 12-MM. PIG.

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WITH 4 PLATES.

It has been my privilege to study, with Prof. Charles S. Minot, the transverse sections of a 12-mm. pig embryo forming Series 5 of the Harvard Collection. Numerous sections of this embryo are to appear in Prof. Minot's new "Laboratory Text-book of Embryology." To show the relation of these to one another I have made four reconstructions which are here separately presented as the basis of this paper. It is thought that this particular pig is distinguished from all other embryos of corresponding size by the detail and completeness with which the entire animal has been portrayed. Similar figures of the human embryo are found in Pl. XX, Vol. 5 of the *Journal of Morphology* (Mall, 91), and in Taf. II of His's contribution "Zur Geschichte des Gehirns," 88.

The reconstructions were made generally by the method of His. The contour of the brain and pharynx was taken from wax models prepared by Dr. J. L. Bremer; elsewhere the shading has been inferred from studying the cross sections. Since the umbilical cord was cut away in the embryo of series 5, that region was supplied from another transverse series of a 12-mm. pig, No. 518 of the Harvard Collection.

The general description of the illustrations is left to the lettered figures. Only the more interesting features are presently to be described; first, those concerning the brain, nerves, and sense organs; then those involving the pharynx, digestive tract, and viscera; finally, those relating to the vascular system.

Brain, Nerves, and Sense Organs.—The exterior of the brain and nerves appears in Plate I; the internal aspect of the brain in Plate III; and the internal view of certain nerves in Plate IV. Unfortunately the depression between mid-brain and diencephalon has been exaggerated in some of the figures. In the median plane the superficial surface is not indented at this point. The rounded outer wall of the diencephalon shows no trace of the epiphysis which begins to form in a pig of

20 mm. and becomes well defined in one of 24 mm. The hind brain possesses three well marked neuromeres followed posteriorly by a fourth shallow one. In a 9 mm. pig there are five which are distinct.

Of the nerves shown in Plate I, the fifth is noteworthy as possessing no ciliary ganglion. Its ophthalmic division is not connected with either the third or fourth nerves, though it passes very near the latter. It finally divides into a shorter frontal and a longer nasal branch (Dixon). Ciliary ganglia have been drawn as if belonging with the fifth nerve by both His and Mall, but as shown by Dixon, 96, and admitted by Prof. His, this was an error. No ciliary ganglion could be found in this pig. The motor tract of the fifth nerve passing into the inferior maxillary division is drawn in Plate IV.

The seventh nerve, Plate I, appears as a bundle of fibres free from cells passing out from the lower part of the lateral wall of the medulla. Its course within the brain proceeds from a point near the median line directly outward, transverse to the cerebral axis. Outside of the medulla a large ganglionic mass is placed over the motor bundle in equitant fashion. That part toward the fifth nerve is the geniculate ganglion from the inferior end of which passes a clump of fibres to fuse with the motor bundle already described, and form the main trunk of the facial nerve. The geniculate ganglion is in close contact with the acoustic ganglion and in a few sections is inseparable from it. From the geniculate ganglion there arises a slender fasciculus, the *pars intermedia* of Wrisberg. It proceeds backward under the entering root of the eighth nerve, to the wall of the medulla, Plate IV. After penetrating into the brain, the fibres lie just ventral to the oval bundle, and may be traced a short distance caudad, running parallel with the cerebral axis. Duval has followed them to the upper end of the glosso-pharyngeal nucleus (Quain). The slender *pars intermedia*, the large geniculate ganglion and the motor root are parts of a single nerve, secondarily united with the acoustic ganglion. Researches establishing this opinion are cited by Thane, 95, Van Gehuchten, 97, and Wiedersheim, 02. The further course of the nerve is shown in Plate I. It divides into *prae-trematic* and *post-trematic* branches, but the division is under the spiracle or auditory cleft and not over it as in fishes. The anterior branch of the seventh nerve passes into the mandibular arch as the *chorda tympani*; the remainder lies behind the auditory groove in the hyoid arch.

The eighth nerve shows its upper vestibular and lower cochlear branches, but its ganglion is not yet subdivided.

The trunk of the ninth nerve is cellular for some distance before it

enters the medulla, but possesses no distinct ganglion other than the ganglion petrosum. Just beyond the ganglion a very slender branch, not drawn in the figure, passes upward and forward over the second cleft. This is Jacobson's nerve. The main stem passes down behind the cleft where it is seen dividing into the lingual branch which extends forward into the hyoid arch, and a smaller pharyngeal branch which remains in the third arch. Notwithstanding the changed relations to the second cleft (such as has occurred in the seventh nerve) the lingual branch is presumably comparable with the prae-trematic and the pharyngeal with the post-trematic of fishes. In this embryo there was no connection between the ninth and tenth nerves.

The tenth nerve arises from the large jugular ganglion, extending from which is a beaded commissure ending in a small knob. In the track of the commissure, but separated from it, and lying beyond it, is an irregular ganglionic mass. After another interval there appears a small fragment, and then follows the first cervical ganglion notably smaller and more dorsally placed than those which succeed it. The irregular ganglionic mass is not connected with the hypoglossal nerve in series 5, but in series 518 a slender bundle unites the two structures. This, then, is Froriep's ganglion. Its relation with the commissure is far more striking than its resemblance with a spinal ganglion. I have found it connected with the commissure in pigs of 17 mm., as did Froriep in a sheep of 12.5 mm. He considered the connection unimportant and described the "vagus ganglion" as passing beneath the hypoglossal ganglion. In his figures (82, Pl. 16) the latter is drawn of the same form and texture as the spinal ganglia, and very different from the diffuse prolongation of the vagus ganglion. In a dissected pig of 17 mm. I could find no such difference: the hypoglossal ganglion appeared as a detached part of the ganglionic chain running forward to the vagus. This commissure in 17 mm. embryos could not be subdivided into definite ganglia; it was characterized by irregular swellings and spurs. In the adult it remains as one or two hypoglossal ganglia. Froriep and Beck, 95, p. 689, in all of the six hogs examined, found a single hypoglossal ganglion and in one case two. In man they are quite constantly absent and the degeneration extends to the first cervical ganglion which may even be macroscopically lacking.

Below the ganglion nodosum the vagus nerve gives rise to several branches passing between the third and fourth branchial clefts. One branch passes under the third cleft into the arch in front of it. There is a branch behind the fourth cleft and the system ends with the large recurrent laryngeal nerve. The laryngeal plexus appears to be derived from the nerves to the degenerated gill clefts.

The spinal accessory nerve begins at the level of the sixth cervical ganglion. Its fibres are very closely associated with the hypoglossal ganglia; in series 518 it rests against, and in places is nearly surrounded by the first cervical ganglion. The passage of fibres between the latter and the spinal accessory nerve has been found in man by Kassander, and confirmed by Froriep and Beck, 95 (p. 694).

Of the sense organs, only the nasal cavity need be noted. Plate 2 is drawn to show the relations of the pharynx and some other internal structures to the surface markings. The nasal cavity appears with the external naris opening broadly on the surface. Toward the mouth the two edges of this cavity are brought together by the growth of the median nasal process on the inside, and of the lateral nasal and maxillary processes (separated by the lachrymal groove) on the outside. Caught between the internal nasal and maxillary processes, the walls of the nasal opening are compressed to form a raphe of semicircular outline as shown in the figure. This raphe extends to the roof of the oral cavity. At its internal end it is a mere plate, indicating the position of the internal naris. In the 14-mm. pig the raphe has disintegrated and mesenchyma extends from side to side. The membrane is at its internal end, after becoming broad and thin, ruptures. Hochstetter, 92, states that "the primary choanae of mammals arise from a breaking through of the hind end of the nasal pit by a tearing apart of the membrana bucconasalis, and there exists in mammals no primary connection between the nasal and buccal cavities." Peter, 02, pp. 54-55, adopts this interpretation. The new opening, however, appears to involve only a part of the raphe made by the fused lips of the primitive nasal opening. The fusion is permanent except in the region of the from the entodermal tract.

Pharynx, Digestive Tract, and Viscera.—The structures connected with the roof of the mouth are shown in Plate II, and in median section also in Plate III. Beginning anteriorly there first appears the hypophysis, having a slender outlet and a broad, thin, spade-like body, flattened parallel with the brain wall. It tends to fork at the infundibular gland and possesses an inconstant knob near the junction of its body and duct. Behind the duct there is still to be seen Seessel's pocket; between it and the hypophysis the oral membrane formerly separated the stomadæum from the entodermal tract.

The floor of the oral cavity is shown in relief in Plate III. Most anteriorly are the large mandibular arches. From the broad dorsum of each arises an elongated eminence, rounded in cross section. In the median line between them, there is a groove in the caudad part of

which is found a low elevation, the tuberculum impar of His. Kallius, *or*, p. 42, has named this pair of mandibular elevations the lingual folds, and states that they form almost the entire body and tip of the tongue. The tuberculum impar is the source of the posterior part of the lingual body and of the septum. A shallow transverse groove still marks the fusion of tuberculum impar and the root of the tongue. The thyroid duct which opened into this groove has become obliterated, and the circumvallate papillæ which are to develop along its course have not yet appeared. That the root of the tongue is formed by a fusion of the second and third arches, as stated by His, **85**, p. 65, could hardly be determined at this stage.

Behind the tongue there is a short, low, bilobate protuberance, the epiglottis. Beyond this the ventral wall of the pharynx presents a round, dorsally directed elevation, which soon becomes indented in the median line. Thick conical masses, the arytenoid folds, appear on either side of this groove. The notch between them becomes a long, slender slit. The trachea, after separating from the œsophagus, continues in this slit-like form, its lateral walls being in close contact except at their dorsal end, where a minute passage exists. Further caudad the ventral prolongation disappears, and the trachea is then a simple tube, Plate III. The subsequent development of the larynx has not been adequately described.

The oral cleft, forming one of a pair of lateral wings at the beginning of the digestive tract, is represented in Plate II. The auditory cleft rises dorsal to the pharyngeal wall, and passes to the auditory groove. It does not open to the exterior. Its internal orifice is drawn in Plate IV, in which it is seen to end behind a conical mass pendant from the side of the pharyngeal roof. The anterior part of the Eustachian opening meets the beginning of the oral wing.

The second pharyngeal pouch runs posteriorly outward, parallel with the course of the pharynx. It opens freely into a well marked external groove which subsequently deepens and separates the lower jaw from the neck. There is no indication of a "Verschlussplatte" in series 5; in series 518, an oblique plate is present on both sides, but appears to be broken through. In a 10-mm. pig, the clefts opened to the exterior but remnants of the plates existed. As yet no indication of the tonsils appears in connection with the second cleft.

The third pouch is a slender tube passing outward, at right angles with the pharynx to its small "Verschlussplatte." Just within the plate it gives rise to a slender tube passing ventrally, parallel with the external groove of the second cleft. This diverticulum may represent

an elongated contact with the ectoderm, since its course is parallel with the corresponding part of the second cleft. De Meuron, 86, p. 104, states that in no class of mammals other than vertebrates can anything be found comparable with this ventral cœcum.

The closing plate of the third cleft lies very near a deep ectodermal pocket which opens externally by a clear-cut nearly round hole, and extends internally along the course of the tenth nerve, ending in an epithelial proliferation. A very slender tube from the pharynx runs toward this mass. The pocket, gland and tube mark the course of the fourth cleft.

From the base of the entodermal part of the fourth cleft there is another pocket tending to pass around in front of the trachea. De Meuron considered this to be a rudimentary cleft. It may, however, be a ventral branch of the fourth cleft comparable with that of the third. Both of these ventral processes occupy parallel positions in the embryo.

In a 12-mm. pig, the cervical sinus is mainly the ectodermal part of the fourth cleft as above described. Its rounded opening has not yet been concealed by the opercular extension of the hyoid arch. The closing plate of the third cleft is becoming involved in the orifice of the sinus anteriorly. Posteriorly the outlet of the sinus is in contact with the ganglion nodosum forming Froriep's epibranchial organ, 85. The epithelial proliferation shown in Plate II is below the level of the ganglion.

The thyroid gland is represented in the 12-mm. pig by its somewhat branched median anlage in the second arch, and by the ventral arms of the fourth cleft. The latter, known also as the post-branchial bodies or lateral thyroids, encircle the trachea, become detached from the pharynx, and, in the higher mammals only, connect with the median thyroid.

The thymus is derived mainly from the ventral arm of the third pouch which also encircles the trachea, approaching its mate from the opposite side. In the 12-mm. pig there is an epithelial mass connected with the entoderm of the third arch and with the adjacent ectoderm. In the 14-mm. pig, this tissue has apparently fused with that at the tip of the cervical sinus, and the resulting mass is also in contact with the ganglion nodosum. Froriep, 85, p. 32, found that his study of the epibranchial organ was complicated inasmuch as the cell mass, connected on one side with the ganglion of the tenth nerve, was united on the other with the anlage of the thymus. Such a condition appears in a 17-mm. pig. De Meuron, 86, p. 76, found that in sheep the fourth

arch produced a structure similar to the superior part of the thymus but which remained behind the thyroid gland. As already stated, in the 14-mm. pig this mass has apparently united with the superior part of the thymus. In an embryo of 24 mm. the thymus consists of the approximated and proliferated ends of the ventral arms of the third clefts. From each of these a slender cord passes upward and backward to join the considerable cell mass near the vagus. This connection is broken, and the small upper part has been variously called the carotid gland, the parathyroid body or, more recently, the epithelial body (Maurer, 02).

The right lung is figured in Plate III. Its elongated condition as compared with the human lung is noteworthy. Above the bifurcation of the trachea there is a budding bronchus which is to supply the upper lobe of the right lung. No corresponding branch is found on the opposite side. This asymmetry of the lungs, described by Aeby, has been found well developed in the lowest of existing mammalia (Wiedersheim, 02, p. 434). With this, its early embryonic appearance is in full accord. Keibel, 97, found the tracheal bronchus in a 9.6-mm. embryo; in the Harvard Collection it is well developed at 9.0 mm.

The stomach is already a *pig's* stomach, possessing in its cardiac portion a well marked diverticulum.

The liver comprises four large lobes which are visible before the embryo is sectioned. Along its lower surface there extends a pouch, exceeding in diameter the intestine from which it arises and into which it empties. Its cylindrical epithelium is quite unlike that of the hepatic cylinders, but resembles somewhat the intestinal mucosa. This large diverticulum ends blindly, its terminal portion being separated from the liver by mesenchyma. Sometimes a knob-like bud is found on its surface. Nearer the intestine these buds are more numerous. Some of them terminate in hepatic cylinders; others end blindly, or are found as detached cysts in the liver. Later all but one of these hepatic ducts are obliterated, and the diverticulum into which it empties has become in part the cystic duct and in part the gall-bladder. Brachet, 96, p. 666, describes similarly the development of the rabbit's biliary ducts. There is first a single intestinal diverticulum, from the proximal two-thirds of which the hepatic cylinders proliferate, and of which the quiescent distal part is retained as the gall-bladder. From its embryological history, it is to be expected that the hepatic ducts possess glands "resembling those of the gastric cardia" and that in the distended gall-bladder such glands should be absent.

The pancreas consists of two closely applied divisions. The ventral

anlage empties into the bile duct close to the intestine. The dorsal and larger portion, separated from the ventral by the portal vein, opens into the duodenum below the bile duct. The adult pancreas is formed of a band of gland-tissue extending from the biliary duct to the duct of Santorini, which opens into the intestine 15 cms. lower down.² From this band extend two tails which seem to correspond with the two anlagen. The ventral duct, that of Wirsung, is represented by impervious fibrous tissue. The duct of Santorini, from the dorsal anlage, is the only one retained in the adult pig.

The intestine extends into the umbilical cord as a simple loop. After receiving the yolk stalk which is now very slender and scarcely pervious, it returns to the body. A dilatation marks the position of the cœcum, which in the adult is a voluminous pouch without an appendix.

The rectum, just before entering the cloaca, is nearly occluded by an epithelial proliferation which separates the intestinal and urinary tracts. In a 20-mm. pig the anus is distinct from the urogenital sinus, and the proliferation has wholly disappeared. I have found a similar plug in rabbits, and Keibel, 96, has figured one in an 11.5-mm. human embryo. He describes it as an "accidental and insignificant adhesion." Gasser discovered a corresponding structure in the chick which has been fully described and its function explained by Minot, 00, 2.

The urogenital system consists of very large Wolffian bodies outlined in Plate IV, and of the genital ridges. The kidneys are represented by their pelves, Plate III. From the latter, the slender ureters pass to the Wolffian ducts, which in turn unite with the allantois and enter the cloaca.

The cloaca is closed by its "membrane," or rather by the approximation of its borders which form a raphe. This is to open at its ends, giving rise to the anal and urogenital apertures, and to remain fused between them, forming the perineal raphe.

Heart, Arteries, and Veins.—The heart, because of its trabecular structure, must be drawn diagrammatically. In Plate III it is shown cut through on the left side of the median septa. The constriction between the auricles forms a partial septum. Below this and toward the left side of the embryo is the large foramen ovale, bounded partly by the auricular wall and partly by the thin wavy septum superius. This septum is attached ventrally to a thick mesenchymal mass, from which

² In man, His (85, pp. 19 and 24) has figured the dorsal anlage in its later stages as emptying below the bile duct, as in the pig. Hamburger, Schirmer and others find the duct of Santorini opening above the bile duct.

proceeds the shelf-like anlage of the atrio-ventricular wall and mitral valve. The left auricle passes caudad into a funnel-like prolongation, the pulmonary vein. As in man, this is at first a single tube, but later is taken up into the auricle so that its several branches enter by separate orifices.

The left ventricle is cut off from the right by a trabecular partition, capped dorsally by a mass of dense mesenchyma which bounds the ill-named interventricular foramen. This foramen opens into the space a, b, c, shown in a section of the heart on the right of the median septa, Plate IV. From here the blood may proceed either through the aorta or the pulmonary artery. The aorta and pulmonary artery are separated by a pair of folds united above, but distinct below. The fold on the left side, which has been cut away, passed over into the interventricular septum near b. The other extends along the right cardiac wall, ending in the tricuspid anlage. These folds fuse so as to connect a with b, and b with c. The only outlet for the persistent interventricular foramen is then into the aorta (Born, 89, p. 339). The cut tissue near b is not involved in the division of the bulbus arteriosus just described. It represents a clump of trabeculae passing from the right wall and sectioned just before uniting with the median septum. It is connected with the tricuspid trabeculae. Instructive cross-sections at this level have been drawn by Hochstetter, 02, p. 55.

The right auricle still has a single opening for the ducts of Cuvier and the inferior vena cava. They unite in the sinus venosus which empties between its two valves. The valves are united above, forming the septum spurium. In man the septum spurium and a part of the left valve are used in closing the foramen ovale; parts of the right valve persist as the Eustachian valve and valve of Thebesius.

Arteries.—The arterial system is represented in Plate III. The pulmonary artery leaves the heart by a single trunk, which divides into two arches of equal calibre, passing to the right and left aortae respectively. From the right arch a large stem, and from the left a slender one, unite and proceed to the lungs. Only the left arch and its stem contribute to the adult pulmonary artery as described by Bremer, 02.

The aorta also begins as a single trunk which bifurcates, forming right and left divisions. Beyond the bifurcation the ventral section of the aorta continues to the tongue and jaw as the external carotid artery. External and internal carotid arteries are united by the carotid arch. A very short section of ventral aorta represents the common carotid artery.

Proceeding caudad, the internal carotid artery passes into a slender,

degenerating portion of the dorsal aorta extending to the aortic arch, beyond which it becomes a large trunk which unites with a similar vessel from the opposite side to form the median dorsal aorta.

From the median aorta there arise pairs of intersegmental arteries. These formerly continued in single column along the right and left aortæ, but after the development of the vertebral anastomosis they lose their aortic origin. In the 12-mm. pig the seventh intersegmental artery is the first to arise from the right aorta. From it the vertebral and subclavian arteries originate.

The subsequent development of these vessels has been figured by Rathke, 43. The minute common carotid arteries become very long stems and fuse with one another below. Near their junction arises the right subclavian, of which the right aorta down to the 7th intersegmental artery forms a small section. Common carotids and right subclavian come from an innominate artery, not yet formed in the 12-mm. pig. The left subclavian leaves the aorta separately. Caudad from the 7th intersegmental artery, the right aorta is obliterated.

The arteries of the brain have nearly their adult arrangement. The vertebrales unite in a long basilar artery with many lateral branches. In front of the pons it forks, forming the posterior communicating arteries, which pass into the internal carotids. A branch extending between optic stalks and brain forms the anterior cerebral artery which by anastomosing with the opposite side will complete the circle of Willis. In front of the mid-brain are the posterior cerebral arteries.

The branches of the dorsal aorta are the regular pairs of intersegmental arteries, the scattered mesonephric arteries and, in the median line, the coeliac axis and the omphalo-mesenteric artery. The last named formerly encircled the intestine (Hochstetter, 02, p. 114), but the left half of the loop has disappeared, and it now passes to the yolk sac on the right of the intestine. The large umbilical branches and the caudal extension of the aorta complete the arterial system.

Veins.—The veins are shown chiefly in Plate IV. The anterior cardinal system arises as a plexus between the developing hemispheres. The small vessels unite in a median stem, the anlage of the superior longitudinal sinus. This soon divides into two branches which pass around to the under side of the brain, thus forecasting the lateral sinuses. It receives the ophthalmic vein, later subdivided into ophthalmic vein and cavernous sinus. Many branches from the mid-brain region unite with those just described and form the internal jugular vein. The 12-mm. pig agrees very closely with the 6-mm. guinea-pig studied by Salzer, 95,

The internal jugular vein passes between the Gasserian ganglion and

the brain; thence outside of the otocyst, and nerves seven to eleven inclusive, finally becoming internal to the twelfth nerve near the ganglion nodosum. Originally internal to all these nerves, it later becomes external to them all (Salzer).

A vein coming from the side of the tongue passes outside of the tenth nerve and enters the internal jugular at the level of the lateral thyroid pocket. The corresponding vein from the left side begins in the median line, along which it continues a short distance before turning to one side. In a 14-mm. pig the right vein is the median one. Anastomosis between the two is probable. These vessels, which to my knowledge have never been described, are found in 6-mm. pigs, running along the dorsal pericardial wall and proceeding from as far forward as the second arch. In a pig of 20 mm. the anterior cardinal veins have approached so near that the intervening space is less than the diameter of one of them. Where they are nearest these *transverse veins* are found, passing ventral to the arteries, dorsal to the cords of the thymus, and just caudad from the thyroid, with which they are closely connected. Here the very short left innominate vein is formed, uniting the anterior cardinals. That part of the right cardinal between the anastomosis and the heart subsequently disappears.

Near the duct of Cuvier the anterior cardinal vein is split for some distance, and the subclavian vein arises from its outer part. That section of the external jugular which is near the heart appears to be cut off from the internal jugular by the growth of slender mesenchymal partitions. After the disappearance of the posterior cardinal vein, the right duct of Cuvier becomes a continuation of the internal jugular vein, and with the migration of the subclavian vein, adult conditions ensue. Shortly before birth, these veins are arranged like a four-tined fork, the handle being the vena cava superior (duct of Cuvier and anterior cardinal), the inner tines being the internal jugulars (anterior cardinals), and the outer tines representing the external jugulars from which the subclavians pass off laterally.

The posterior cardinal veins arise near the tail and enter the Wolffian bodies where they become divided into sinusoids (Minot, oo, 1). They form distinct trunks as far cephalad as the cross anastomosis between the subcardinal veins. This section of the right posterior cardinal becomes a part of the inferior cava, the corresponding portion on the left forms a part of left spermatic vein. A prominent anterior trunk unites with two others and proceeds to the duct of Cuvier. This section of the posterior cardinal vein loses its connection with the heart on the right side, but retains it on the left, forming the hemiazygos

vein. The fusion of azygos and hemiazygos is described by Parker and Tozier, 98.

The subcardinal veins, Lewis, 02, are formed by an anastomosis of Wolffian sinusoids. The cephalad portion of the right subcardinal conveys the blood from posterior cardinal to the liver, and is a part of the inferior vena cava. That on the left disappears.

The umbilical veins, which in the cord of series 518 are fusing with one another, separate in the embryo and extend through the body wall to the liver. Here the left umbilical vein is broken into sinusoids except for a quite open passage to the portal vein. The larger right umbilical vein passes through the liver as the ductus venosus Arantii which joins with the portal vein and inferior vena cava to form the vena hepatica communis.

It remains to describe the portal vein, the hepatic relations of which appear in Plate IV. It is a continuation of the omphalo-mesenteric vein as shown in Plate III. That vein, beginning with branches from the yolk sac, crosses the abdominal cavity in a detached bit of mesentery and passes along the left side of the duodenum where it receives the superior mesenteric vein. The mesenteric vein begins in the intestinal loop, not in the yolk sac. Similar conditions have been found in the cat by Dexter, 02, from whose work it appears that the mesenteric vein is a new branch, and not one of the omphalo-mesenteric vessels, as has generally been supposed.

Prof. Minot has shown in his laboratory text-book that the thorough study of a few embryos is for students the shortest way to a comprehensive knowledge of embryology. As a means for correlating special embryological investigations, the complete description of single embryos is a promising but almost untried experiment.

NOTE.—It should be understood that though the results here presented have been drawn upon in part in the making of a text-book, the present study is complete in itself and independent of the text-book. This paper accepted for publication in No. 1, Vol. 2, was unavoidably delayed till now by circumstances beyond the control of the author.—EDITOR.

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EXPLANATION OF PLATES.

PLATE I.—Pig Embryo of 12.0 mm. Reconstruction from transverse sections, Series 5.

To show especially the cephalic nerves. *c. 1, c. 2, c. 3*, Cervical nerves. *Cbl*, Cerebellum. *com*, Ganglionic commissure. *Dien*, Diencephalon. *ex*, External branch of the spinal accessory nerve. *F*, Froriep's ganglion. *G. 5*, Gasserian ganglion. *H*, Cerebral hemisphere. *j*, Jugular ganglion. *L*, Lens. *M. b*, Mid-brain. *Mdb.*, Mandibular process. *Md. ob*, Medulla oblongata. *Max*, Maxillary process. *n*, Ganglion nodosum. *Na*, Nasal pit. *Op*, Optic cup. *Ot*, Otocyst. *Rec. l*, Recurrent laryngeal nerve. *Ven. IV*, Roof of fourth ventricle. *3*, Oculomotor nerve. *4*, Trochlear nerve. *5op*, Branches of the ophthalmic division of the trigeminal nerve. *6*, Abducens nerve. *7*, Geniculate ganglion of the facial nerve. *8*, Vestibular ganglion. *9*, Petrosal ganglion. *10*, Vagus nerve. *11*, Spinal accessory nerve. *12*, Hypoglossal nerve. ——— x 20 diams.

PLATE II.—Pig Embryo of 12.0 mm. Reconstruction from transverse sections, Series 5.

The embryo has been drawn as if transparent to show the form of its pharynx, and the relations of the pharyngeal gill pouches to the grooves on the outer surface of the embryo. *car*, Carotid gland. *Cbl*, Cerebellum. *CS*, Cervical sinus. *Dien*, Diencephalon. *H*, Cerebral hemisphere. *Hy*, Hypophysis. *Inf*, Infundibular gland. *Lat. Th*, Lateral thyroid. *l. gr*, Lachrymal groove. *m*, Maxillary process. *M. b*, Mid-brain. *Mdb*, Mandibular process. *Md. ob*, Medulla oblongata. *na. ex*, External naris. *ni*, Internal naris, closed by an epithelial plate. *Oe*, Oesophagus. *Op*, Eye. *Ot*, Otocyst. *Sp. c*, Spinal cord. *Th*, Median thyroid gland. *thym*, Thymus. *Tra*, Trachea. *1, 2, 3, 4*, Entodermal pouches of the corresponding gill clefts. ———x 20 diams.

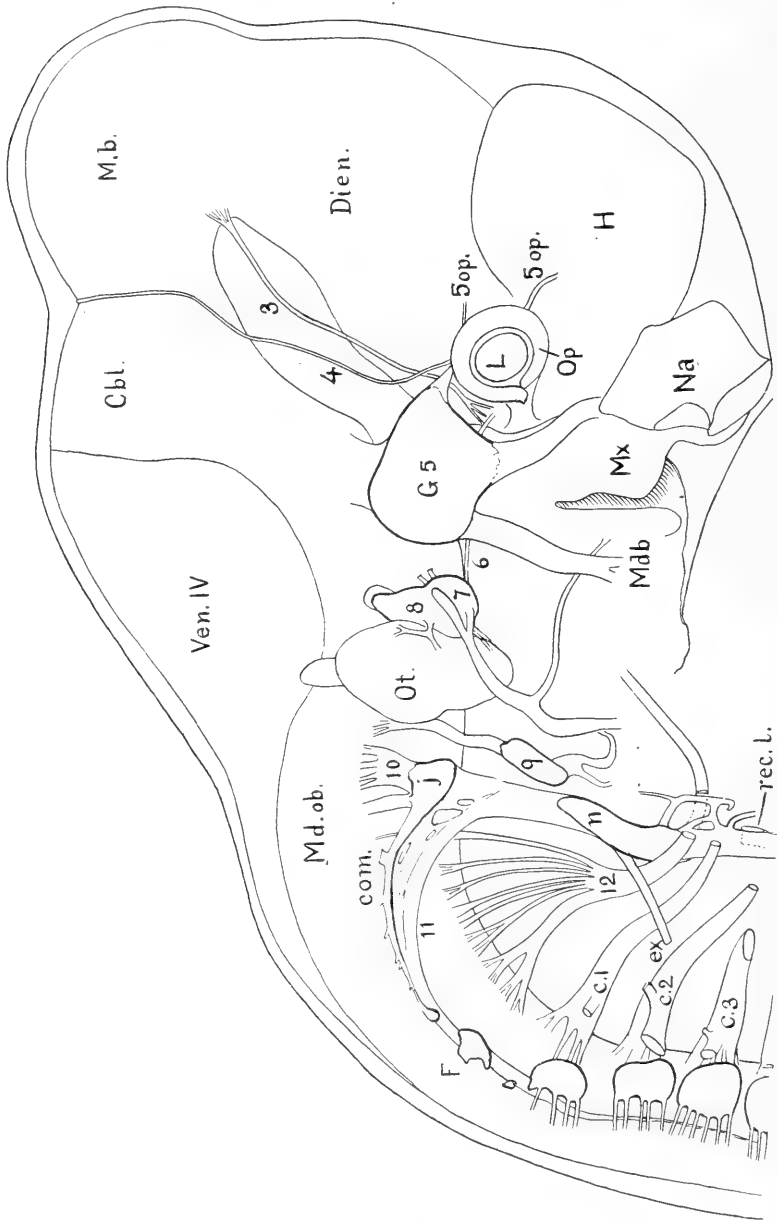
PLATE III.—Pig Embryo of 12.0 mm. Reconstruction from transverse sections, Series 5 and 518.

For the most part the organs represented are in or near the median plane. The drawing illustrates especially the alimentary tract, the arterial system, and the heart. *A. bas*, Basilar artery. *A. cau*, Caudal artery. *All*, Allantois. *Ao*, Median dorsal aorta. *Ao. d, Ao. D*, Right dorsal aorta. *A. s*, Subclavian artery. *Au*, Left auricle. *A. um*, Umbilical artery. *A. vi*, Vitelline artery (Omphalo-mesenteric). *c*, Coeliac axis. *car. e*, External carotid artery. *car. i*, Internal carotid artery. *Cbl*, Cerebellum. *cl*, Cloaca. *cl. mem*, Cloacal membrane. *d*, Left duct of Cuvier. *Dien*, Diencephalon. *D. V*, Ductus venosus Arantii. *ep*, Epithelial plug in the rectum. *Epgl*, Epiglottis. *f*, interventricular foramen opening into the space a, b, c, of Pl. 4. *Fm*, Foramen of Monro. *f. o*, Foramen ovale. *g*, Gall-bladder. *In*, Entodermal wall of the intestine. *is*, An intersegmental artery. *Ki*, Renal pelvis. *Lar*, Larynx. *Li*, Liver. *Lu*, Lung. *M. b*, Mid-brain. *Md. ob*, Medulla oblongata. *N*, A spinal nerve. *Neu*, Neuromeres. *Oe*, Oesophagus. *op*, Optic stalk. *P. A*, Pulmonary artery. *Pan*, Dorsal anlage of the pancreas, behind the duct

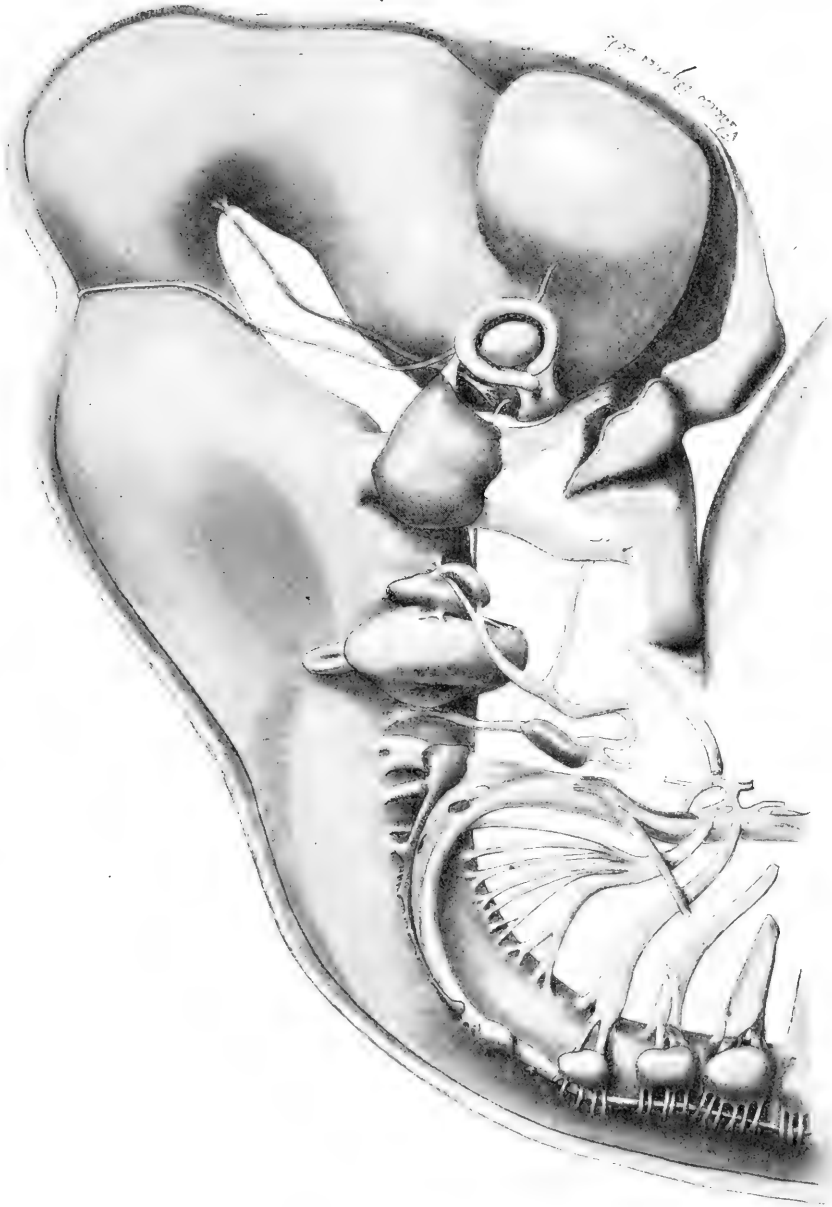
of which is the ventral anlarge. *P. c.*, Peri-cardial cavity, *P. V.*, Pulmonary vein. *Sp. c.*, Spinal cord. *St.*, Stomach. *t.*, Posterior portion of the tongue. *T. i.*, Tuberculum impar. *Tra.*, Trachea. *Um. d.*, Right umbilical vein. *Ven.*, Left ventricle. *V. mes.*, Superior mesenteric vein. *V. port.*, Portal vein. *V. vi.*, Vitelline vein (Omphalo-mesenteric. *W. D.*, Wolffian duct. *x.*, Anastomosis between the right and left cardinal systems. *Yk.*, Yolk sac. *Yk. s.*, Yolk stalk. —x 13.5 diams.

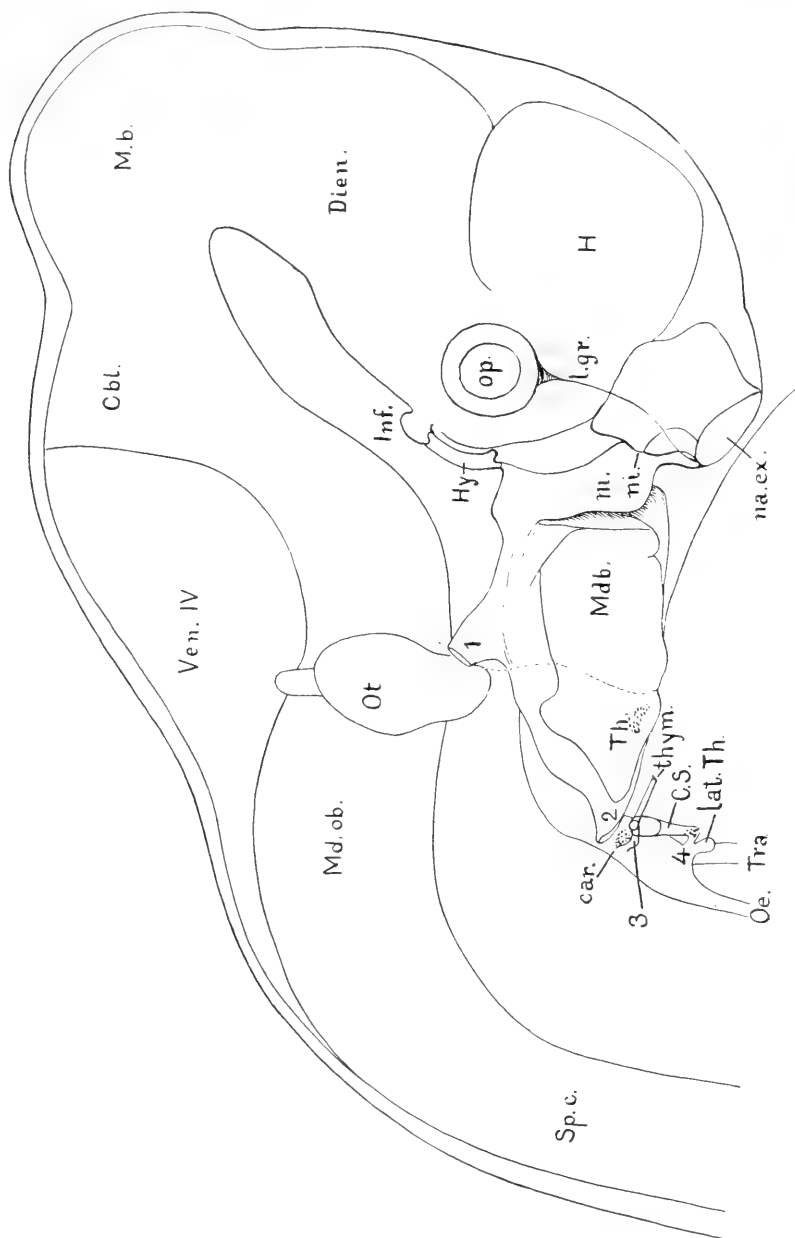
PLATE IV.—Pig Embryo of 12.0 mm. Reconstruction from transverse sections, Series 5.

The section is on the right of the median plane, and shows chiefly the heart and venous system. *A.*, Umbilical artery. *a.*, Aortic septum. *All.*, Allantois. *Ao.*, Aorta. *Au.*, Right auricle. *b.*, Bundle of trabeculae. *c.*, wall between bulbs arteriosus and auricle. *card'*, *card''*, Superior and inferior sections of the posterior cardinal vein. *cl. 1.*, *cl. 2.*, *cl. 3.*, *cl. 4.*, Entodermal pouches and their pharyngeal openings of the corresponding gill clefts. *c. om.*, Dotted outline of the omental or lesser peritoneal cavity. *d.*, Left duct of Cuvier. *D. C.*, Right duct of Cuvier. *D. V.*, Ductus venosus Arantii. *F. W.*, Foramen of Winslow. *F. pp.*, Pleuro-peritoneal foramen. *gen.*, Genital tubercle. *G. R.*, Genital Ridge. *Jug'*, *Jug''*, Jugular or anterior cardinal vein. *Li.*, Liver. *l. s.*, anlage of the lateral sinus. *mx.*, Transverse vein. *P.*, Pulmonary artery. *p. c.*, Pericardial cavity. *Pl.*, Dotted outline of pleural cavity. *Rec.*, Rectum. *Sc.*, Subcardinal vein. *Scl.*, Subclavian vein. *sls.*, Anlage of the superior longitudinal sinus. *Ur.*, Ureter. *Um. d.*, Right umbilical vein. *v.*, Valves of the sinus venosus. *Ven.*, Right ventricle. *V. H. C.*, Vena hepatica communis. *v. op.*, Ophthalmic vein. *V. P.*, Portal vein. *W. b.*, Wolffian body. *W. D.*, Wolffian duct. *x.*, Anastomosis between the right and left cardinal systems. —x 13.5 diams.

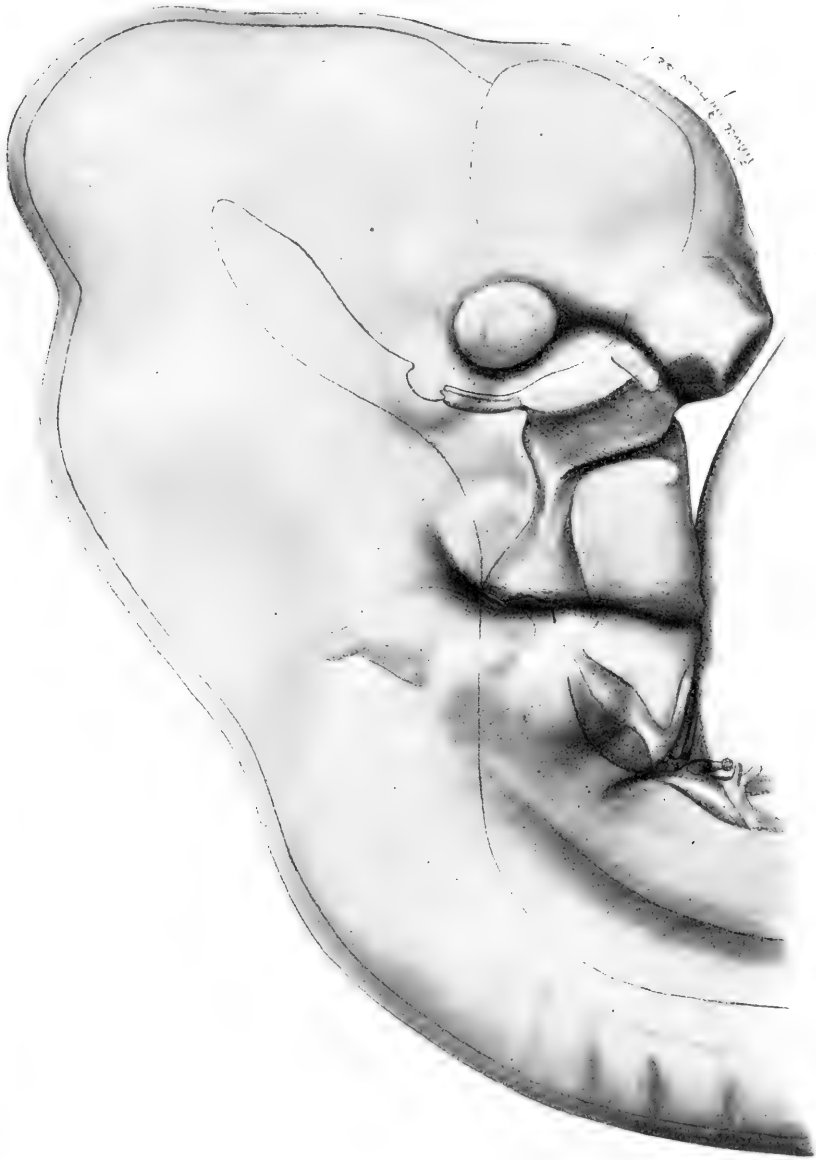


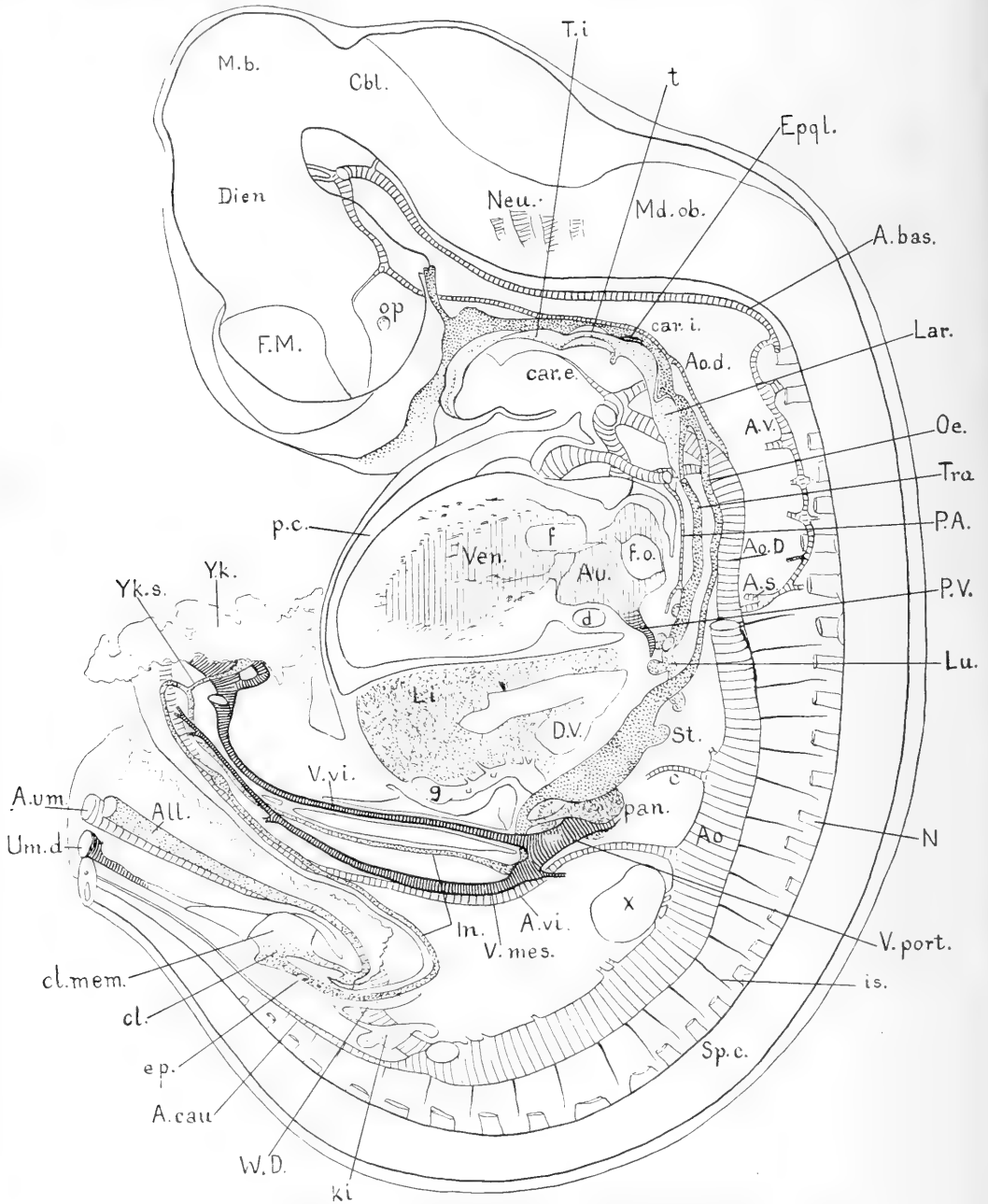
ANATOMY OF HEAD AND NECK--ESPECIALLY THE CEPHALIC NERVES
 (Refer to explanation of plates for details)



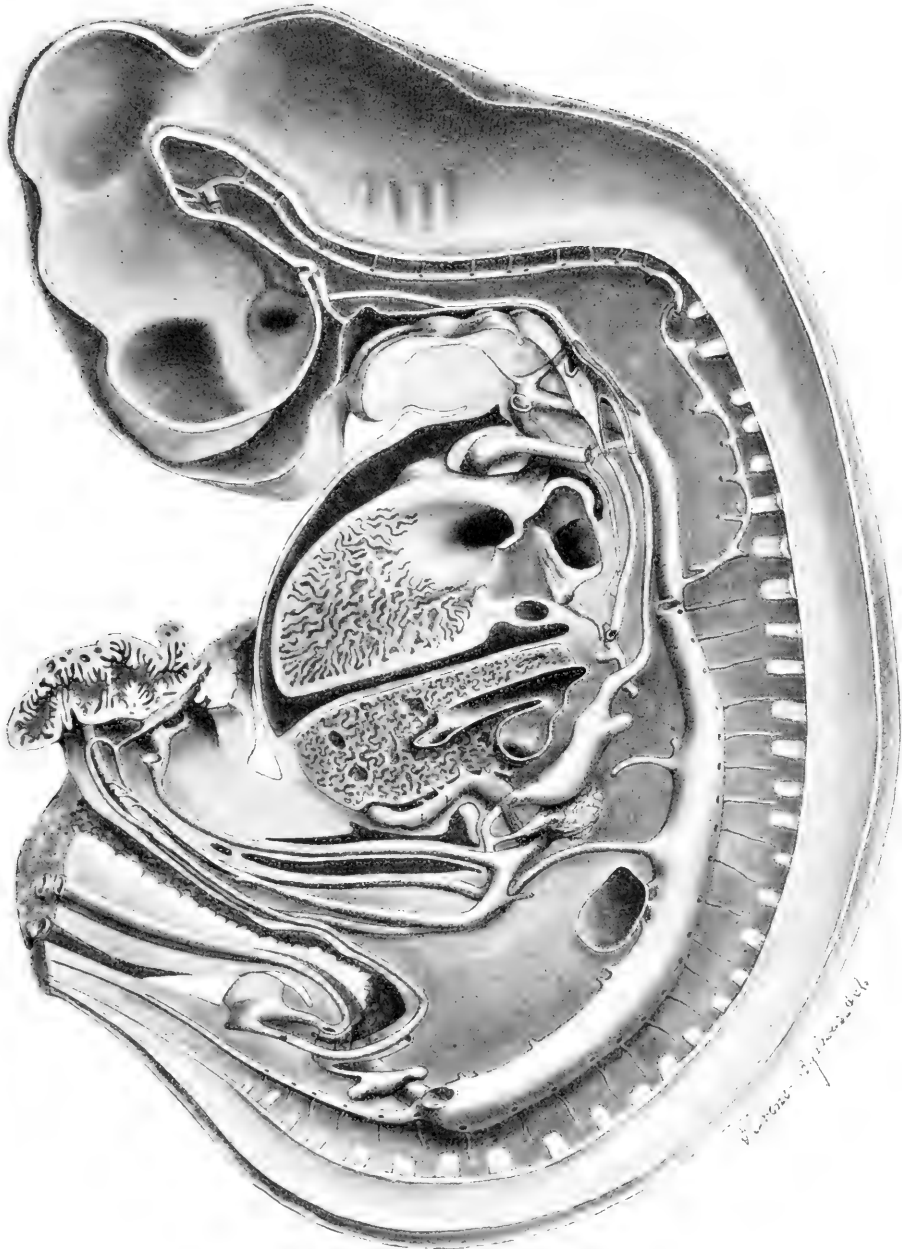


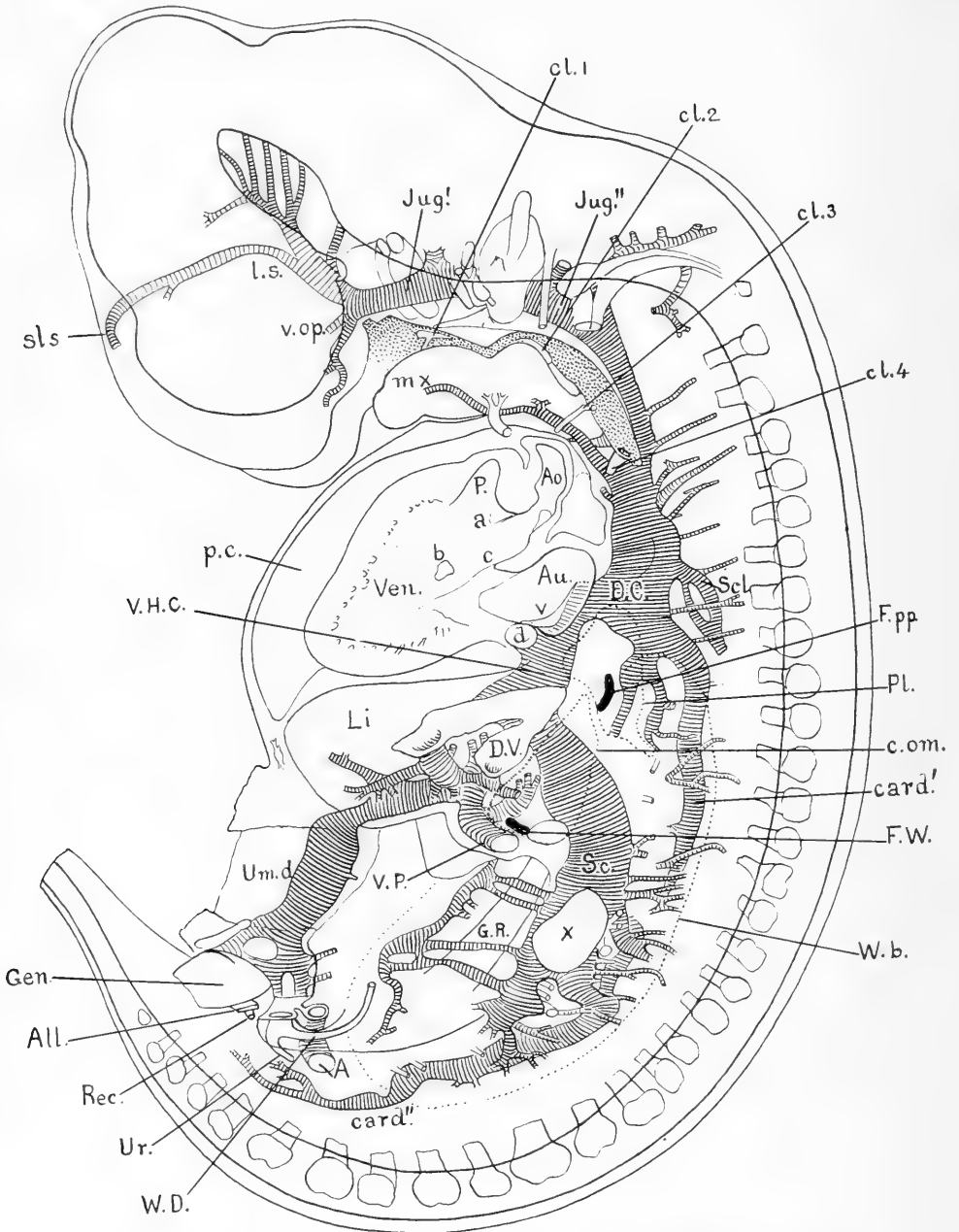
ANATOMY OF HEAD AND NECK--ESPECIALLY THE PHARYNX
 (Refer to explanation of plates for details)



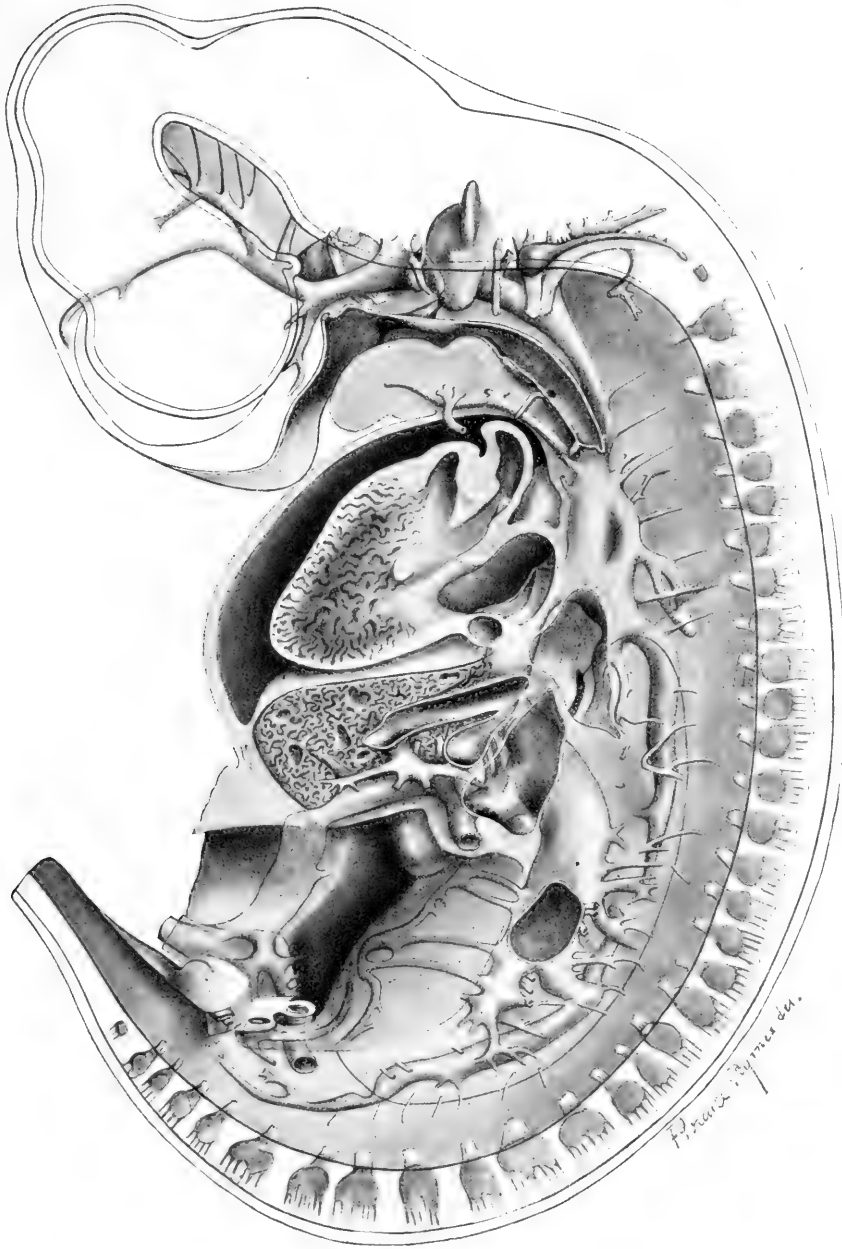


MEDIAN ORGANS--ESPECIALLY ALIMENTARY TRACT, ARTERIAL SYSTEM, AND HEART
(Refer to explanation of plates for details)





TO THE RIGHT OF MEDIAN PLANE--ESPECIALLY VENOUS SYSTEM AND HEART
(Refer to explanation of plates for details)





THE EFFECT OF FATIGUE ON THE NUCLEI OF VOLUNTARY MUSCLE CELLS.

BY

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WITH 4 TEXT FIGURES.

While a great deal of work has been done concerning the effect of fatigue on the cells of the nervous system, I can find nothing in the literature on similar changes in the nuclei of muscle cells. In an article by Scheffer¹ the subject of the histological effect of muscle fatigue is taken up from a different standpoint.

Below are given the results of a number of experiments upon embryonic and adult muscular tissue. The muscle in the tail of the tadpole was used for the first series of experiments and the gastrocnemius of the frog for the second. The work was undertaken at the suggestion of Dr. C. R. Bardeen.

A. TAIL MUSCLES OF TADPOLE.—Various methods for fatiguing the swimming muscles of the tadpole were used, that of keeping the animal constantly irritated by means of a long haired brush revolving within the dish, proving the best. A shaft was suspended perpendicularly in the center of the dish its upper end bearing a wheel connected by a belt to a water wheel. At the lower end of the shaft an arm was attached which extended out from the center to the edge of the glass dish a short distance above the surface of the water. To this arm the brush was attached along its lower border, the hairs of the brush extending to the bottom of the dish and stirring up thoroughly the water and animals when the apparatus was set in motion and the arm revolved about the central shaft. After the animals became too fatigued to swim against the current produced by the apparatus, the hairs rubbing over them would stimulate the tadpoles to further movements. A stage was finally reached when no further movements could be obtained even upon violent stimulation such as pinching with forceps or pricking with a needle. In

¹Scheffer, W., Ueber eine mikroskopische Erscheinung am ermüdeten Muskel. *Münchener Med. Woch.*, 17 Juni, 1902.

all cases control animals were selected from the same lot of tadpoles, attention being paid to the size and similar conditions.

Fatigued and control tadpoles were dropped into the same dish of killing fluid, carried through all subsequent steps together, imbedded parallel to one another, and cut with the same stroke of the section knife. It would seem from this that the differences between the fatigued and the control cells must be due to the fatiguing process.

Experiment 1.—Tadpoles stimulated for 72 hours in the water wheel apparatus and then teased with a needle until motionless. Killed with warmed corrosive-acetic fixative.

Experiment 2.—Tadpoles stimulated 3 hours by rapidly moving wheel and teased until motionless. The time required to tease this set of animals to a motionless condition was much less than the time required for set number one. Killed in picro-acetic fixative.

Experiment 3.—Tadpoles stimulated for 24 hours and teased as above. Time required to tease to motionless condition longer than for set two. Killed in picro-acetic fluid.

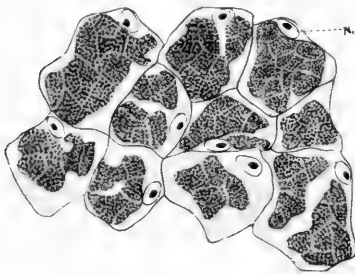


FIG. 1.

FIG. 1. Resting muscle cells. Tail of tadpole. $\frac{1}{12}$ oil immers. Carm. Zeiss. N. = Nucleus.



FIG. 2.

FIG. 2. Fatigued muscle cells. Tail of tadpole. $\frac{1}{2}$ oil immers. Carm. Zeiss. N. = Nucleus.

In staining the tissue a variety of dyes were used, methylene blue and eosin giving the best results, the blue forming a definite contrast to the red.

In the sections of fatigued muscle the nuclei appear shrunken and crenated to a greater or less degree, where the normal nucleus (Fig. 1) shows a regular outline and is better defined. The fatigued nuclei (Fig. 2) appear more lightly staining and less granular than the control. Further the sections of fatigued muscle take the blue stain more lightly as regards the whole section than does the resting muscle.

Tadpoles kept in the fatiguing apparatus for the longer periods of time became so accustomed to the stimulation and the strange surroundings, that they required a longer teasing with the needle to bring to a condition where they were unable to respond to stimuli. Stimulation for as short a period as three hours produced changes as marked, to all appearances, as those due to the longer periods of stimulation.

B. GASTROCNEMIUS OF FROG.—The sciatic nerve of one side was carefully dissected out and severed through as small an aperture as possible.



FIG. 3. Normal resting muscle. Gastrocnemius of frog. $\frac{1}{2}$ oil immers. Carm. Zeiss.

This was done well above the knee to exclude any effect of air contact upon the muscle. The nerve was stimulated with an induction current too weak to produce complete tetanus. The stimulation was continued until no further response was obtained, then the tissue in both legs was killed by the injection of picro-acetic acid through the abdominal aorta, thus insuring identical conditions in this respect for both muscles. After fixation the skin about the muscles was ruptured for the first time and two muscles, stimulated and control, carried together through the same jars of reagents as described above.

Where the normal nuclei are regular in outline and show a marked granular appearance (Fig. 3) those of the fatigued muscle are shrunken, irregular in outline (Fig. 4) and more homogeneous. The granules or the nuclei are finer and stain less intensely than those of the resting muscle nuclei.



FIG. 4. Stimulated muscle. Gastrocnemius of frog from $\frac{1}{2}$ oil immers. Carm. Zeiss.

In the figures typical sections are represented, many of the sections showing even more marked differences, nuclei in some cases being shrunken to half their original size.

Experiments were performed attempting to demonstrate the effect of fatigue on heart muscle nuclei. Kittens were used and both vagi severed in the animal experimented upon to allow an increased heart rate. A control animal of approximately the same size was used in each case. Although a greatly increased heart rate was obtained and the animals kept alive for periods up to ten hours, no histological evidences

of fatigue could be demonstrated in the nuclei. The result is not a surprising one when we consider the power this tissue has of recovery from katabolic changes.

SUMMARY.

The following changes are demonstrable in the nuclei of muscle cells as a result of activity:

1. The nuclei are shrunken and present a very irregular outline. This shrinkage and distortion increases with the length of the stimuli up to a certain point when no further visible change is shown, no matter how long and severe the fatiguing process.

2. The nuclei of fatigued muscle cells are less densely granular and take stains less deeply than the nuclei of resting cells.

THE GROWTH AND HISTOGENESIS OF THE CEREBRO-SPINAL NERVES IN MAMMALS.

BY

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WITH 15 TEXT FIGURES.

In the following article are given the results of a study of the histogenesis and the general mode of growth of the cerebro-spinal nerves in mammals. Owing to the ease with which the material could be obtained pig-embryos have been those chiefly used, but in addition embryos of man, guinea-pigs and mice have been studied. In all of these animals the development of the nerves seems to be essentially similar.¹

I. OUTGROWTH OF THE CEREBRO-SPINAL NERVES.

In the mammals the development of the peripheral nerves, with the exception of the optic and olfactory, begins by an outgrowth of naked processes from cells lying in the motor root-zone of the central nervous system and in the sensory ganglia. The naked processes belonging to a given cerebro-spinal nerve are usually grouped in bundles which extend out separately into the mesenchyme surrounding the central nervous system but which soon are collected into a common nerve-trunk. This method of development has been clearly described by His in the human embryo, and can readily be verified in any of the mammals more commonly studied. If a pig embryo 8 mm. long, for instance, be fixed in Zenker's fluid and hardened in alcohol, the thoracic nerves may readily be dissected out. At this period bundles of fibres from the motor-root zone and from the spinal ganglion of each thoracic segment have become grouped into a spinal nerve which extends towards but does not enter the body-wall. One of these nerves, with its sensory-root and ganglion, motor-root, and main-trunk intact, may be isolated, together with a slight amount of the surrounding mesenchyme, stained in Dela-

¹The literature on the general subject of the development of the peripheral nerves in vertebrates has been recently reviewed by Harrison, Dohrn, Fürbringer and Nussbaum, each from a different standpoint.

field's hæmatoxylin, followed by Congo-red, dehydrated, cleared, and then mounted in balsam. Clearer pictures may thus be obtained in early embryos than by the osmic-acid, picro-carminé method used by Vignal.

In a specimen thus prepared (Fig. 1), the bundles of nerve-fibres may be seen surrounded by branched, anastomosing mesenchyme-cells. Here and there an elongated cell may be seen closely applied to a bundle of fibres, but special sheath-cells of this kind are infrequent. In places single fibres or small bundles consisting of two or three fibres entirely free from sheath-cells may be followed for nearly half a millimeter. After teasing the tissue of the spinal ganglion or that from the ventral

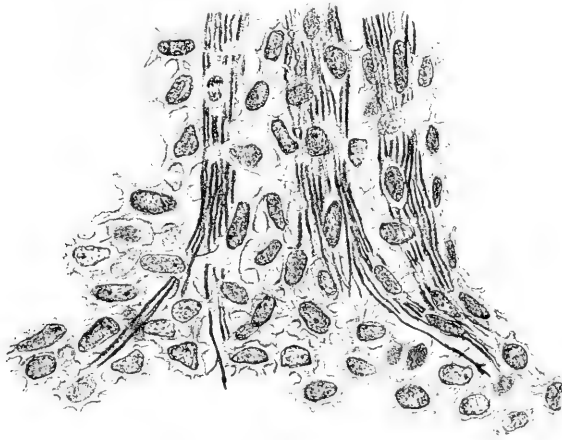


FIG. 1. Portion of the tip of an intercostal nerve isolated from a pig-embryo 8 mm. long. 720 diam.

root-zone of the spinal cord, cells may be seen which give rise directly to the nerve-fibres, but no cells of this kind are to be found among the cells accompanying the bundles of nerve-fibres constituting the nerve-trunk.

As the nerve grows forward new nerve-fibres grow in rapidly from behind, and the nerve-fibres as they grow forward give rise to groups of fine fibrils.

The cells found scattered among the nerve-fibres and nerve-fibrils multiply actively. As the new cells are formed certain of them give rise to a skeletal framework for the support of the nerve-fibrils. The periphery of the nerve, also, at an early period becomes covered with a fairly complete membrane formed of anastomosing cells. The cells within the nerve give rise to branched processes which anastomose with

one another and with the peripheral layer of cells. In the meshes of this framework the bundles of nerve-fibrils run.

In Fig. 2 is shown the extremity of the ventral division of a spinal nerve of a pig 10 mm. long. This nerve was isolated and stained by the method described above. The advancing tip of the nerve is com-

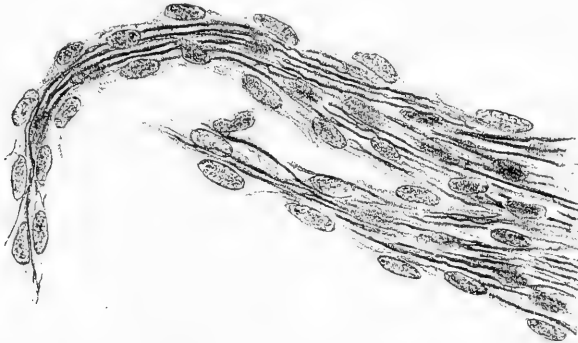


FIG. 2. Nerve-tip isolated from an intercostal nerve of a pig-embryo 10 mm. long. 720 diam.

posed of a few fibrils ensheathed by two cells. Behind this the nerve-fibrils and the sheath-cells rapidly increase in number. A short distance behind the tip the nerve has been partially split during the process of isolation. The curving of the tip is due to mounting.

The various constituent elements of the nerve may be isolated by teasing. The cells applied to the more compact bundles of fibrils present the appearance shown in Fig. 3, *a*. Fig. 3, *b*, shows a cell in the process of division; Fig. 3, *c*, two cells with a nerve-fibre passing between them; and Fig. 3, *d*, two fibres and two cells from the extreme tip of a growing nerve. With care it is possible to isolate nerve-fibres or bundles of fibrils free from any cellular covering for considerable distances. No nerve-fibres can be seen arising from cells within the nerves. The cells are, however, sometimes so closely applied to small groups of fibrils as to give rise to the appearance of protoplasmic continuity between sheath-cells and nerve-fibrils. This is especially apt to be the case in longitudinal sections.



FIG. 3. Elements isolated from the ventral trunk of a spinal nerve of a pig-embryo 11 mm. long. 720 diam.

Fig. 4 shows a cross-section of the median dorsal branch of a thoracic nerve of an embryo 18 mm. long. This nerve is similar in struc-

ture to the main ventral branch of an embryo of 10 mm. About the periphery of the nerve cells may be seen which give rise by flattened anastomosing lateral processes to an inclosing membrane. Within the body of the nerve many cells may be seen giving rise to processes which anastomose with one another and with processes arising from the marginal cells. On staining in hæmatoxylin and then in the Van Gieson mixture the processes of the marginal cells and of the internal cells take a purplish tint, while the cross-sections of the nerve-fibrils appear orange in color. A slight bluish tint, often taken by the areas intervening between the nerve-fibrils and the sheath-cells, indicates that some substance is present there. This corresponds to the homogeneous material which Vignal has described as constituting the stroma of the bundles of nerve-fibres.

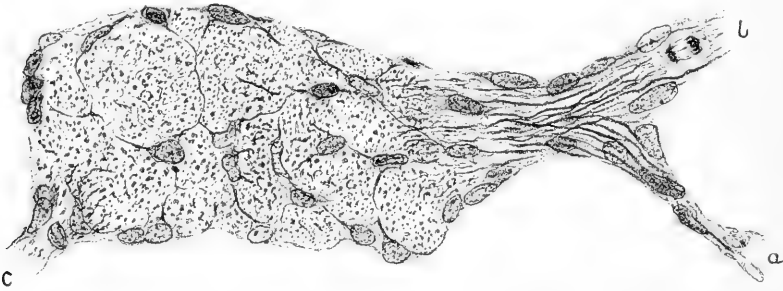


FIG. 4 Cross-section of the median ramus of the dorsal division of a thoracic nerve of a pig-embryo 18 mm. long. *a, b, c* branches arising from the main trunk. 720 diam.

The processes taking place after the formation of the primary embryonic nerves may be conveniently divided into two groups, those underlying the distribution of nerves during development and those underlying the histogenetic changes taking place within the growing nerves. We shall now consider each of these groups in turn.

II. NERVE DISTRIBUTION DURING DEVELOPMENT.

After the formation of the primary trunks of the cerebro-spinal nerves growth towards the areas which they are to supply becomes very active. In case of the sixth cranial nerve in man the nerve-trunk extends directly to the anlage of a single peripheral organ. In most instances, however, the conditions of nerve growth are far more complex. The primary nerve trunks give rise to primary branches each of which is destined for a more or less complex area of the body. Thus the fifth cranial nerve gives rise to its three chief branches, the cervical and

lumbo-sacral nerves give rise to the main branches destined for the limb-plexuses, and the thoracic nerves give rise to dorsal and ventral divisions and to branches for the sympathetic system. Frequently the primary branches extending outward from the main nerve-trunk of a given cerebral or spinal nerve become combined with certain branches derived from another nerve, and thus give rise to a common peripheral trunk containing fibres derived from two or more sources. Thus in man, a branch from the tenth joins the trunk of the ninth cranial nerve and the fibre-bundles of the eleventh cranial nerve, themselves derived from a series of anlagen, become to a greater or less extent bound up with the main nerve-trunk derived from the anlage of the tenth cranial nerve. In the region of the limbs, by the processes of anastomosis and of plexus-formation, fibre-bundles immediately connected with the large areas of the spinal cord become united into a few nerve-trunks which can grow forward with a minimum expenditure of energy towards a region of ultimate distribution.

The forces which direct the early embryonic nerves toward the anlagen for which they are destined are at present shrouded in mystery. There is much, however, which indicates that to a certain extent the nerves take a path of least resistance offered by the surrounding tissues and that they are guided to a considerable extent by the more fixed structures lying in the line of their general growth. The nature of these paths of least resistance can best be studied, however, in connection with the development of specific nerves. Thus the intercostal nerves are, to a considerable extent, guided by the costal processes of the embryonic vertebral column and by the myotomes. There is certainly the possibility, however, that given regions may exert a specific directive attraction on the nerves which are destined to supply them.

As a result of the primary nerve distribution certain nerves are directed toward various cutaneous areas and certain nerves are directed into the anlagen of the muscular apparatus. It is convenient to take up separately the distribution of these two sets of nerves.

The distribution of the cutaneous nerves may be followed with comparative ease during the early stages of embryonic development. Up to the period when a human or a pig-embryo reaches a length of two centimeters the cutaneous nerves may be followed readily in serial sections of embryos hardened in Zenker's fluid and stained in iron hæmatoxylin followed by Congo-red or in other intense stains. The relations of the nerves may best be understood by making reconstructions in wax or projection drawings. Thus in a previous article in this Journal, Lewis and I have pictured the peripheral cutaneous nerves of the body-wall and

limbs in several early human embryos. Grosser and Fröhlich have made a valuable special study of the development of the thoraco-abdominal cutaneous nerves in man and have compared the conditions found in early embryos with those found in the adult.

After pig-embryos have reached a length of from two to three centimeters it is possible to get very instructive pictures by means of impregnation with gold-chloride. My best preparations have been obtained by placing a portion of the embryo first in lemon juice for ten or fifteen minutes, then in a one per cent solution of gold-chloride for an hour, finally reducing in a twenty per cent solution of formic acid in the dark. Separate layers of tissue may be isolated and spread out in glycerine, or the specimen may be embedded and cut. By these methods the various stages in the formation of the peripheral plexuses may be most readily followed.

From the primary cutaneous rami extending toward the skin from the main nerve-trunks in the deeper parts branches are given off which run in various directions parallel with the epidermis but some distance below it. From these branches the main subcutaneous nerve-plexuses directly arise. The formation of these subcutaneous plexuses seems to be due to the tendency of branches sent by two nerves into a common region to be attracted toward the same area and to fuse into a common trunk on reaching it.² In Fig. 5 the larger, darker nerves here represented as the most superficial, form a portion of the main subcutaneous plexus arising from branches of the lateral rami (Tr.) of the dorsal divisions of two thoracic nerves of a pig embryo 4 cm long. While this plexus is being formed branches are given off from the nerves forming it. These extend towards the epidermis, just below which another plexus with finer meshes arises. In Fig. 5 this second plexus is shown in process of formation. The nerves entering into this latter plexus stain much lighter than the main nerve-trunks. As development proceeds from the stage illustrated in Fig. 5, more and more branches are given off from the plexuses there shown, finer plexuses are formed, and ultimately nerve-fibrils are distributed to the various end-organs and structures characteristic of the skin and subcutaneous tissue. The details of these latter processes I have not attempted to follow.

² Nerves growing into a given region from two or more directions do not always thus anastomose to form plexuses. Thus Mertens has shown that although the lateral cutaneous branches of the fourth and fifth intercostal nerves supply overlapping areas, anastomoses between the nerve branches revealed by dissection are infrequent. A bundle of fibres constituting a nerve may cross over or through another nerve without real anastomosis of the two trunks.

A study of the development of the peripheral cutaneous nerves leads to the belief that some sort of stimulus to growth is exerted upon the nerves by areas lacking innervation. In Fig. 5 numerous areas may be seen into which nerve branches proceed from several directions.

Kühn's interesting experiments on the regeneration of nerves in the dorsal cutaneous region of the frog have an important bearing on the mode of forward growth of nerves. When an area of the skin was deprived of its nerve supply by cutting two or three main nerve-trunks distributing branches to it, he found that from nerves in the neighboring regions new nerve-fibres extended into the deprived area. In this inner-



FIG. 5. A portion of the nerve-plexus formed by the lateral cutaneous branches of the dorsal divisions of two thoracic nerves of a pig embryo 4 cm. long. Tr. Main trunk of each nerve. 38 diam.

vation new nerve-paths and peripheral plexuses not corresponding with the old were often formed, or the growth of the new fibres showed no regular order. This last was especially true of nerve-fibres arising from the central ends of the cut nerves.

During embryonic development nerve-fibres derived from very different sources and destined for a different ultimate distribution often take common paths for a part of their course. Good examples of this may be seen in the distribution of the vaso-motor nerves and in the relations entered into between the trigeminal nerve, the facial nerve and the cervical nerves. Popowsky has called attention to the development of anastomoses between the fifth and seventh cranial nerves.

A given cutaneous area with the nerves distributed to it may during

development be shifted extensively with respect to neighboring parts. Grosser and Fröhlich have called attention to this phenomenon in the dorsal and thoraco-abdominal regions of man.

Having thus briefly considered the mode of distribution of cutaneous nerves during development, we may take up the development of the nerves distributed to the voluntary motor-apparatus. In order that a description of this process may be clear, it is necessary to consider briefly the general features of the development of the musculature.

The muscles are differentiated from a mass of pre-muscle tissue which is variously derived in different parts of the body in the mammals. Thus the dorsal and thoraco-abdominal musculature arises from tissue derived from the myotomes, and the musculature of the leg from the mesenchyme of the limb-bud.

At the time when differentiation begins in this pre-muscle tissue two distinct groups of cells may be distinguished, myoblasts and embryonic connective-tissue cells. The former in part multiply rapidly by indirect division and in part become elongated into spindle-shaped muscle-fibres.

These muscle-fibres are usually grouped into bundles, new fibres being constantly added at the periphery of the bundles by elongation of myoblasts. Meanwhile, the skeletal tissue of the muscle becomes differentiated from the connective-tissue cells. The latter grow into and break up the primitive bundles of muscle fibres into smaller bundles. Each muscle fibre finally becomes surrounded by a certain amount of connective tissue, but usually groups of fibres become surrounded by a denser connective tissue than that surrounding any individual fibre.

In the simplest muscles the muscle fibres are parallel, of about equal length, and are attached at each end to a tendon running transverse to their course. In mammals these conditions may be seen in an anterior segment of the *rectus abdominis* muscle of a small rodent.

In most muscles the arrangement of the bundles of muscle fibres is far more complex. They run in various directions, interdigitate, and are so complexly combined that it is difficult to get an accurate idea of the internal architecture. Very often each muscle fibre is innervated about midway between its extremities. In the segment of the rectus mentioned above, gold-chloride specimens show a band of motor-endings running across the muscle midway between the two transverse tendons which limit it. In Fig. 6 there is represented a portion of the nerve-plexus distributed to the *M. transversus abdominis* of a guinea-pig embryo 8½ cm. long. A few bundles of muscle-fibres are shown in out-

line. The centre of these bundles may be seen to correspond closely to an area of distribution of motor-endings, here represented as black dots.³

The most important problem connected with the development of the nerves belonging to the muscles is the mode of distribution of the nerves within the muscle. Mainly on theoretical grounds Fürbringer, Eisler and others have supported the view that the nerve and muscle cells are

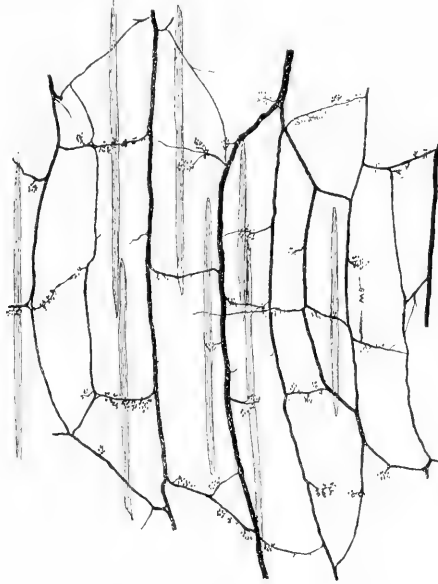


FIG. 6. A portion of the nerve-plexus distributed to the transversalis musculature of a guinea-pig embryo $8\frac{1}{2}$ cm. long. 11 diam.

closely associated from a period of development long preceding the differentiation of the permanent muscles. No good histological evidence has been brought forward in support of this view. On the contrary, the independent development of the nerves belonging to the muscles may be followed step by step from the primary embryonic nerves up to the union

³Mays (1884), in his splendid contribution to the subject of the intramuscular distribution of nerves, has called attention to the fact that muscle-fibres are often innervated approximately midway between their extremities. Bardeleben and Frohse have made valuable studies of the nerve distribution in human muscles, but the methods used did not enable them to expose the full richness of the intramuscular nerve distribution. Frohse was able to trace nerves to muscle bundles a millimeter in diameter. Nussbaum has lately given a good review of the more recent work on the relation of nerves to muscles-

of nerve and muscle fibres at a comparatively late period of muscle development.⁴

As the mass of premuscle tissue in a given region becomes differentiated into the individual muscles characteristic of that region, paths for nerve growth are offered in the loose, vascular mesenchyme which separates the various muscles. The nerves extend out rapidly toward the various muscles and the various parts of each muscle which they are to supply. When the area to be supplied by a given nerve or set of nerves is considerable, the nerves, as they are spread out, may branch and give rise to coarse plexuses. Fig. 7 shows such a plexus in process of formation in the area between the internal oblique and the transversalis muscles of a pig-embryo 4 cm. long.



FIG. 7. A portion of the nerve-plexus formed on the surface of the *transversus abdominis* muscle of a pig-embryo 4 cm. long. 11 diam.

From the intermuscular nerves branches are given off which enter the muscle substance and make

their way, rapidly ramifying, toward the middle of each bundle of muscle fibres constituting the muscle (see Fig. 8). In simple muscles, like the segment of the rectus above mentioned, there is little or no plexus formation during the period of intramuscular distribution. But in complex muscles where the bundles of muscle fibres interdigitate, plexus formation is active during this period. As in the skin, so here, this plexus formation seems to be due to an attraction which causes branches to grow from several sources toward a given area.

In the course of development of the muscles new fibres may be differentiated in one or more directions, and toward these the intrinsic nerves of the muscle extend to be distributed. This may be beautifully fol-

⁴ In many of the lower vertebrates there is good evidence that the motor roots of the spinal nerves become associated at an early period with the musculature of the myotomes. But in these vertebrates the myotome musculature is functional. In mammalian embryos, on the other hand, I have been able to find no good evidence of union of motor-root fibres with the myotome cells. Branches from the spinal nerves do not begin to enter the dorsal and the thoraco-abdominal musculature until the latter begins to be differentiated from the myotomes. This I have previously shown in describing the development of the thoraco-abdominal musculature of the pig. The myotomes are probably no more functional in mammals than are the branchial clefts.

lowed in muscles like the *latissimus dorsi*. Nussbaum has shown that the distribution of nerves belonging to a muscle indicates the direction of development of that muscle. Popowsky's interesting work on the development of the facial nerve illustrates this principle well. In addition to this active extension of nerve distribution on or within a muscle, the bundles of muscle-fibres comprising it may shift their relative posi-

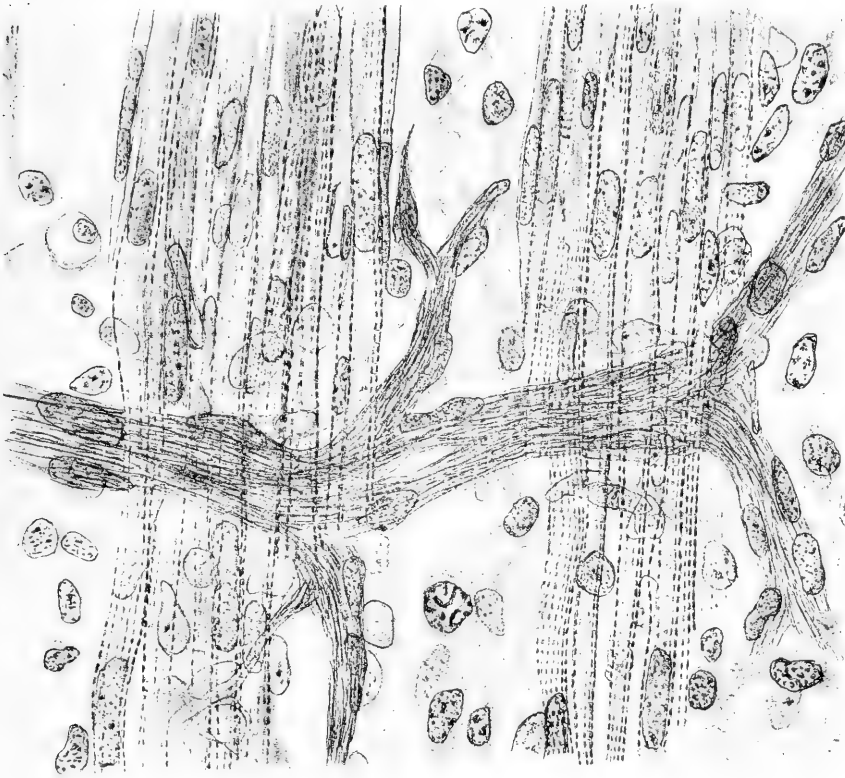


FIG. 8. A portion of a segment of the rectus muscle of a pig embryo 39 mm. long. An intramuscular nerve may be seen distributing branches in the loose mesenchyme separating the bundles of muscle-fibres. 720 diam.

tions, as in certain segments of the *rectus abdominis* of the larger mammals, and the muscle as a whole may shift its position in relation to other parts of the body, and thus the nerves may be passively altered in their relations.

In addition to the nerves furnished to the muscle-fibres during development, nerves are also furnished to various sensory endings lying in the muscle, to its associated skeletal apparatus and to the blood-vessels.

The development of this sensory and vaso-motor apparatus can only be followed with satisfaction when better methods for differentially staining developing nerves have been devised. Methylene-blue, which is so good for adult tissues, seems to act much less specifically on developing nerve-fibres. Gold-chloride used on fresh tissues is excellent for the study of the grosser tissue relations, but the tissues are so altered by the acids used in reducing the gold that the finer histological details are many of them lost. The Apáthy method of using gold-chloride on fixed tissues does not seem to give good results with mammalian embryos. In young embryos Congo-red gives an excellent stain for nerve-fibrils, but it is not a stain sufficiently specific for the complex tissue relations of later embryonic development. The changes, however, taking place in nerve-trunks may be traced both in teased specimens and in sections, by means of the usual methods of technique, and the development of the nerve-endings on the striated muscle-fibres may be followed, although less perfectly than one might wish, by the use of the gold-chloride method combined with other methods of technique. We shall now consider certain of the histogenetic phenomena disclosed by these methods. It is convenient to describe first the processes connected with the forward growth and secondly those connected with the internal differentiation of the nerves.

III. HISTOGENESIS IN THE DEVELOPING NERVES.

a. Processes Taking Place at the Growing Tip.

A description has above been given of the histological structure of the primary embryonic nerve-trunks. Each nerve is composed of bundles of embryonic fibres and fibril-groups. The nerve as a whole is fairly completely ensheathed, while the constituent fibre-bundles are supported and partially ensheathed by anastomosing cells. When a nerve-trunk gives rise immediately to large primary branches, as is the case with the spinal and most of the cranial nerves, these branches are similar in structure to the primary nerve-trunks. The nerves which arise by direct forward extension of the primary branches, such, for instance, as the ventral tip of each intercostal nerve and the nerves which arise from the fusion of two or more primary branches, such as the nerves arising from the brachial and lumbo-sacral plexuses, send forward a few fibrils closely accompanied by, perhaps preceded by, sheath-cells. Behind this tip the ingrowth of bundles of fibrils and the multiplication of these fibrils by branching causes the nerve-trunk rapidly to increase in thickness toward the central nervous system (see Fig. 2). When the nerves

first formed give rise to secondary branches, the peripheral cells of the nerve multiply in the vicinity of the future branch and give rise to a tube-like projection into which the nerve-fibrils extend. In Fig. 4 at "a" may be seen a branch of this kind in process of formation. Whether a few nerve-fibrils first extend outward and then sheath-cells multiply so as to cover them, or the tube-like process is first formed, or the two processes are simultaneous, it is difficult to decide. Perhaps all three modes occur.

The forward growth of the nerves takes place by essentially the same processes both when the growing tip represents the extremity of an original nerve and when it represents the extremity of a branch. In the cutaneous nerves, branching and forward extension is so rapid that the growing extremities of the nerves soon become small in calibre. In Fig. 9 is shown the extremity of a branch of a lateral cutaneous ramus of the ventral division of a spinal nerve of a pig 14 mm. long. The nerve is composed of a small bundle of fibrils inclosed by flat endothelial cells. At "a" a few of the fibrils branch off into another level.



FIG. 9. Tip of a branch of the lateral cutaneous ramus of the ventral division of a spinal nerve of a pig 14 mm. long. 720 diam.

At "b" what appears to be a naked axis-cylinder process extends outward into the surrounding mesenchyme. This process is enlarged at the end like the two fibres pictured in Fig. 3, *d*. This enlargement corresponds to that described by Cajal as the growing extremity of a nerve-fibre. Unless we assume that the sheath-cell belonging to this fibre was cut off in sectioning, we must take the fibre to be a naked branch of the nerve. At *c* a few nerve-fibrils are also extending forward, but they are covered by a process of a sheath-cell. The more the nerves branch the finer the branches become. The ultimate branches consist of a few fibrils either naked or ensheathed by a series of greatly elongated sheath-cells.

Leontowitsch has made an extensive study of the nerves in the adult human skin. His results, obtained by methylene-blue methods, are of great value, although it is probable that certain of his conclusions will not be accepted without further support. Leontowitsch divides the nerves of the skin into two groups, the medullated nerves and their branches, and the non-medullated nerves, or nerves of Remak. The latter he again divides into two groups, Type I and Type II. The most primitive portion of the nervous apparatus of the skin, according to Leontowitsch, is composed of the "Remak" cells of Type I. These are cells

which give rise to true plexuses by the anastomosis of long, narrow branches which extend outward from the cell-body in various directions. Four such plexuses may be distinguished: a deep one in the corium, a middle and a subepithelial in the papillary layer, and an intra-epithelial. The Remak nerves of Type II likewise are composed of anastomosing cells which give rise to a true plexus. The protoplasm of the processes of these cells, however, is much more developed than in those of Type I, and there seems to be much less branching of the processes. Often the protoplasm of these cells shows a distinct fibrillation. Certain cells seem to be in a state of transition between Type I and Type II. The medullary nerves terminate in arborizations, telodendrites, in which plexus formation is slight or does not exist. The ramifications of the medullary nerves may resemble the Remak fibres for a distance, or they may at once pass over into naked processes which are marked by plate-like varicosities and terminate either "free" or in sense-organs. Leontowitsch thinks that there is constant physiological regeneration going on in the skin and that this takes place by a transformation of the "Remak" cell-plexuses into the peripheral portion of the "neurite" of the central ganglion cell. He can explain his findings only on the hypothesis advanced by Schwann, Balfour, and numerous recent investigators that the nerves arise by differentiation from a chain of anastomosing cells.

Although Leontowitsch makes the statement that the tyro can distinguish between connective-tissue cells and the cells he figures as belonging to Remak nerves Type I, I do not think that he makes the distinction clear either in his text or figures. The cells of the Remak nerves Type II may well be taken for sheath-cells surrounding small bundles of fibrils such as are known to exist in the sympathetic system, the intestinal plexuses, and in the whole peripheral nervous system during early embryonic development. Gold-chloride and methylene blue both show an affinity for the sheath-cells as well as for the nerve-fibrils. Although I have not had an opportunity to repeat Leontowitsch's work extensively, my own studies on the nerves of the skin lead me to believe that there is nothing there to disprove the hypothesis that the sensory nerves of the skin are developed from nerve-fibrils which have grown out from central ganglion cells and which multiply greatly in number by branching. The growing fibrils are closely accompanied by sheath-cells until near their ultimate termination. The ensheathed paths, but not the contained fibrils, may either anastomose freely or to no considerable extent, according to the region in which the branching takes place.

Galeoti and Levi in a recent valuable contribution have described

the growing extremities of nerves on their way to muscle cells in the regenerating tail of a lizard. The nerve-fibres they describe are composed first of a chain of cells within which later the axis-cylinder processes become differentiated. They used gold-chloride impregnation in their studies. In many respects the growing nerves which they picture resemble those which I have seen in mammalian embryos and have described above as the "sheath cells." I have found that as a rule in early embryos the gold-chloride is precipitated, not in the axis-cylinder fibrils, but in the stroma of the nerves and in the sheath-cells.⁵ It seems, therefore, possible that the cells described by Galeoti and Levi were cells which ensheath nerve-fibrils not revealed by the methods they used. What they describe as developing axis-cylinders appears somewhat like a beginning deposit of myelin about axis-cylinder processes. For myelin in the early stages of development, gold-chloride has an especial affinity.

In general the growing extremities of the nerves within the developing muscles resemble those of the skin except that, as a rule, larger bundles of fibrils are contained within the nerve-sheaths until the final branchings take place which serve to distribute fibrils to the individual muscle cells composing the muscle bundles. Fig. 8 shows the branching of a nerve growing out to supply several muscle bundles of the rectus muscle of a pig 39 mm. long. Up to this stage the growing tip of the nerves may be easily distinguished in well stained sections.

The final union of the growing tip of the nerve with muscle-cells seems, in the rectus muscle of the pig, to begin in embryos of 8 cm., but definite endings are few until considerably later. The formation of nerve-endings cannot be satisfactorily followed in mammalian embryos, owing to the great number and the small size of the cells. So far as I have been able to determine, the steps in the formation of the end-plate are as follows:

An ensheathed bundle of nerve-fibrils extends transversely across a number of bundles of muscle fibres. As each bundle is reached an ensheathed nerve branch is sent into the midst of the muscle-fibres.

⁵ Kaplan has shown that his excellent ink-stain for axis-cylinder processes does not stain these in embryos before the appearance of the myelin sheath. The same thing seems to be true of the aniline stains for axis-cylinders. In staining Auerbach's and Meisner's plexuses with gold-chloride, as a rule the individual fibres composing the fibre-bundles are not distinct. The gold seems to be distributed in the stroma of the bundles. Apáthy also has called attention to the fact that gold-chloride usually stains the stroma of axis-cylinders, but not the contained fibrils when used before fixation. For Apáthy's haematein and gold-chloride stains the nerves of mammalian embryos do not seem adopted.

From this latter branch nerve-fibrils are sent out in company with sheath-cells to each muscle-fibre. A sheath-cell becomes applied to the surface of the muscle-fibre, while the protoplasm of the latter in the vicinity of the sheath-cell becomes granular and nuclei collect about the granular area. At the time of the formation of the end-plate, the muscle-fibre possesses both peripheral and central nuclei. I have elsewhere (1900) given pictures of cross-sections of muscle-fibres which seem to show a wandering of central nuclei toward the surface of the cell. The nuclei which collect about the granular area of the muscle-fibre seem to arise from the surface nuclei. They represent probably the nuclei of the sole of the adult muscle-plate while the nucleus of the cell which accompanies the nerve-fibre to the muscle-fibre, probably represents a nucleus of the sheath, or possibly a nucleus of arborization. Fig. 10 shows an early stage in the union of nerve-fibres and muscle-cells.

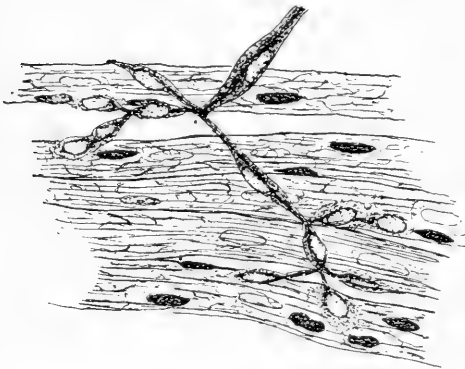


FIG. 10.

FIG. 10. An early stage in the union of nerve and muscle-fibres. From a gold-chloride specimen of the rectus muscle of a pig 19 cm. long. 720 diam. For the sake of contrast the surface nuclei are represented very much darker than they appear in the specimen.

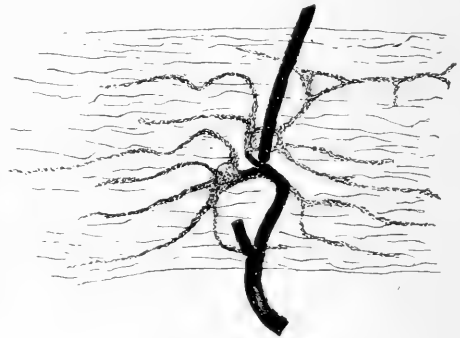


FIG. 11.

FIG. 11. Nerve, nerve-ending, and sarcolemma from a portion of the rectus muscle of a frog. 720 diam.

Union of nerve-fibres and muscle-cells does not begin to be common until the embryo has reached a length of 15 cm., and it continues for a considerable period after this time. So far as I have been able to determine, a definite sarcolemma forms after the nerve-fibre and sheath-cell have joined the muscle-cell. By the digestion of specimens hardened in osmic acid I have been able to isolate delicate sarcolemmata from muscle-cells of the rectus of pig embryos 20 cm. long, but not from younger embryos. This valuable digestion method of Chittenden also enables one to show the relation of the sarcolemma to the sheath of

Schwann. If muscle-fibres with the terminal nerves running to them be hardened in osmic acid or impregnated with gold-chloride and then digested in pancreatin, the protoplasm of the muscle-fibre disappears, but the sarcolemma, the sheath of Schwann, the myelin sheath, and some portions of the nerve-endings, probably the stroma, are left undigested. With care these digested specimens may be stained and mounted in glycerine or in balsam.⁶ In all successful specimens which I have prepared in this way, I have found the sheath of Schwann inseparably connected with the sarcolemma and the undigested portion of the end-plate closely united to and apparently on the under surface of the latter. The most satisfactory specimens are obtained with the muscles of frogs. See Fig. 11. It seems probable that the sarcolemma is formed through the action of the surface nuclei of the muscle-fibre, in response, possibly, to stimuli arising from the union of the nerve with the muscle-fibre; and it is so formed that it incloses that portion of the nerve which is spread out over the protoplasm of the muscle.

Various stages in the development of end-plates in muscle-fibres of mammals were described in 1892 by Mays. To the descriptions in Mays' most valuable paper I have nothing to add. In a study of the development of end-plates in pigs, mice, and guinea-pigs, I have seen specimens corresponding to many of Mays' pictures. In certain respects what I have seen corresponds to the description given by Galeoti and Levi of the formation of end-plates on the regenerating muscle-fibres of the lizard. This last paper and that of Mays both contain good summaries of the literature on the subject of the development of nerve-endings.

b. Internal Differentiation of the Nerves.

From the neuroblasts and from the spinal ganglion cells processes of considerable thickness are sent out into the peripheral nerves. It has been mentioned above that these processes soon begin to give rise at their extremities to groups of fibrils. During the early stages of development these fibrils may either be gathered in small compact groups, each of which represents an axis-cylinder process or they may be so scattered within the nerve that it is impossible to distinguish definite groups of fibrils corresponding to axis-cylinder processes. It seems probable that these embryonic fibrils increase in thickness as well as in length and in turn give rise at their extremities to new groups of fibrils. It is possible

⁶ The capillary cells and the white fibrous tissue are also left undigested. By staining heavily in Delafield's haematoxylin and then counter-staining in Congo-red, the sarcolemma, the capillary cells and the sheath of Schwann take a blue tint, and the fibrous tissue a red.

that the fibrils may increase in size and multiply by dividing longitudinally somewhat in the manner which Heidenhain has described for the fibrils of muscle-cells. When a nerve branches certain of the fibrils belonging to a given axis-cylinder process may be diverted into the branch while others may continue in the main trunk. Mays showed that in the frog a given nerve-fibre gives rise to a large number of peripheral branches. Dunn has recently shown that in the sciatic nerve of the frog there is a constant increase in the number of fibres as the periphery is approached. Although there is at the same time a decrease in area of cross section of the individual fibres, this is more than offset by the increase in number of fibres. All this goes to show that the fibrils connected with a given ganglion cell must increase very greatly in number and mass as one passes from the central toward the peripheral areas. The growth and longitudinal division of fibrils therefore probably constantly increases in amount as the fibrils extend outwards. The fibrils of embryonic nerves seem to be larger than the "primitive" fibrils described by Apáthy and by Bethe in adult nerves. The relations of the latter to the former can only be determined when methods have been devised which will stain primitive fibrils in young embryos.

The relations of the fibrils to the sheath-cells are difficult to determine in very small peripheral branches. The sheath-cells are so closely applied to the fibrils that it becomes mainly a matter of judgment to decide whether the fibrils are surrounded by or are embedded within the sheath-cells. In the large nerve-trunks first formed near the central nervous system sheath-cells appear scattered within the nerve as well as about the periphery (Fig. 2), and this, too, may lead to dispute as to the relation of the cells within the nerve to the nerve-fibrils. It is in peripheral nerves of a moderate size found during the earlier stages of embryonic development that the absence of genetic continuity between nerve-fibrils and the intrinsic cells of the nerve becomes most clear. Thus in Fig. 12 is shown a cross section of the median branch of the dorsal division of a thoracic nerve of a pig embryo 14 mm. long. Some of the surrounding mesenchyme is also shown. This nerve is composed of a large bundle of fibrils surrounded by a single layer of flat anastomosing cells. No cells are to be found among the fibrils, although the nerve may be followed for a considerable distance through a series of sections.

After a nerve of this kind has become considerably distended by ingrowth of new fibrils from behind, cells begin to wander from the investing sheath in among the fibrils. These cells give rise through anastomosis of their membranous processes to a skeletal framework similar

to that previously described in page 234. Kolster has described the invasion of cells of the sheath in among the nerve-fibrils which it surrounds in the nerves of *Salmo trutta*.

During the growth of the nerves the elementary bundle or bundles of fibrils of which it is composed become further broken up into secondary bundles by the invasion of fibrous tissue from the investing sheath. Thus, each intercostal nerve of the pig is at first composed of but a single funiculus, but later it becomes divided into two main bundles of fibrils, and these again are further subdivided. Fig. 13, *a*, shows a cross-section of an intercostal nerve of an embryo 8 cm. long. Above is a rather small compound bundle of fibrils, and below is a much larger one. Each of these is in turn divided into several funiculi. The septa sepa-

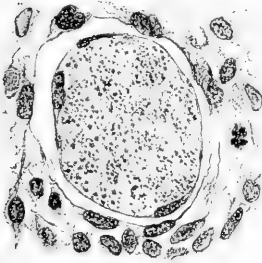


FIG. 12.

FIG. 12. Cross-section of the median branch of the dorsal division of a thoracic nerve of a pig embryo 14 mm. long. 720 diam.

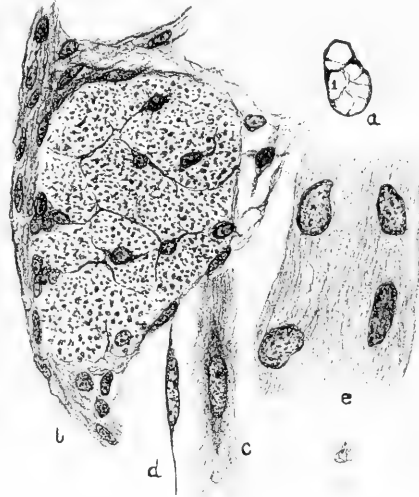


FIG. 13.

FIG. 13. *a*, Cross-section of an intercostal nerve of an embryo 8 cm. long; *b*, cross-section of the bundle of nerve-fibres designated "1" in "a"; *c*, An isolated cell corresponding to the cells shown in section in the bundle of nerve-fibres in "b"; *d*, longitudinal section through one of these cells; *e*, small portion of the membranous sheath surrounding the bundle of fibres shown in "b." *a*, 76 diam.; *b*, *c*, *d* and *e* 720 diam.

rating the funiculi last formed are delicate. This is shown in the septum at the lower margin of the funiculus pictured in Fig. 13, *b*, an enlargement of "1" in Fig. 13, *a*. But these septa are always lined toward the funiculus by a layer of flat, anastomosing cells. In Fig. 13, *e*, is shown a portion of such a membrane isolated from a funiculus of an intercostal nerve of a pig 8 cm. long and stained in hæmatoxylin and safranin.

The invasion of tissue which breaks up the elementary bundles into

secondary funiculi, seems to accompany the blood vessels which penetrate the nerve at various places along its course. In consequence of the irregular manner in which the septa arise, the funiculi of the embryo, like those of the adult, branch and anastomose freely along the course of the nerve. New funiculi may also be added to the nerves during the process of plexus formation.

In the further development of the nerve-trunks the most interesting questions are those concerned with the development of the myelin sheath and the sheath of Schwann. The work of Vignal is of most fundamental importance in this connection. In general the observations which I have made correspond with Vignal's. Certain details in the development of the sheath of Schwann can, however, be better studied in sections than by the teasing method employed by Vignal. Gurwitsch in studying this question made use of the Apáthy gold-chloride method, which he found a specific stain for the membranous sheaths of the developing nerve-fibrils. By the use of the Van Gieson stain I have been able completely to confirm the valuable work of Gurwitsch.

In Fig. 13, *b*, at the left, two projecting masses of cells seem to be on the point of contributing new cells to the interior of the nerve bundle. By the anastomosis of the flattened lateral processes of these intra-funicular cells, a membranous framework is formed which serves to divide the nerve-fibrils into groups. The membranes run parallel with the nerve-fibrils and thus appear as fine lines in cross-section (Fig. 13, *b*) and usually so in longitudinal sections (Fig. 13, *d*). They may be stained in sections, when Zenker's fluid has been used, by the Van Gieson or by the Mallory connective-tissue stain. The processes extending from the intra-funicular cells have been taken by some investigators to be nerve-fibres. The longitudinal section shown in Fig. 13, *d*, might suggest a bipolar nerve cell. But the processes take a purple stain in the Van Gieson mixture and a blue stain by the Mallory method, while the nerve-fibrils take on quite a different color in each case. Owing to the great delicacy of the membranous process of the cell, one is apt to obtain in teased preparations only the nucleus and a bit of the more granular entoplasm immediately about it. With care, however, specimens may be obtained like that shown in Fig. 13, *c*, in which a considerable portion of the membranous exoplasm is retained intact. The membranous processes appear to have a slight fibrillation. Before the intrinsic cells of the developing nerve have become differentiated into sheath-cells they multiply by indirect division (Figs. 3, *b*, and 4). After they become thus differentiated, direct cell division takes place. The line of division may be in the long or in the transverse axis of the nucleus

of the cell. After the sheath of Schwann is formed, cell division does not take place in its component cells. In regeneration, however, according to most observers, indirect division takes place in the cells which arise from the cells of the sheath of Schwann. These processes remind one of those taking place in muscle-cells. Myoblasts divide by indirect division. The central nuclei of the elongated spindle muscle-fibres multiply by direct division and so do also the peripheral nuclei which later appear. In regeneration, on the other hand, the myoblasts which arise from the muscle-fibres multiply by indirect division.

After they begin to appear the intra-funicular cells increase rapidly in number and give rise to membranous septa which divide the fibrils into smaller and smaller bundles and finally surround small groups of fibrils with a septum, the sheath of Schwann. Fig. 13, *b*, shows the membranous septa of bundles of fibrils in a pig-embryo 8 cm. long. Considerable groups of fibrils are enclosed. Fig. 14, *a*, shows a cross-section of a small portion of a nerve of an embryo 15 cm. long. The septa here form sheaths of Schwann about small dense bundles of fibrils, although not all the fibrils are thus inclosed.

Gurwitsch suggests the possibility that the membranous septa which he describes might be taken to represent endoneurium. In that case one would expect to find two sorts of cells within the funiculus, one set belonging more intimately to the nerve-fibrils, the other giving rise to the membranous septa. Gurwitsch, however, shows that stage by stage the development of membranes within the fasciculus may be followed until the sheaths of Schwann appear. A study of a large number of sections and teased preparations has served to convince me that Gurwitsch is correct in his interpretations. The endoneurium develops comparatively late. It is very slight at the time of the formation of the sheath of Schwann.

There is a vast amount of literature connected with the genetic origin of the cells of the sheath of Schwann and of the relations of these cells to the axis-cylinder. Those who assume that the latter structure arises by fusion of parts derived from a chain of cells, usually consider that the cells of the sheath have an ectodermal origin. In the mammals, as well as in the lower vertebrates, a certain number of cells wander out from

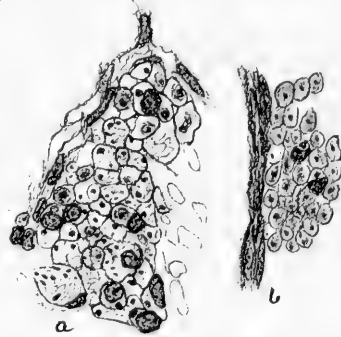


FIG. 14. *a*, Cross-section from the centre of an intercostal nerve of a pig-embryo 15 cm. long; *b*, Cross-section of several fibres near the margin of an intercostal nerve of a pig-embryo 20 cm. long. 720 diam.

the spinal ganglia and cord along with the bundles of axis-cylinder processes. These cells may contribute in part to the origin of the cells of the sheath of Schwann, but my observations lead me to believe with Vignal and Gurwitsch, that the latter arise in mammals, in the main at least, from the mesenchyme. I agree with Gurwitsch that the sheath of Schwann is an exogenous structure which has quite a different genetic origin from that of the nerve-fibre. When once the sheath of Schwann is formed it does, however, undoubtedly enter into intimate physiological relations, "symbiosis," with the axis-cylinder process which it incloses.

Indeed, throughout the period of the development of the nerve-fibrils as well as in the adult life, the elaboration of nerve-sheaths shows that they must play a vital part. In the embryo, at least, their function is doubtless mainly nutritional. The early nerves are composed of nerve-fibrils within a sheath of anastomosing cells. In addition to the fibrils there is contained within the sheath some substance either fluid or semi-fluid in nature, which serves to "float" the growing fibrils and to furnish them with nutrition. Vignal has described this substance as homogeneous. It deserves much more careful study from the micro-chemical standpoint than it has yet received. The perineural sheath in nerves before the sheath of Schwann has appeared has, in all likelihood, specific action in determining the physical and probably also the chemical characteristics of this stroma.

For the formation of a medullary sheath a special cellular sheath about each nerve fibre is not absolutely necessary. As Gurwitsch has pointed out, formation of myelin about an axis-cylinder process may begin before the corresponding sheath of Schwann is complete. I have observed this also in the pig. Kolster in a valuable study on the development of the nerve-fibres in *Salmo trutta* has shown that a medullary sheath may develop about fibres in a nerve in which no cells have as yet passed from the perineurium into the midst of the fibres which it surrounds. Apáthy has paid special attention to the interfibrillar substance of nerve-fibres and has shown that it may present many characteristics of myelin.

As a rule, however, in mammals the sheath of Schwann, as shown by Vignal, completely incloses the axis-cylinder fibrils before formation of the medullary sheath begins. In Fig. 15, *a*, is shown a fibre of this kind dissected from the intercostal nerve of a pig 15 cm. long. The cells comprising the sheath here shown are nearer together than is common at the period when the sheath is first formed. The average distance between nuclei at the period under discussion seems to be about a tenth of a milli-

meter, though variation is great. Fibrils free from cells for a distance of over a millimeter can be dissected from pig embryos six to eight millimeters long. It therefore seems highly improbable that the cells of the sheath of Schwann, which form segments of a tenth of a millimeter or less in length, could have anything to do with a segmental formation of the corresponding axis-cylinder.

Within the sheath of Schwann the axis-cylinder lies at first apparently surrounded by a fluid, judging from the space which intervenes between it and the thin wall of the sheath.⁷ Only in the vicinity of the nucleus is the wall thick. Here there is a mass of granular protoplasm. About the axis-cylinder myelin is deposited, owing apparently to the action of the axis-cylinder on the surrounding fluid. At first the deposit of myelin seems usually to be fairly evenly distributed (Fig.

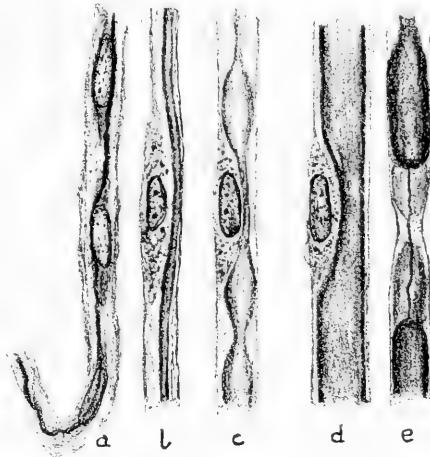


FIG. 15. Nerve-fibres illustrating various stages in the development of a medullary sheath. 720 diam.

15, *b*), but soon it is much more active in some areas than in others, giving rise to the beaded appearance shown in Fig. 15, *c*; and finally, the sheath becomes filled out (Fig. 15, *d*). The formation of myelin seems to continue in the vicinity of the nodes of Ranvier after the sheath has become completely filled out elsewhere. Fig. 15, *e*, shows a fibre in which a "segment" of lighter myelin is being formed on each side between a node of Ranvier and the darker, more fully formed myelin of the nerve-fibres. This suggests that the internodal segments of the nerve-fibres grow at their extremities by addition there of new material. Whether the "beads" and the secondarily-formed segments of myelin of the nature just described have anything to do with Lantermann's segments, is open to question. The various stages in the formation of myelin pictured by Vignal may be readily confirmed.

The changes taking place in the nerves and nerve-fibres after birth have been described at length by Westphal. What he describes as free axis-cylinders seem to be fibres in which the sheath of Schwann is com-

⁷ In osmic acid specimens the sheath usually shrinks down against the axis-cylinder process. This may be prevented by the use of formalin before the nerves are subjected to osmic acid treatment.

pletely filled with a substance resembling embryonic myelin, that is, of fibres approximately like that shown in Fig. 15, *d*. Often when myelin is being very actively formed, it is difficult to distinguish the axis-cylinder from the surrounding myelin. Differentiation of the embryonic myelin into the adult form begins at the periphery of the fibres and proceeds toward the centre. This process has been carefully studied by Westphal. I may mention here again that, while neither by the Weigert method nor by the use of osmic acid is embryonic myelin stained so dark as that of adult fibres, gold-chloride has an especial affinity for embryonic myelin.

The intercalation of new segments of the sheath of Schwann at the nodes of Ranvier during the later stages in the development of the fibres has been described by Vignal and has deserved more attention than it has received. The processes he describes may be readily confirmed. The progressive myelinization of nerve-fibres from the center towards the periphery may also be readily confirmed. In pig embryos 20 mm. long the nerve-fibres in the main trunk of an intercostal nerve are most of them covered with embryonic myelin. In the peripheral nerves distributed to the anterior segments of the rectus muscle, on the other hand, one finds only rarely a fibre in which the myelin has been formed up to the final branches distributed to the individual muscle-fibres. None of these final branches seem to be medullated.

SUMMARY.

In the development of the peripheral nervous system it is convenient to recognize several stages, although it is difficult to draw a sharp line of demarcation between them. The first stage is that of the differentiation of the motor nuclei and sensory ganglia; the second includes the period of outgrowth from the region of the central nervous system to various peripheral anlagen; the third, the development of branches from the primary nerves to the various parts differentiated from these anlagen; and the fourth, the development of functional unity between the nerve-fibres and the structures to which they are distributed. During the second period the proximal nerve-plexuses are formed, during the third the coarser peripheral plexuses, and during the fourth the finer terminal plexuses. During the second, third and fourth stages there may take place considerable shifting in relative position of the structures to which the nerves are distributed.

The axis-cylinder fibrils of the nerve grow out by continuous extension from central cells. They divide and branch extensively as they proceed from the region of the central nervous system outwards. They

leave the central nervous system and spinal ganglia in naked bundles (Fig. 1) but soon become intimately related with sheath-cells which accompany them closely throughout the period of growth. At the growing tip of a nerve it is difficult to decide whether the axis-cylinder fibrils or the sheath-cells proceed (Figs. 2, 4 and 9). Posterior to this the nerve gradually becomes distended with fibrils by ingrowth from behind and by multiplication due to division. In an early embryonic nerve of moderate size one finds many hundred fibrils inclosed by a sheath of flattened cells, but with no cells among them (Fig. 12). In such nerves one can most easily see that the fibrils are not differentiated parts of cells lying in the nerve. In addition to this it is possible to isolate from embryos one to five or six centimeters in length unensheathed nerve-fibril bundles from one-half to a millimeter long. When the sheath of Schwann is formed in embryos ten to twenty centimeters in length, the nuclei of the sheath are about a tenth of a millimeter apart. There is, therefore, no segmentation in the axis-cylinder fibrils corresponding to the cells of the sheath of Schwann.

Union of nerve and muscle fibres takes place before the formation of the sarcolemma. The latter membrane becomes so closely united to the sheath of Schwann that no line of demarcation can be seen between them in specimens from which the muscle substance has been digested. The terminal apparatus of the nerve is more resistant to digestive fluids than the muscle substance, and is closely attached to the under surface of the sarcolemma (Fig. 11).

The sheaths of the nerves serve to maintain the stroma in which the axis-cylinder fibrils grow. At first large numbers of fibrils are ensheathed within the main trunks of the nerves, but by proliferation of sheath-cells smaller and smaller bundles are inclosed until finally but a small group of fibrils is inclosed within each sheath of Schwann. The work of Gurwitsch on the formation of the sheath of Schwann is confirmed. Myelinization is due to influences exerted by the axis-cylinder fibrils on the surrounding stroma.

During development the nerve funiculi may be broken up into smaller funiculi by invasion of tissue of the investing sheath.

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THE MICROSCOPIC STRUCTURE OF CORTICAL AREAS IN MAN AND SOME MAMMALS.

BY

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WITH 4 PLATES.

INTRODUCTORY.

The first step toward dividing the cerebral cortex into structural areas corresponding with the functional localization, determined by the experiments of Fritsch and Hitzig, was made when the giant cells of Betz were discovered and found to be characteristic of the motor area. These cells, described by various authors for man, were later identified by Bevan Lewis in the pig, sheep, cat and other animals, and found to be also present in isolated groups behind the motor area.

Nissl's method of staining nerve cells has, as I believe, furnished us with a means of carrying such investigation further than was possible by the older technique.

We are as yet unable to distinguish specific differences between cortical nerve cells. It is, for instance, impossible to show such a difference between cortical nerve cells in the auditory and those in the visual path. We can, however, say that the entire cortical visual center, considered as an organ, differs from the auditory or other cortical centers.

In order for us to determine whether any relation can be shown between the variations in the structure of the different regions in the cortex, on the one hand, and the function of these respective regions on the other hand, we must examine the largest possible number of brains, not only of those of one species of animals, but also those of animals in different stages of phylogenetic development.

From such comparative studies it has been found to be true that in animals whose organs of sense are equally well developed, but have not, on the whole, reached a high degree of specialization, no great differences in the structure of the cortex can be observed. This seems to be the case with the brain of the pteropus, the cat, and somewhat less so of the dog. On the other hand, in correlation with the special develop-

ment of a given sense organ, the corresponding cortical area presents a marked specialization as compared with the surrounding regions. In the brain of the horse, for instance, the olfactory region seems to be very highly developed, and is plainly distinguishable from the remaining cortex. The other organs of sense in that animal do not seem to have reached such a high degree of development, and the cortical areas corresponding to these organs are accordingly less developed and less marked. In the brain of the monkey and of man, we find several regions characteristically developed and sharply defined, a fact which corresponds to the development of the sense organs associated with these several regions.

Much confusion has arisen in comparing the findings of different investigators who have used dissimilar methods.

Another source of error lies, I believe, in the fact that only small pieces of the cortex taken from different regions were examined. There have never been made, to my knowledge, entire sections through the cerebral cortex, especially that of the human brain, for this purpose, and on that account a continued picture was not obtained. The sections which I have prepared were made through the entire hemisphere, frontally, horizontally, as well as sagittally, thus presenting a nearly continuous picture. A disadvantage of these entire sections, however, is met in the fact that in many places the cortex was not cut perpendicularly, and hence the cells assumed a different shape. These pictures can be easily recognized, however, if one has a little experience in microscopy of the cerebral cortex. The principal cause of the general lack of agreement as to the structure of the cortex is, however, due to the laying down of general conclusions drawn from a study of the brains of lower animals without sufficient comparison with the human cortex which is very specially constituted.

The investigations of Fritsch and Hitzig in 1870 followed by those of Munk, Ferrier, Hitzig, Goltz, Flechsig, Duret, Carville, Luciani, Tamburini, Horsley, Schäfer and others have furnished us with a solid experimental basis for a localization of function in the cerebral cortex of the lower animal; while the results of human clinico-pathological cases, which have lately been examined as extensively as our methods will permit, have made it possible to institute valuable comparisons here. If, however, we undertake to compare the results of our experimental investigation of animal brains with those obtained in clinico-pathological cases of human brains, we must not forget that the different centers vary in animals and man and also among animals themselves, with regard to their situation in the cortex. Such variation is to be explained by the fact that a specially developed cortical center in

an animal will probably occupy more space than those not so highly developed, and thus displace the other less developed centers, so that these may come to occupy a position different from that in other animals. Thus according to the experimental investigations of Munk, the visual center in the monkey of lower types is in the operculum; but an attempt to locate it in man in the corresponding region would result in great confusion, as it is not situated on the lateral surface of the hemisphere in man as in the monkey, but on the medial surface. This displacement of the visual center in man is very likely brought about by the more highly developed association centers which occupy the lateral surface of the hemisphere in the parietal and occipital lobes.

It is true, some investigators still adhere to the idea that the visual center is situated on the lateral surface of the hemispheres, but such is not the case in man.

As a result of one or more of the sources of error just enumerated we find the following greatly differing views maintained:

Meynert found five layers almost everywhere in the cortex, except in the occipital lobe where he described eight layers. Other investigators, as for instance *Ramón y Cajal*, consider only four layers as the common type, the cortex presenting, however, here and there a few slight variations which can yet be considered part of the four-layer type. In his later writings, *Ramón y Cajal* differs slightly from his former opinion. He says, concerning the sight-center in the occipital lobe, "The investigations which I have made on the human cortex, as well as on that of the dog and cat by both Nissl and Golgi methods, have led me to distinguish the following layers:

1. Plexiform layer (called molecular layer by authors generally, and "cell-poor layer" by Meynert).
2. Layer of small pyramids.
3. Layer of medium-sized pyramids.
4. Layer of large stellate cells.
5. Layer of small stellate cells. (Called "layer of granules" by other authors.)
6. Second plexiform layer, or layer of small pyramidal cells, with arched axon.
7. Layer of giant pyramidal cells (solitary cells of Meynert).
8. Layer of medium-sized pyramidal cells, with arched ascending axon.
9. Layer of fusiform and triangular cells (fusiform-cell layer of Meynert).

In the human motor cortex *Ramón y Cajal* recognizes the following layers:

1. Plexiform layer (layer poor in cells of Meynert, molecular layer of some writers).
2. Layer of small and medium sized pyramids.
3. External layer of giant pyramids.
4. Layer of small stellate cells. (Granule-cell layer of authors.)

5. Internal or deep layer of giant pyramids.

6. Layer of polymorphic cells (fusiform and medium-sized pyramids of some writers).

Von Monakow seems to share the view formerly expressed by *Ramón y Cajal*. *Golgi* describes three layers, and even the cortex of the occipital lobe, according to this author, contains only three layers.

Koelliker divides the cortex into four and six-layer types, as follows:

1. The white cortical layer of the stratum zonale, poor in cells.
2. Layer of small pyramidal cells.
3. Layer of medium-sized and large pyramidal cells.
4. Layer of polymorphous cells.

In many convolutions, he found, as did *Hammaberg*, six layers, thus:

1. Stratum zonale.
2. First layer of small pyramidal cells.
3. First layer of medium-sized and large pyramidal cells.
4. Second layer of small pyramidal cells.
5. Second layer of medium-sized and large pyramidal cells.
6. Layer of polymorphous cells.

Obersteiner assumes a type of five layers:

1. Layer of neuroglia cells, or stratum moleculare.
2. Layer of small pyramidal cells of outer nerve-cell layer.
3. Layer of large pyramids, formation of the cornu ammonis or middle nerve cell layer.
4. Layer of the small irregular cells, granule formation, or mixed nerve-cell layer.
5. Layer of spindle cells, claustral formation.

According to *Obersteiner*, a few slight variations occur which are, however, not so important as to prevent their inclusion in the five-layer structure. He is unable to find the eight layers of *Meynert*, and believes that nowhere, and especially in higher animals, do sharp differences appear in the structure of the cortex.

Bevan Lewis described, in the cortex, a structure of five and six layers. The five-layer structure is found in man and monkeys in front of the central sulcus, corresponding to the anterior central gyrus. In the lower animals which he examined, he found it surrounding the fissura cruciata. This five-layer type is, according to him, characteristic of the motor area. The six-layer type is found behind the central sulcus and is believed to be characteristic of the sensory cortex.

Hammaberg, who made a great number of accurate investigations of the human cerebral cortex, seems to incline towards the opinion of *Lewis*.

COMPARATIVE ANATOMY OF CORTICAL REGIONS.

I shall now endeavor to describe the cortex of various animals, comparing the functional centers according to structure and localization. I have examined sections of six different animals, which are phylogenetically fairly well separated from one another.

1. Pteropus. 2 Horse. 3. Cat. 4. Dog. 5. Monkey (Macacus Cynomolgus), and 6. Man.¹

OLFACTORY REGION.

The olfactory center is of variable extent in the animals examined, being largest in the horse and smallest in man. That portion of the cortex which can undoubtedly be considered the olfactory cortex, presents in the pteropus, horse, cat, dog, monkey, and man, a rather characteristic structure, which is due to the fact that the cells in the outer polymorphous cell layer, arrange themselves in smaller and larger groups, thus giving to this layer an interrupted appearance. In some places, especially in the olfactory tract, these cells lie so close together (not in groups) and are so deeply stained, that one can distinguish plainly between this layer and the same layer in other cortical centers.

In the pteropus, this peculiar structure extends over a comparatively large area of the ventral and lateral parts of the hemisphere; its limits are difficult to describe precisely, owing to the fact that this brain contains no fissures which could be used as landmarks.

In the dog, cat, and monkey, this type is limited to the hippocampal gyrus and seems to extend into the posterior portion of the gyrus fornicaus; it then passes into the olfactory tract, where nearly all the pyramidal cells disappear, only a few polymorphous cells remaining in place of the pyramidal cells.

In the human cortex this type is confined to a very small area in the hippocampal gyrus bordering on one side, on the formatio cornu ammonis, of which it seems to be the continuation, while on the other side it is in contact with the seven-layer type.

One can plainly see, when approaching the olfactory region from the seven-layer type (to be described under a separate heading), the granule-cell layer disappear and the pyramidal cells diminish in number and finally seem to be transformed into polymorphous and spindle shaped cells, which lie between the characteristic outer layer and inner layer of polymorphous cells.

In the cortex of the horse's brain, this type occupies a more promi-

¹Of the horse and of man, I lost considerable material, especially the temporal lobe of man, so that at present my sections will not suffice to give a complete picture of the cortex of horse and man. I have, however, noted in the body of the text certain observations, and should add here that, in a horse's brain, the finer structure differs from that of the cortex of other animals in that one sees clearly, with the exception of a few limited regions, six layers in which two stripes, the stripes Gannari or Baillarger, can be plainly seen.

ment position; it is present in the gyrus fornicatus where the latter passes into the hippocampal gyrus, and in the markedly developed anterior portion which passes from the medial to the lateral frontal surface of the hemisphere. This addition to the gyrus fornicatus gives to the brain of the horse the aspect of possessing a large frontal lobe. Such, however, is not the case, for in the brain of the horse the characteristic structure of the frontal lobe is absent. I believe we may consider this extensive cortical region as a part of the olfactory center. A peculiar feature of this region, however, is the presence of large motor pyramidal cells, evidently signifying that the olfactory and motor centers are here merging into one another.

MOTOR AREA.

This area is mainly distinguished by the large pyramidal cells of Betz. These giant cells are not similar in shape or in size in different animals. In the horse they average about 0.44 mm. in length and 0.374 mm. in width. In the pteropus the length of the largest cell is 0.36 mm. and its width at the base 0.18 mm. In the cat, however, these giant cells measure 0.612 mm. in length and about 0.468 mm. in width at the base of the cell. In the dog they measure 0.72 mm. by 0.324 mm.; in the monkey, 0.468 mm. by 0.316 mm.; in man, 0.54 mm. by 0.36 mm. These large pyramidal cells of the human cortex frequently show a mass of pigment surrounding the nucleus, which I have not seen in pyramidal cells of lower animals.

In the cortex of the pteropus, the cat, the dog, the monkey and of man, the motor area presents a structure of five layers.

In the horse we can also assume five layers, but the inner stripe of Baillarger is here so clearly defined that it can be considered a special layer, making a six layer type, though such a distinction would be arbitrarily based on the position of the large pyramidal cells in the upper portion of the stripe of Baillarger, leaving the lower portion poor in cells, and giving it the appearance of a distinct layer.

In the motor area of the human cortex, there is present a suggestion of the granule-cell layer. This granule-cell layer does not appear clearly if at all in the motor area of lower animals.

The motor cortex in the dog, the monkey and in man (less clearly so in the cat, horse and pteropus) is much wider than the sensory cortex lying behind it, but the cells in the sensory cortex lie much more closely together and are also much smaller.

The ratio of the depth of the motor cortex compared with the sensory cortex is in:

Dog as	2.210 : 1.690
Monkey	2.340 : 1.590
Man	3.510 : 1.820

It is evident from these figures that this difference between the motor and sensory cortex is least in the dog and most in man.

In the pteropus, the large cells are distributed over a relatively large cortical area in the anterior portion of the hemisphere on its lateral as well as on its medial surface. They are situated in the fourth layer of the five layer type. For the reason that relatively large cells are found in the pteropus in such large numbers, and are spread over so large an area, I am inclined to doubt that these really represent the motor cells only. These cells, being in a parapyknomorphic state, do not differ from the other pyramidal cells in the same region, whereas the motor or large pyramidal cells in higher animals are in a pyknomorphic state, compared with the parapyknomorphic state of the smaller pyramidal cells in the same region.

In the cat and the dog, these cells lie in a limited area surrounding the *fissura cruciata*.

In the monkey, they lie in the well defined anterior central gyrus, but isolated cells are still found in the posterior central gyrus. They do not, however, reach as far ventralward in the posterior central gyrus as the stem of the fissure of Sylvius, but only as far as the lower extremity of the central sulcus of Rolando, which is shorter comparatively in the monkey than in man. The large pyramidal cells in the posterior central gyrus are not so large as the same cells in the anterior central.

In the human cortex, the large pyramidal cells are found in the anterior central gyrus. Both in size and in numbers they reach their highest point of development in the dorsal portion of the anterior central, but diminish in both respects as they approach the ventral extremity of this gyrus. Anteriorly from the anterior central gyrus they occur only in small numbers in the posterior extremity of the upper and middle frontal gyri.

On examination of the motor area, with a low power lens (a. a. Zeiss), one observes the peculiar fact that in lower animals the large pyramidal cells are crowded closely together and presumably on that account occupy a limited area, while in man the cells are more scattered and cover a comparatively larger area of the cortex. Posteriorly from the anterior central gyrus, the boundary being formed by the central sulcus (*fissure of Rolando*), the motor type passes abruptly into the seven layer type, while toward the frontal lobe the transition into the seven layer type is gradual. This latter type in the frontal lobe resembles the parietal

type in that it can be divided into seven layers, but differs from it with regard to the structure of the pyknomorphous or deeply stained pyramidal cells.

The motor cortex of the animals studied, presents the following five layer type:

1. Layer of glia or tangential fibers.
2. Outer layer of polymorphous cells.
3. Layer of parapyknomorphous pyramidal cells.
4. Layer of large pyknomorphous pyramidal cells (Betz's pyramidal cells or Lewis' ganglionic cells).
5. Inner layer of polymorphous cells.

The pyramidal cells of the third layer are distinguished not only by their smaller size, but also by the structure of their chromatic substance, which is more or less reticular. We can therefore designate these cells according to Nissl's nomenclature as arkyochrome cells. The large pyramidal cells of the motor area, on the other hand, as well as a great number of the pyknomorphous cells of the fourth and sixth layers of the parietal and temporal regions present the characteristic stichochrome structure.

THE SEVEN-LAYER TYPE.

It is difficult to give this type a functional name, because it extends, in the human brain, over a very large area, in which we must look for more than one function. In the human brain it is found in—

- (1) The whole parietal lobe, which we can assume with tolerable certainty to be in part the cortical center of sensation.
- (2) The entire lateral portion of the occipital lobe.
- (3) The whole frontal lobe.
- (4) The temporal lobe, wherein a few modifications are found.
- (5) The præcuneus.
- (6) The region of the island of Reil, where again some slight modifications occur.

It is probable that in this cortex are situated the different centers of association, which have been described by Flechsig.

In the brain of the monkey this type is comparatively less extensive in proportion to the well defined motor and visual centers.

In the cortex of the dog and cat, it occupies a much smaller area and is not so clearly defined. Owing to the absence of the frontal lobe in these animals, this type is entirely wanting in front of the motor zone.

In the Pteropus this type is nowhere present in the cortex.

THE SEVEN LAYER TYPE MAY NOW BE COMPARED WITH THE FIVE LAYER TYPE (MOTOR AREA) AS FOLLOWS:

The first layer (layer of glia and tangential fibers, molecular layer) is similar in structure to that of the motor area, but is narrower. The second layer is similar to that in the motor area. The third is also similar to that of the motor region, but is much narrower in many places, especially on the convexities of the convolutions. The fourth is a layer of pyknomorphous pyramidal cells, which can be distinguished from the third layer by the more intense staining of the cells. This layer does not exist as such in the motor region. The fifth layer is Hammaberg's fourth layer, or the layer of granule cells of other authors. Koelliker named it the second layer of small pyramids. This layer does not exist in the motor region of the brains of the lower animals I have examined; in man just a trace of it is seen in the motor region, but it is not sufficiently developed to permit one to distinguish it as a separate layer. The sixth layer is again a layer of pyknomorphous pyramidal cells, the ganglionic cells of Lewis. This layer seems to be a continuation of the fourth layer of the motor region. The seventh layer is the inner layer of polymorphous cells. This layer corresponds to the fifth of the motor region.

We therefore have the following layers in the seven layer type:

1. Layer of glia or outer layer of tangential fibers.
2. Outer layer of polymorphous cells.
3. Layer of parapyknomorphous pyramidal cells.
4. Outer layer of pyknomorphous pyramidal cells.
5. Layer of granule cells.
6. Inner layer of pyknomorphous pyramidal cells.
7. Inner layer of polymorphous cells.

In the dog, the monkey and in man, the transition from the motor to the seven-layer type can be distinctly recognized. In man, monkey, and dog, less distinctly in the cat, the large pyramidal cells of the motor area become smaller at the point of transition and arrange themselves in two rows, between which the granule-cell layer (fourth layer of Hammaberg, Ramón y Cajal's layer of small stellate cells) is distinctly seen, giving to this type its characteristic appearance.

The granule-cell layer is always present in this type. The two layers of pyknomorphous pyramidal cells, however, are subject to variation. There are places in the cortex where the outer layer of pyknomorphous pyramidal cells is wanting and their place is taken by the parapyknomorphous pyramidal cells of the third layer, so that in these places the fourth layer is absent. Then again, there are places where the inner pyknomorphous pyramidal cells are missing and where, more or less clearly, can be seen a light stripe, which is known as the inner stripe of Baillarger. This condition is most frequently found in the human

cortex, so that it can be accepted as the rule there. In the dog and monkey, on the other hand, the inner layer of pyknomorphous pyramidal cells is very distinctly developed and spread over a fairly large area. Now if, as is generally done, small pieces of the cortex are cut here and there from the surface of the hemispheres, it may happen that either the outer or the inner layer of pyknomorphous pyramidal cells alone is present (in most places the outer layer, as it is present almost everywhere in the seven-layer type), a study of such pieces might lead one to believe that the inner or outer layer of pyknomorphous pyramidal cells does not exist at all. In those places where the internal layer of pyknomorphous pyramidal cells is absent, it is difficult to recognize a seven-layer type, if by absence of these cells the stripe of Baillarger is not plainly brought to view. I have not as yet been able to definitely fix the exact points, where these variations occur, but one can see that these pyknomorphous pyramidal cells are present in greater numbers in the dorsal than in the ventral portion of the parietal lobe. It is also noticeable, that the inner layer of pyknomorphous pyramidal cells disappears as the occipital lobe is approached, so that posteriorly the stripe of Baillarger comes more into view.

The seven-layer type is found in the dog, behind the fissura cruciata, and extends backward to within 2 cm. of the occipital pole. It is found less sharply marked in the temporal lobe and is entirely absent in front of the fissura cruciata.

In the monkey the seven-layer type is most distinctly marked in the parietal region lying between the central sulcus and the external occipital fissure, or ape cleft. In the temporal lobe this type undergoes a modification, which will be described below. In front of the fissure which corresponds to one of the frontal fissures in man (Munk calling it "Harkenfurche" in the monkey), this type is again evident and its limits coincide with those of the frontal lobe.

In the human cortex, this type extends, as I have stated before, over a very large area. It is found in the parietal lobe and in the præcuneus. It occupies the entire lateral surface of the occipital lobe, and extends, modified, into the temporal lobe.

On examining this type, the question suggests itself, what may the function of this seven-layered cortex be? Extirpation experiments performed on the Monkey, especially those of Munk, seem to show that the muscular sense is located in the parietal lobe. But he points out two areas in the monkey showing this type, the destruction of which is not followed by any focal symptoms. Of these two cortical regions, one lies in front of the frontal sulcus, Harkenfurche, which undoubtedly corresponds to the frontal lobe in man, and the other is a small area at the posterior dorsal extremity

of the inter-parietal sulcus in front of the ape cleft. The observations in regard to this type in the human cortex do not agree and are not conclusive as Von Monakow points out. His discussion of the three cases of Vetter, Grasset, and one of his own, together with a later case of Starr and McCosh, permit us to conclude that it is fairly probable that in the monkey and man, the parietal area is in part the center for muscular sense, and as the sensory fibers (continuation of the lemniscus) run into the parietal lobe, the center for tactile, pain and temperature sense lies in part also there and probably extends to the anterior central gyrus.

In the frontal lobe, lesions have occurred accompanied by no focal symptoms, but in larger lesions confined to this region, peculiar changes in the individual's character have been observed, such as loss of the sense of morality and decency.

It has been found that all these areas show a nearly similar structure, namely, that of seven layers. In how far are we able to say they resemble each other functionally? Flechsig, basing his opinion upon his investigations of the development of the medullary sheaths, declared the parietal lobe to be one of four association centers; the other three being in the frontal lobe, in the region of the island of Reil, and in the temporal lobe. Flechsig also found, that the structure was the same in these different regions.

That the parietal lobe is only an association center, as is believed by Flechsig, seems to be incorrect, considering the clinico-pathological observations, and, according to the investigations of v. Monakow, the fibers continue from the lemniscus, extend principally into the parietal lobe. Nevertheless, the structure of the parietal cortex is similar to that of the frontal cortex.

The investigations of Golgi, Martinotti, Ramón y Cajal and Koelliker have shown, that in the layer of granule cells are found the cells of Martinotti, or that most of these granule cells are Golgi cells of type II. The Martinotti cells possess ascending axones, which are partly distributed in the outer layer of tangential fibers, and partly end in horizontal fibers before reaching the outer layer. We can, therefore, judging from the course of the axones, say that these cells do not send out centrifugal impulses.

The granule cells present the smallest numerical development in the motor area, but are found in great numbers in the parietal region, where they form a new layer. These cells are most numerous in the visual center, which undoubtedly is the most specialized center in the cortex of man and monkey.

These granule cells—judging from their anatomical structure, from their position in the cortex, and from the fact that they are found in greater numbers in those centers in the cortex, in which probably a greater number of centripetal impulses are received, while they occur in less numbers in those centers in the cortex, in which probably fewer centripetal impulses are received—probably are intermediate cells, which receive the centripetal impulses, and transmit them further by their ascending axones to the dendrites of the pyramidal cells (association and projectional cells), whence they reach their destination in a descending direction. Such impulses need

not come from the periphery, but may come from different regions of the cortex.

AUDITORY REGION.

This center is, judging from its structure, still a part of the seven-layer type, but as the localization is known with a fair degree of certainty, I will describe it, as others have done, as the auditory center.

Experimental investigation made on animals has shown that the temporal lobe is the seat of the auditory center. Thus, Munk has caused deafness by extirpating the temporal lobe in monkeys; and in man, on the basis of clinico-pathological observations, the auditory center was also located in the temporal lobe. Flechsig has followed the auditory fibers from the lower auditory centers directly to the transverse temporal gyri and to the superior temporal gyrus opposite the transverse gyri.

I have succeeded in preparing sections of the temporal lobe of the pteropus, cat, dog and monkey; but in the brain of the horse the stain of the sections was not a good one, and of the human brain the greater part of the temporal lobe was injured in preparing. I shall, therefore, be able to describe this, as well as several other portions of the cortex in man and the horse, only later on.

In the pteropus I have not been able to find any important differences from the general type; in the cat and dog indistinctly; but in the monkey I have found more plainly the following deviations from the contiguous parietal type. In the temporal lobe, principally two layers of cells increase in size—the granule layer and inner layer of polymorphous cells. One can also notice that in the inner layer of pyknomorphous pyramidal cells the pyramidal cells increase in number, this being not so conspicuous as the increase in the two aforementioned layers. The inner layer of pyknomorphous pyramidal cells adjoins a little more closely the granule-cell layer, and therefore the stripe of Baillarger is plainly visible between the inner layer of polymorphous cells and the inner layer of pyknomorphous pyramidal cells, thus suggesting a structure of eight layers. *The most striking feature of the cortex in the auditory region* is the enormous increase of cells in the granule cell layer, and in the inner layer of polymorphous cells, as compared with what is found elsewhere in the seven-layered cortex.

VISUAL CENTER.

The visual center has aroused the greatest interest on account of experimental and clinical observation. But up to the present, it still seems unsettled as to where it is located and how far it extends in the

cerebral cortex. The greatest number of experiments regarding the localization of this center in the cerebral cortex of animals have been made by Munk and Ferrier.

Ferrier considers himself justified in the belief that the visual center is situated in the angular gyrus.

According to *Munk* the visual center is found in the occipital lobe. In the dog it does not, however, extend as in the monkey to the occipital pole, but is believed by him to be situated more anteriorly and laterally.

Where is the visual center situated in the human cortex? Many investigators have endeavored to answer this question, but unfortunately the observations of these investigators have not in all cases led to the same results.

Henschen concludes that the visual center is confined exclusively to that region of the cortex which is situated around the anterior two-thirds of the calcarine fissure.

According to *Viallet* the visual center is found in the entire mesial surface of the occipital cortex, and does not extend over the convex surface of the hemisphere.

Seguin locates the visual center in the cuneus only.

Von Monakow believes that all facts necessarily speak in favor of the view that the visual area occupies besides the entire cortex of the occipital convolutions proper (cuneus, lingual lobe, gyrus descen. 01-03), also at least the posterior portion of the angular gyrus.

Other investigators, as *Ferrier*, *Gowers*, *Angelucci*, *Bianchi*, *Luciana*, and many others locate the visual center on the lateral as well as medial surfaces of the hemisphere.

It is evident, from all these differing opinions, that the visual center has not yet been located with certainty in the human cortex.

Structure.—The visual center in the cortex of the monkey has been determined beyond any doubt, and accurately located by the experiments of Munk. This sphere is situated in the occipital lobe behind the parieto-occipital fissure, or ape cleft. I have shown that anatomically this cortical sphere presents a typical and characteristic structure and can clearly be distinguished from adjoining areas. This sudden transition in structure from the parietal to the visual cortex is very striking and sharply marked. It is situated at the posterior margin of the ape cleft, in the depth of which the parietal type is still present.

A comparison of the cortex of the visual region with the adjoining cortex of the parietal region, reveals first of all the fact that the radiating fibers in the cortex do not appear in the visual region as is so plainly the case in the parietal region; and consequent upon that fact the first layer, or layer of tangential fibers, is not as wide here as in the parietal region. In addition, it may be noticed that everywhere in the visual

cortex an enormous number of granule cells appear. The second, third and fourth layers can at first sight be distinguished only indistinctly; but after a more careful examination of the field one does see that in the second layer the cells are set more closely together than in the third, and, owing to that again, the fourth layer becomes more conspicuous. Besides, there are in this fourth layer somewhat larger cells than in the second and third. Below the fourth layer one sees very plainly a layer of tangential fibers (the stripe of Baillarger), in which here and there are found large, fusiform, irregular cells. Then, below this layer, there is a very conspicuous and marked granule-cell layer. Then follows another layer of tangential fibers (inner stripe of Baillarger), in which again here and there are found large fusiform cells. Lastly, the inner layer, or layer of polymorphous cells, differs from the layer of polymorphous cells in the parietal and motor regions. It is almost twice as wide as in the above mentioned two types; is more sharply marked by the great number of cells found therein, and besides there are seen scattered here and there large, intensely stained, irregular cells which have been described by Meynert, who named them "solitary cells."

There are, therefore, six layers, if we consider the second, third and fourth layers as one. If we, however, count each one separately, then there are eight layers, as follows:

1. Layer of glia cells, or outer layer of tangential fibers.
2. Outer layer of polymorphous cells.
3. Layer of parapyknomorphous pyramidal cells (here, however, the cells have a more irregular shape).
4. Layer of granule cells, with somewhat large, irregular cells, among which are also found pyramidal cells.
5. Layer of tangential fibers (outer stripe of Baillarger), in which stripe irregular cells are found.
6. Layer of granule cells (inner layer).
7. Layer of tangential fibers (inner stripe of Baillarger).
8. Layer of polymorphous cells (inner layer).

In the dog and the cat the visual cortex is not plainly distinguishable from the remainder of the cortex. One can see, however, that it contains more granule cells than the parietal cortex. *Another fact which strikingly coincides with this is the corresponding lack of development of the lateral geniculate body in the brain of the dog and cat*

In the monkey, whose visual cortex is very highly developed, the development of the lateral geniculate body is correspondingly more marked than in the dog and cat. The lateral geniculate body of the human brain is like the monkey's.

It is very likely that the phylogenetic secondary sight centers (cortex) of the dog and cat have not relieved the phylogenetic primary sight centers (Thalamus and corpora quadrigemina) of their functions (in the sense of Steiner) to such a degree as in the brain of the monkey and man; hence the lack of development of the cortex and lateral geniculate bodies in dog and cat. It is possible that Goltz was not entirely wrong when he said that after the destruction of the entire cortex of the dog he could still see to some extent.

If this cortex, which presents such a characteristic structure in the monkey, and which is so sharply and so plainly differentiated from the adjoining parietal cortex, alone represents the visual cortex in the monkey, why should it not likewise alone represent the visual cortex in man? We may assume, with fair certainty, this to be the case. As the visual region can be sharply defined by its structure, its localization also ought to be definitely fixed. It has been demonstrated that the visual region nowhere passes over the margin of the longitudinal fissure onto the convex surface of the hemisphere, and that in the cases examined by myself, it assumes a pyramidal shape. The point of the pyramid lay in the anterior extremity of the calcarine fissure, the base posteriorly at the margin of the longitudinal fissure. The upper side of the pyramid projected as far as above the middle of the cuneus, the lower side down to the gyrus fusiformis and partly into it.

It is possible that the visual region varies in different brains. This variation may be due to the calcarine fissure, the course and extent of which is variable in different brains.

GENERAL.

In conclusion, a few general remarks on the arrangement of the cells of the cerebral cortex seem desirable.

In the human cortex, the seven-layer structure seems to coincide, according to its situation, with the association centers of Flechsig. He says:

“The plainly evident differences in the structure of the cortex of the central gyri, the calcarine fissure, the hippocampal gyrus, etc., have already been known for a long time, though strange to say they have not been sufficiently appreciated. On the other hand, it requires subtle research to demonstrate, for instance, differences between the cortex of the second frontal gyrus of the inferior parietal gyrus, of the second temporal gyrus, etc. If we measure the ganglion cells for their largest sizes, we obtain differences which can be expressed in figures, to be sure, but the type, as a rule, remains the same. We must, however, not overlook the fact that the border regions of sensory and association centers present occasionally

transitional types. The cortex of each sensory area is evidently composed of two differently constructed sets of layers:

1. The layers of specific elements (the spindle cells of the gyrus fornicatus, the granule cells of the visual sphere, the giant cells of the central gyri, the cylindrical cells of the auditory area, etc.); and

2. The elements of the association centers which spread over the entire cortex.

The association centers contain in their cortex elements only of the latter kind, but these layers also pass into sensory centers, so that the latter frequently present slight resemblances of the structure of the association centers.

I cannot agree to everything Flechsig says here. That in some places, as, for instance, in the motor area, giant cells and in the cornu ammonis characteristic cells are found, is, no doubt, plainly evident. But I cannot agree with him when he says, that in the visual area only, granule cells are found, or that in the auditory region only cylindrical cells are found, or that only in the anterior portion of the gyrus fornicatus are found the large characteristic spindle cells. The granule cells which he finds only in the visual region, are found almost everywhere in the cerebral cortex, not in equal numbers, however, as I have already pointed out. The cylindrical cells, which he claims to have found only in the auditory area, I have not been able to find in that part of the temporal lobe, of which I have obtained good specimens, and some of the sections have surely been made through the auditory area.

The main distinction between the different cortical regions does not appear so much in the individual cells as it does in the composition of the entire cortex. It is true that the large giant pyramidal cells are very characteristic of the motor area, and in the visual area those cells, which may be considered analogous to the pyramidal cells in the adjoining areas, are no more so distinctly pyramidal in shape. These modifications can probably be brought into accord with the following facts: I have already pointed out that in the visual area the cells are no more arranged in rows perpendicularly to the upper surface of the cortex, and that the fiber striations are no longer so conspicuous. We may conclude from this, that the radiating fibers are not developed so well in the direction of the outer layer of tangential fibers as in the stripes of Baillarger. In consequence, these two inner layers of tangential fibers, or stripes of Baillarger, are enormously developed. (The fifth and seventh layers of the eighth layer type.) This is followed by, or is the result of, the fact that the cells do not send one large dendrite to the periphery, giving them a pyramidal shape, but send many dendrites to the inner layers of the tangential fibers, for which reason they become more polymorphous.

One also sees in the innermost, or eighth layer, the solitary cells of Meynert, which were not found to be so large in any other place in the layer of polymorphous cells.

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DESCRIPTION OF FIGURES ON PLATES I, II, III AND IV.

- FIG. 1. Olfactory cortex of *man*.
- A. Layer of glia cells and outer layer of tangential fibers.
 - B. Outer layer of polymorphous cells, cell group formation.
 - C. Mixed cells.
 - D. Inner layer of polymorphous cells.
- FIG. 2. Olfactory cortex of the *Pteropus*.
- B. The characteristic formation of cell groups in the outer layer of polymorphous cells.
- FIG. 3. Olfactory cortex of the *dog's* brain.
- B. The characteristic formation of cell groups in the outer layer of polymorphous cells.
- FIG. 4. Cortex from the anterior portion of the gyrus cinguli (Limbic lobe), where the latter passes onto the convex surface of the hemisphere. (Presumably, the olfactory region in connection with the motor cortex.) *Horse's* brain.
- A. Layer of glia cells and outer layer of tangential fibers.
 - B. Outer layer of polymorphous cells, showing the characteristic cell group formation.
 - C. Layer of parapyknomorphous pyramidal cells.
 - D. Layer of pyknomorphous pyramidal or motor cells.
 - D'. Inner stripe of Baillarger.
 - E. Inner layer of polymorphous cells.
- FIG. 5. Cortex from the motor area of the *dog's* brain.
1. A. Layer of glia cells and outer layer of tangential fibers.
 2. B. Outer layer of polymorphous cells.
 3. C. Layer of parapyknomorphous pyramidal cells.
 4. D. Layer of large, or pyknomorphous pyramidal cells.
 5. E. Inner layer of polymorphous cells.
- FIG. 6. Cortex from the motor area of the brain of the *monkey*. (Anterior central gyrus.)
1. A. Layer of glia cells and outer layer of tangential fibers.
 2. B. Outer layer of polymorphous cells.
 3. C. Layer of parapyknomorphous pyramidal cells.
 4. D. Layer of large, or pyknomorphous pyramidal cells.
 5. E. Inner layer of polymorphous cells.

FIG. 7. Cortex from the motor area of the *human* brain.

1. A. Layer of glia cells and outer layer of tangential fibers.
2. B. Outer layer of polymorphous cells.
3. C. Layer of parapyknomorphous pyramidal cells.
4. D. Layer of large, or pyknomorphous pyramidal cells.
5. E. Inner layer of polymorphous cells.

FIG. 8. Cortex from the parietal lobe of the *human* brain.

1. A. Layer of glia cells and outer layer of tangential fibers.
2. B. Outer layer of polymorphous cells.
3. C. Layer of parapyknomorphous pyramidal cells.
4. D. Outer layer of pyknomorphous pyramidal cells.
5. E. Layer of granule cells.
6. F. Inner layer of pyknomorphous pyramidal cells.
7. G. Inner layer of polymorphous cells.

FIG. 9. Cortex from the parietal lobe of the *monkey*.

1. A. Layer of glia cells and outer layer of tangential fibers.
2. B. Outer layer of polymorphous cells.
3. C. Layer of parapyknomorphous pyramidal cells.
4. D. Outer layer of pyknomorphous pyramidal cells.
5. E. Layer of granule cells.
6. F. Inner layer of pyknomorphous pyramidal cells.
7. G. Inner layer of polymorphous cells.

FIG. 10. Cortex from the parietal lobe of the dog's brain.

1. A. Layer of glia cells and outer layer of tangential fibers.
2. B. Outer layer of polymorphous cells.
3. C. Layer of parapyknomorphous pyramidal cells.
4. D. Outer layer of pyknomorphous pyramidal cells.
5. E. Layer of granule cells. (Layer of small stellate cells, by Ramón y Cajal.)
6. F. Inner layer of pyknomorphous pyramidal cells.
7. G. Inner layer of polymorphous cells.

FIG. 11. Showing the transition from the seven-layer type to the visual area or eight-layer type in the *monkey*.

7. T.—Seven-layer type.
 8. T.—Eight-layer type, or visual region.
- The seven-layer type is as in Fig. 9.

Eight-Layer Type.

1. A. Layer of glia cells and outer layer of tangential fibers.
2. B. Outer layer of polymorphous cells.
3. C. Layer of parapyknomorphous pyramidal cells.
4. D. Layer of granule cells, with fusiform or irregular cells scattered here and there.
5. E. Inner layer of tangential fibers. (External stripe of Baillarger.)
6. F. Layer of granule cells.
7. G. Inner layer of tangential fibers. (Inner stripe of Baillarger.)
8. H. Inner layer of polymorphous cells.

FIG. 12. Showing the transition from the seven-layer type to the visual area, or eight-layer type in *man*.

7. T.—Seven-layer type.

8. T.—Eight-layer type, or visual region.

The layers are the same as in the monkey. Here one can see the solitary cells in the inner stripe of Baillarger.

FIG. 13. Frontal section through the lateral geniculate body of the *dog*, simple and slightly differentiated. The same in the *cat*.

FIG. 14. Frontal section through the lateral geniculate body of the *monkey*, very much more differentiated than that of Fig. 13. The lateral geniculate body in *man* has the same appearance as in the *monkey*.

DESCRIPTION OF PLATE IV.

Horizontal section through the hemisphere of the brain of the *monkey*, (*Macacus cynomolgus*).

C. F., Central Sulcus (Fissure of Rolando).

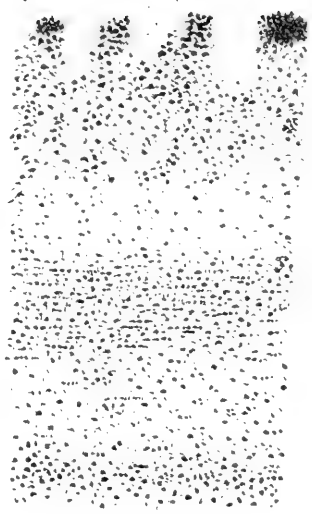
I. P. F., Interparietal Sulcus.

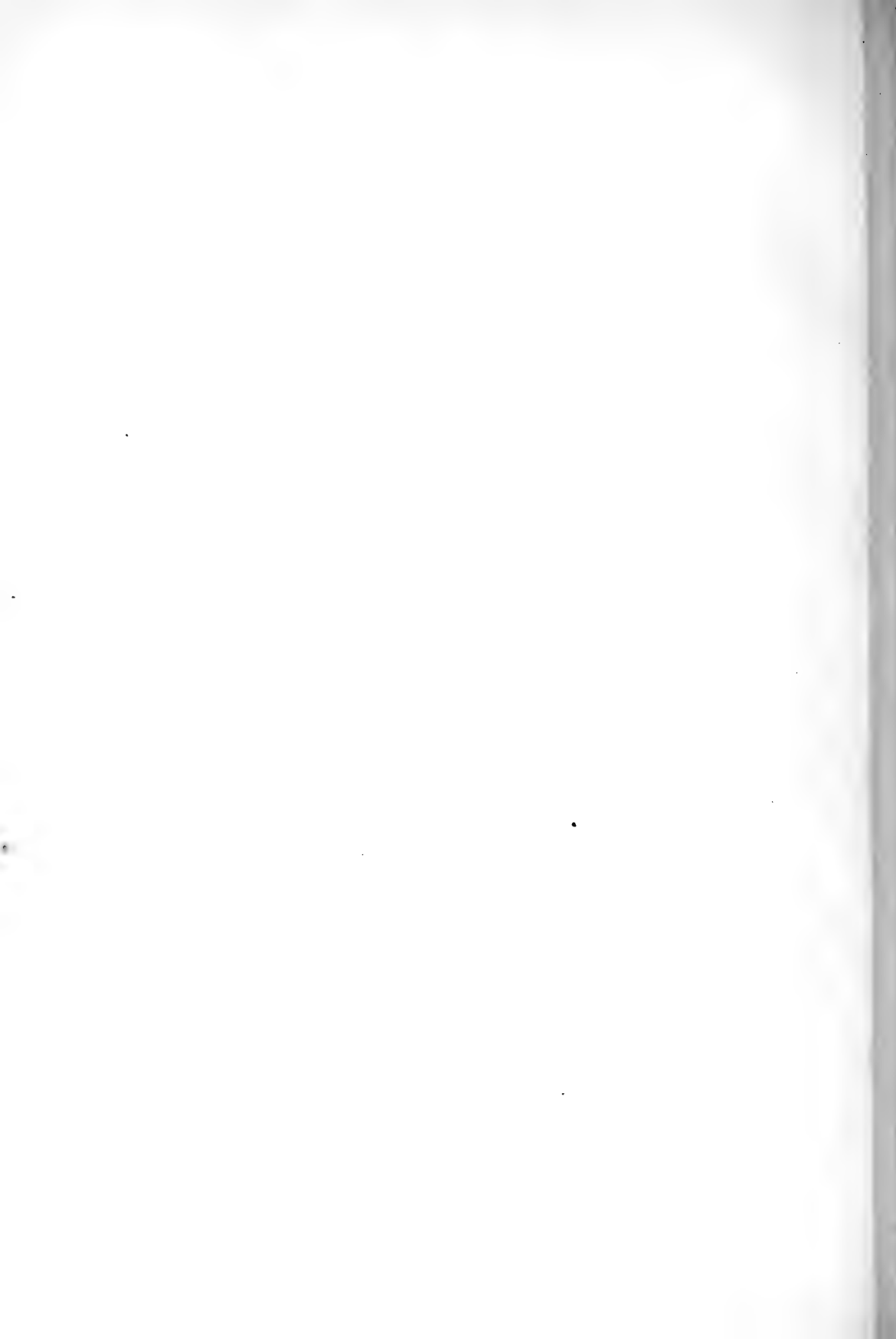
P. O. F., Parieto-occipital fissure.

C., Calcarine fissure.

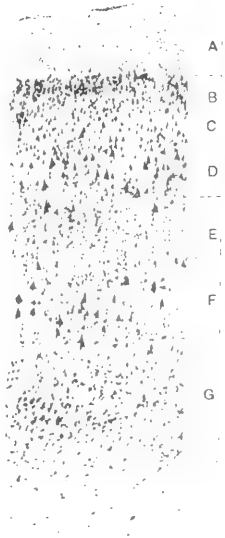
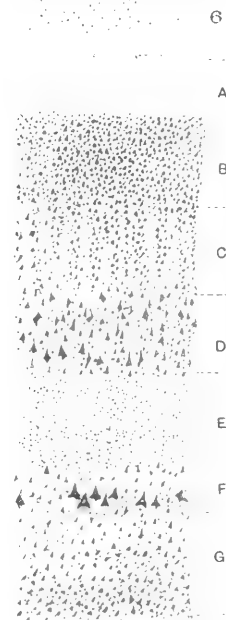
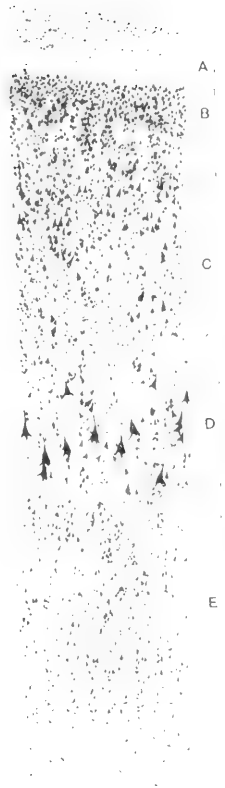
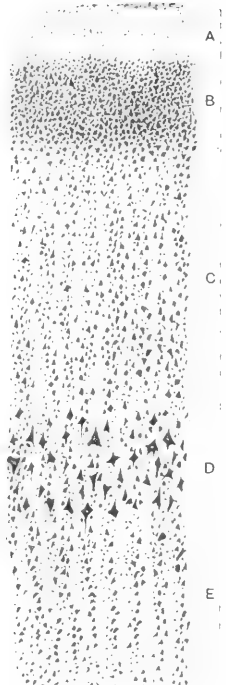
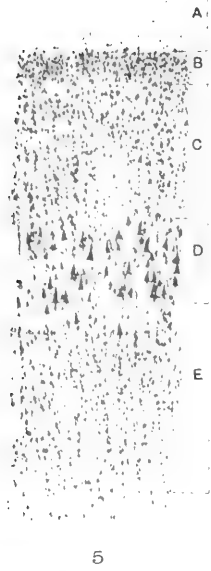
In front of the central sulcus, is the motor area; behind the central sulcus, up to the parieto-occipital fissure, is the region of the seven-layer type; behind the parieto-occipital fissure is the region of the eight-layer type, or visual cortex.







M. G. SCHLAPP.



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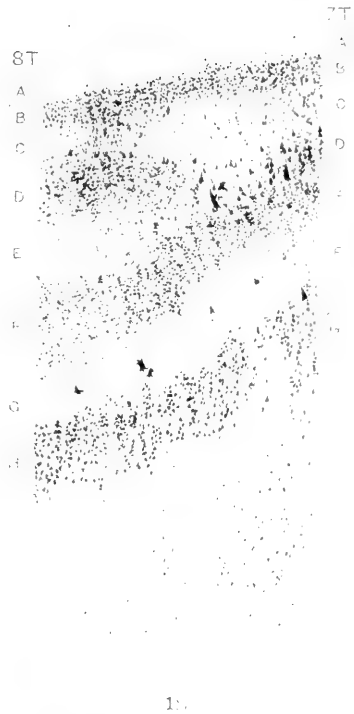
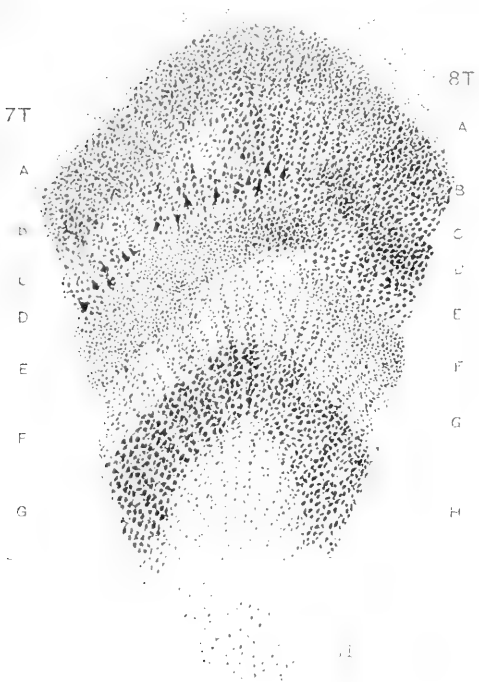
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M. G. SCHLAPP.

CORTICAL REGIONS OF THE BRAIN OF A MONKEY.

(For details refer to explanations of Plates and other Figures.)



THE DEVELOPMENT OF THE POSTCAVAL VEIN IN BIRDS.

BY

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WITH 10 TEXT FIGURES.

This subject was suggested to me by Professor C. F. W. McClure, under whose direction the investigation has been carried on. Professor McClure has shown the greatest kindness and interest during the time of my research in his laboratory, for which I am deeply grateful; and I take unusual pleasure in acknowledging my indebtedness to him for the most valuable assistance throughout my work.

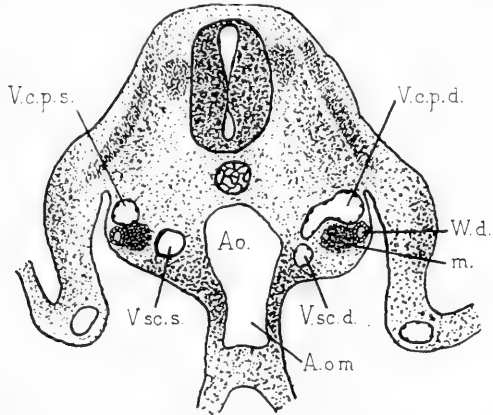
The development of the postcaval vein seems to have been much less investigated in birds than in the higher and lower forms, Hochstetter's articles being the only ones known to the writer as relating to this subject. In reptiles and mammals, on the other hand, the development of the postcava has been worked out in several different orders by a number of investigators. Hochstetter's (88, 93) observations on the chick are very accurate as recorded in his brief general description; a detailed account, however, is lacking. It will be the purpose of the writer in the following pages: (1) To corroborate Hochstetter's general observations on the development of the postcava in the chick; (2) to compare the mode of development in the chick with that in another form, viz.: the English sparrow; (3) to show that a portion of the efferent vessels of the primitive kidney (*Vv. subcardinales*) persists in birds as a part of the postcava in the adult, as Lewis (02) has recently shown to be the case in mammals.

The writer has reconstructed the venous system in a complete series of English sparrow (*Passer domesticus*) embryos, and also in series of chicks (*Gallus gallus*). The veins in the liver region have been reconstructed in wax. The burden of the work is based on the sparrow, but numerous comparisons have been made with the chick and the modes of development in the two forms found to be so very similar, differing in only a few unessential points, that figures taken from both are used for illustration. The accompanying figures (except Figs. 1 and 8) repre-

¹ Presented to the faculty of Princeton University for the degree of Ph. D.

sent actual reconstructions and are not in any sense diagrammatic. *The subcardinal system throughout the series of illustrations is marked with crosses in order to facilitate the tracing of that portion of the postcava through the successive stages of development up to the adult condition.*

The subcardinal veins in the sparrow and chick are first found as a series of unconnected vessels or islands situated on each side between the



² FIG. 1. Cross-section of a very young sparrow embryo, corresponding to a chick 60-70 hours; taken at the level of the A. omphalomesenterica. The asterisk (*) in Fig. 2 indicates the level of the above section. \times about 75.

mesonephros and the aorta (Fig. 1, V. sc. d and s). This is at a very early stage, between the 60th and 70th hour in the chick, when the germ-layers are still flat except in the head region. In Fig. 2 (V. sc. d. and s.), the above mentioned islands are shown; on the right is seen a communication between the postcardinal and subcardinal. These islands subsequently fuse to form continuous vessels in which the bilateral symmetry is complete. This fusion, however,

may not be accomplished until after the proximal part of the postcava is developed.

The development of the subcardinals seems to correspond to the development of the mesonephros: as the mesonephros becomes larger the veins

² LETTERING OF ALL TEXT FIGURES.—In the abbreviations *d* and *s* always refer to dextra and sinistra respectively.

a. (Fig. 6), mesonephric veins. *A. i.* (*d* and *s*), *A. iliaca*. *Ao.*, aorta. *A. o. m.*, *A. omphalomesenterica*. *A. sc.* (*d* and *s*), *A. sciatica*. *A. u.* (*d* and *s*), *A. umbilicalis*. *b.* (Fig. 5), vessels enclosed within ventral side of mesonephros. *c.*, cranial portion of the right subcardinal vein. *d.* (Fig. 7), anastomosis between posterior ends of postcardinals. *D. C.* (*d* and *s*), ductus Cuvieri. *D. V.*, ductus venosus. *ki.* (Fig. 8), kidney. *m.*, mesonephros. *s. g.* (Fig. 8), sexual gland. *Ur.*, ureter. *V. c.* (Fig. 7), *V. coccygomesenterica*. *V. c. i.*, *V. cava inferior* (*V. postcava*). *V. c. i. H.* (Fig. 7), *V. postcava, pars hepatica*. *V. c. i. SC.* (Fig. 7), *V. postcava, pars subcardinalis*. *V. c. p.* (*d* and *s*), *V. cardinalis posterior*. *V. c. p.* (*d* and *s*) (*V. i. i.*), *V. cardinalis posterior* (*V. iliaca interna*). *Vv. g.*, *Vv. genitaliae*. *V. h. r.*, *V. hepatica revehens*. *V. i. c. d.* (Fig. 9), *V. iliaca communis*. *V. i. e.* (*d* and *s*), *V. iliaca externa*. *V. i. l.* (*d* and *s*), *V. intervertebralis lumbalis*. *V. r. m.* (*d* and *s*), *V. renalis magna*. *V. s. s.*, *V. sciatica*. *V. sc.* (*d* and *s*), *V. subcardinalis*. *Vv. sr. s.*, *Vv. suprarenales*, *V. u.* (*d* and *s*), *V. umbilicalis*. *W. d.*, Wolfian duct. *x.* (Fig. 10), dorsal portion of loop around umbilical artery.

increase in length and calibre, and in the earlier stages they are found to extend the full length of this organ. A number of direct communications between the postcardinal and subcardinal veins are present, which pass between the mesonephros and the aorta. In Fig. 4 (sparrow, corresponding to a chick of 90 hours) three of these communications are seen on each side. So long as the mesonephros is small these anastomoses are of considerable size and importance, but as this organ develops they are broken up in the mesonephric circulation, and cease to exist as well-defined vessels. However, the subcardinals may remain in communication, at their anterior ends, with the postcardinals even after the postcava appears (Figs. 4 and 5). In the chick the writer has observed other direct connections between the subcardinals and postcardinals in the form of well-defined vessels enclosed within the ventral part of the mesonephros. These vessels are shown in Fig. 5 (b) (chick, 90 hours) lying at the side of the subcardinals and ventral to the postcardinals. No particular importance is to be attached to them since they, like the other anastomoses between the postcardinals and subcardinals mentioned above, are subsequently broken up in the circulation through the mesonephros. Soon after their first appearance the subcardinals receive blood from the mesonephros through a number of small branches which enlarge as the above organ enlarges. In the figures of the early stages these branches have been omitted to avoid confusion.

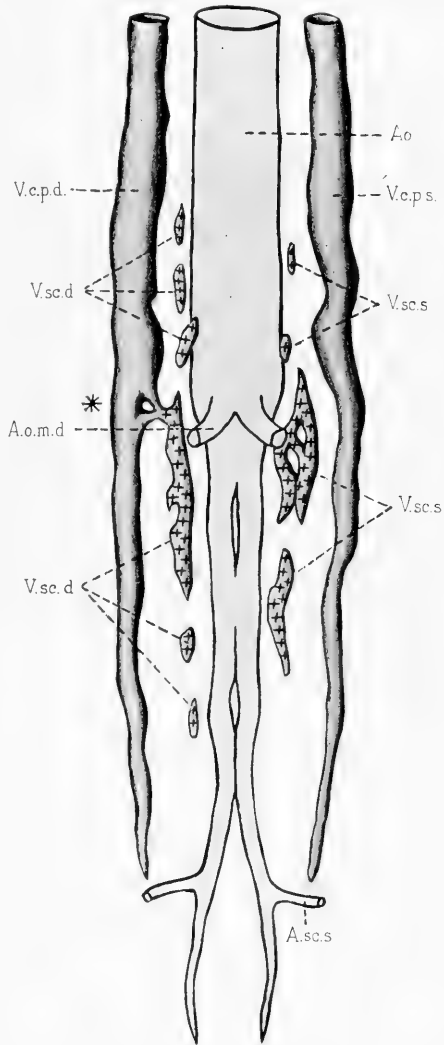


FIG. 2. Reconstruction of the venous system of a very young sparrow embryo, corresponding to a chick of 60-70 hours. Ventral view. $\times 75$. (Explanation of lettering on page 284.)

In his article on the development of the postcaval vein in mammals Lewis (02) has attempted to explain the presence of the subcardinals on the ground that the course of the blood through the postcardinals is impeded by the mesonephric tubules and the recurrent bend of the duct of Cuvier, and hence these vessels are the result of an attempt of the postcardinals to disentangle themselves from the mesonephros. He has apparently overlooked the fact that the subcardinal veins have their ancestors, so to speak, in similar structures in birds and reptiles, which have been described by Hochstetter and others under the name of the efferent veins of the primitive kidney, and consequently have not been called into existence in mammals by any physiological reason. Furthermore, Lewis states that the subcardinals are tributaries of the postcardinals, formed from certain branches of the latter veins which pass ventrad between the mesonephros and the aorta. However this may be in mammals, it is certainly not the case in the chick or sparrow. As has been stated earlier in this article, the subcardinals arise as unconnected vessels or islands, which are without a doubt independent structures; and the connections with the postcardinals are formed later and secondarily.

It is a noteworthy fact that in birds, at least, the subcardinal veins appear and attain a considerable size before the postcava begins to develop. This is plainly seen in Figs. 4 and 5, where the postcava (V. c. i.) is in its incipient stage, and in Fig. 4 is composed of merely a few islands situated in the anlage of the liver and the caval mesentery.

The writer has carefully reconstructed in wax the veins in the liver region and has found almost a perfect agreement with Hochstetter's description and illustrations. However, to clear up some slight doubt in regard to the exact point where the postcava joins the ductus venosus, it has been thought best to insert a figure and brief description of the conditions found in the sparrow at a very early stage of development (Fig. 3, sparrow corresponding to a chick of 90 hours). As shown in this figure the right and left omphalomesenteric veins fuse at a very early stage to form the ductus venosus (D. V.). The sinus venosus (S. V.), which is virtually a continuation of the ductus venosus, is formed by a union of the latter vessel and the two ducts of Cuvier (D. C. d and s), and empties into the right auricle of the heart. The right and left umbilical veins (V. u. d and s) join the right and left ducts of Cuvier respectively some distance from the opening of the latter vessels into the sinus venosus. The postcaval vein (V. c. i.) at this stage has not joined the ductus venosus. But its point of connection, as shown by a closely succeeding stage, is found to be on the dorsal side of the ductus venosus just caudal

to the union of the latter vessel with the ducts of Cuvier (indicated by an asterisk in Fig. 3).

A marked difference is seen here between the relations of the proximal end of the postcava in reptiles, birds and mammals. While in birds it arises as a branch of the ductus venosus (Hochstetter, 88, 93), in reptiles it arises either as a branch of the right omphalomesenteric vein (Lacerta) or as a branch of the union of the latter

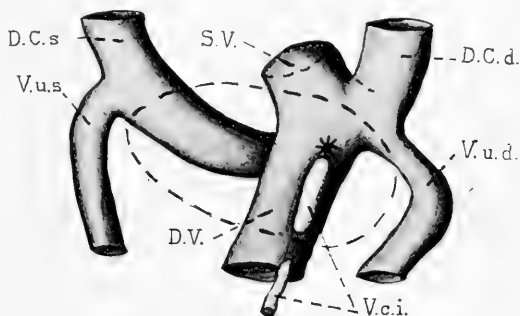


FIG. 3. Drawn from a wax reconstruction of the veins in the liver region of a sparrow embryo; taken from the same specimen as Fig. 4. Outline of liver dotted. Dorsal view. \times about 55. (Explanation of lettering on page 284.)

vein with the right umbilical (Tropidonotus) (Hochstetter, 92). In Echidna (Hochstetter, 96) the right V. hepatica revehens forms the common stem of the postcava and the ductus venosus Aranzii. In the higher mammals thus far observed it arises from the V. hepatica revehens communis (Hochstetter, 93, Lewis, 02).

The postcaval vein in the chick first appears about the 90th hour of incubation, as Hochstetter has observed, though the writer has noticed it in the initial stages somewhat earlier. The liver at this time is composed of merely a few tubules surrounding the ductus venosus. Among the tubules are to be seen a number of small venous islands, or hepatic sinusoids, as Minot has called them. The hepatic portion of the postcava is the result of a fusion of some of these sinusoids lying dorsal to the ductus venosus, that is, in the dorsal part of the right lobe of the liver. At this stage there is also found a series of venous islands extending through the caval mesentery, and ending on the median side of the right mesonephros a short distance anterior to the origin of the A. omphalomesenterica. These islands are in the direct line of the future continuous postcaval vein, and by their fusion, which takes place soon after their first appearance, the portion of the postcava between the liver and the mesonephros is formed.

In his description of the development of the postcava in the chick Hochstetter (88, 93) does not state the fact that it is derived through a fusion of islands in the caval mesentery and through the fusion of a number of hepatic sinusoids. In his work on the mammals, however, he indicates that the postcava arises in some such manner ("durch Erweiterung

und Zusammenfliessen schon vorhandener Venenbahnen," 93, p. 568). Thus it appears that the early formation of the hepatic portion of the postcava takes place on the same principle in both birds and mammals.

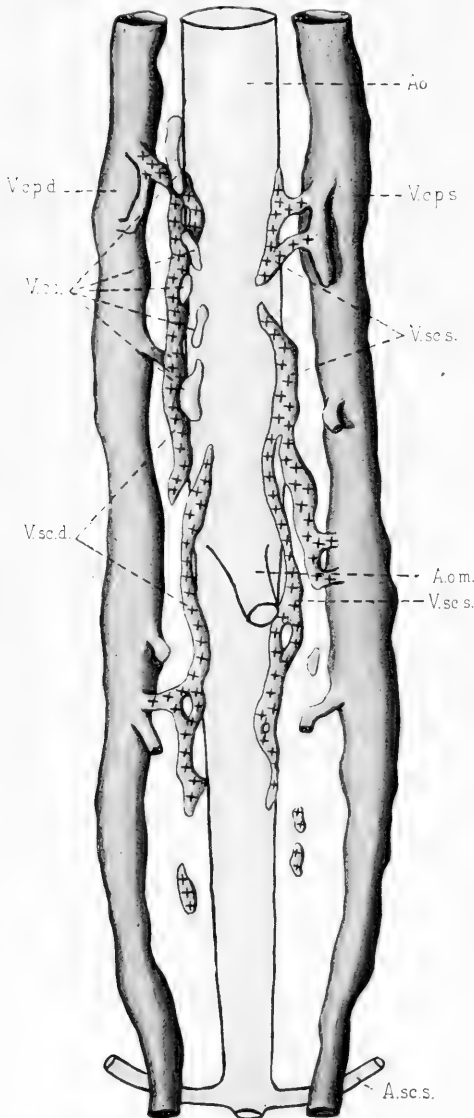


FIG. 4. Reconstruction of the venous system of a sparrow embryo, corresponding to a chick of about 90 hours. Ventral view. $\times 75$. (Explanation of lettering on page 284.)

(V. c. i.), which, however, has not yet joined the ductus venosus, but ends in the hepatic sinusoids. This latter condition is short

The above mentioned islands of the postcava are shown in Fig. 4 (V. c. i.). The anterior island is of sinusoidal origin; the others are situated in the caval mesentery, extending from the liver in front to the median side of the right mesonephros some distance anterior to the origin of the A. omphalomesenterica. At this stage the islands of the subcardinals have not yet undergone a complete longitudinal anastomosis. In Fig. 5, which represents a slightly older stage than Fig. 4, the subcardinal on each side is a continuous vessel extending from a point just caudal to the duct of Cuvier almost to the level of the umbilical arteries—in other words the full length of the mesonephros. At their anterior ends both subcardinals join the postcardinals; all other direct connections between the former and latter veins have been broken up in the mesonephric circulation, with the exception of the vessels described above as situated in the ventral part of the mesonephros (Fig. 5, b). Here the islands of the postcaval vein have also fused to form a continuous vessel

lived, for in an embryo but slightly older than that represented in Fig. 5 the postcava joins the ductus venosus. The postcava after it makes its exit from the caval mesentery joins the right subcardinal some distance in front of the origin of the A. omphalomesenterica. Thus the posterior portion of the right subcardinal becomes the direct continuation of the postcava, and a renal portal system is established on the right side. Soon after this, however, an anastomosis takes place between the two subcardinals ventral to the aorta and caudal to the A. omphalomesenterica, and by this means the blood from the left subcardinal also passes into the postcava. This brings about a complete renal portal system. The anastomosis between the two subcardinals marks the future bifurcation of the adult postcava.

As the mesonephroi enlarge and occupy a considerable portion of the body cavity they grow around the subcardinals, which thus become enclosed within their median side and are carried somewhat ventrad. This brings about a closer relation between the mesonephroi and the subcardinal veins. In consequence of this closer relation the latter vessels increase in size and receive blood from the mesonephroi through large branches, as indicated in Fig. 6 (a) (chick of 5 days' incubation). With the increased amount of blood from the mesonephroi and the en-

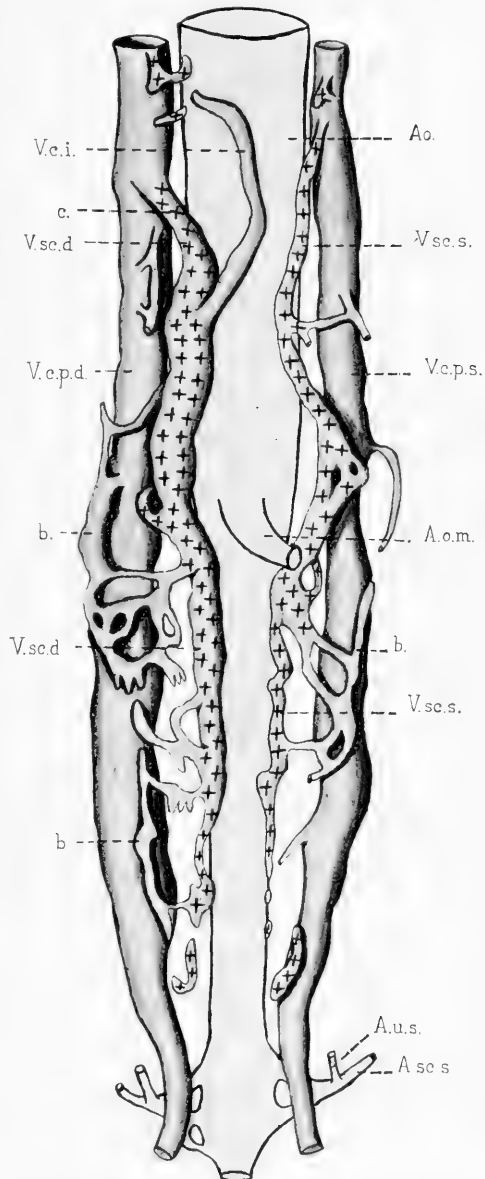


FIG. 5. Reconstruction of the venous system of a chick of 90 hours. Ventral view. $\times 50$. (Explanation of lettering on page 284.)

largement of the subcardinal veins the stem of the postcava attains corresponding proportions. At the end of the 5th day of incubation the subcardinal system has reached its height of development, *and at this stage is seen the immense importance of the subcardinal veins in the development of the postcava. They form the entire efferent system,* and moreover a great quantity of blood passes through the renal portal system, for the anterior ends of the postcardinals by this time have become much diminished in size and are unable to carry a very large proportion of the blood to the duct of Cuvier.

The significance of these subcardinal veins in birds is even better appreciated by a glance at the conditions found in adult reptiles, where the efferent veins of the renal portal system persist in part as paired vessels which connect anteriorly with the unpaired portion of the postcava (Hochstetter, 93). *The efferent vessels in birds are undoubtedly the homologues of the paired portion of the postcava in reptiles.* In mammals also Hochstetter (93, 96) has described a pair of vessels running on the median side of the mesonephros, which unite with the stem of the postcava; McClure has observed the same conditions in Didelphys and Lewis (02) has described these vessels in the rabbit under the name of the subcardinal veins. *The subcardinals in birds are certainly homologous with the vessels in mammals described by the above investigators,* even though a true renal portal system is not established in the higher mammals. Hochstetter has already mentioned the homology of the subcardinal veins, running through the three classes of animals mentioned above, but it has not been brought out with sufficient emphasis.

Fig. 6 (chick of 5 days' incubation) shows the large above-mentioned anastomosis between the two subcardinals caudal to the A. omphalomesenterica. Note the great relative size of the subcardinal veins and the branches (a) from the mesonephroi emptying into them; there are also many smaller branches which have been omitted in the reconstruction. The anterior ends of the postcardinals are seen to be considerably diminished in size. The stem of the postcava has become a relatively large vessel, for it now carries a great quantity of blood to the heart.

The subcardinal veins have been indicated by crosses throughout the series of illustrations; and a comparison of Figs. 2, 4, 5 and 6 will enable one to trace clearly the progressive development of the subcardinal system up to its height at the end of the 5th day of incubation in the chick, and furthermore will enable one to appreciate the vast importance of the subcardinal system in the earlier stages of development.

At about the stage from which Fig. 6 was taken (5th day of incubation) the writer found a most interesting exception to the general plan of development of the subcardinal system in birds, which exception shows a striking combination of the conditions described by Hochstetter in reptiles and Echidna. Anterior to the origin of the A. omphalomesenterica and ventral to the aorta there is present a large anastomosis between the right and left subcardinals, just caudal to the point where the postcava joins the right subcardinal. Such a remarkable similarity to the conditions found in the earlier stages of reptilian development is certainly unusual. Then in addition to the usual anastomosis between the two subcardinals caudal to the A. omphalomesenterica there is also another large anastomosis about midway between the A. omphalomesenterica and the A. iliaca, which reminds one very much of the state of affairs in Echidna, though the fusion takes place to a less degree than in the latter. Having found only this one example in all the specimens examined it would be going too far to assert that the above conditions in the chick are more than accidental, despite the fact that they exhibit such a striking resemblance to reptiles and Echidna.

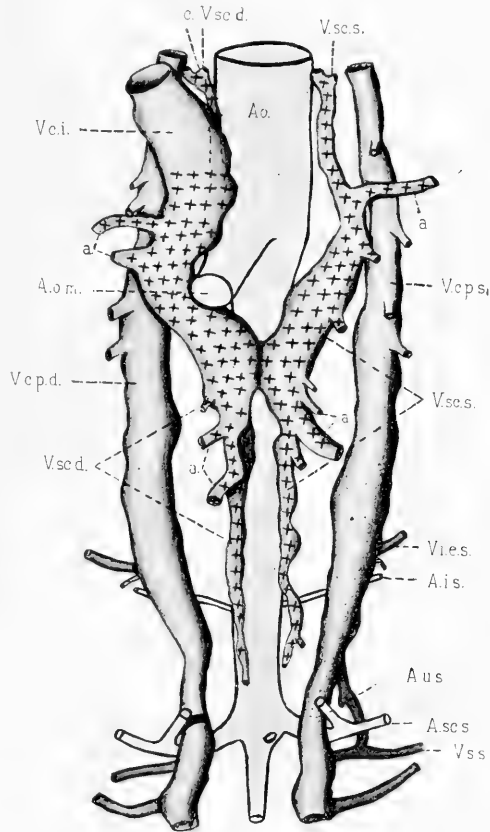


FIG. 6. Reconstruction of the venous system of a chick of 5 days. Ventral view. $\times 37$. (Explanation of lettering on page 284.)

After the 5th day of incubation the subcardinals begin to decrease in importance, for with the gradual atrophy of the mesonephroi they have less and less of the function of efferent vessels to perform. The portion of each vessel caudal to the anastomosis becomes shorter; the anterior end of the left vein diminishes while the corresponding part of the right disappears entirely.

During the process of development the right lobe of the liver enlarges and grows backward, and thus includes the portion of the postcava which was at first situated in the caval mesentery and which is designated in Fig. 7 as *pars hepatica* (V. c. i. H.).

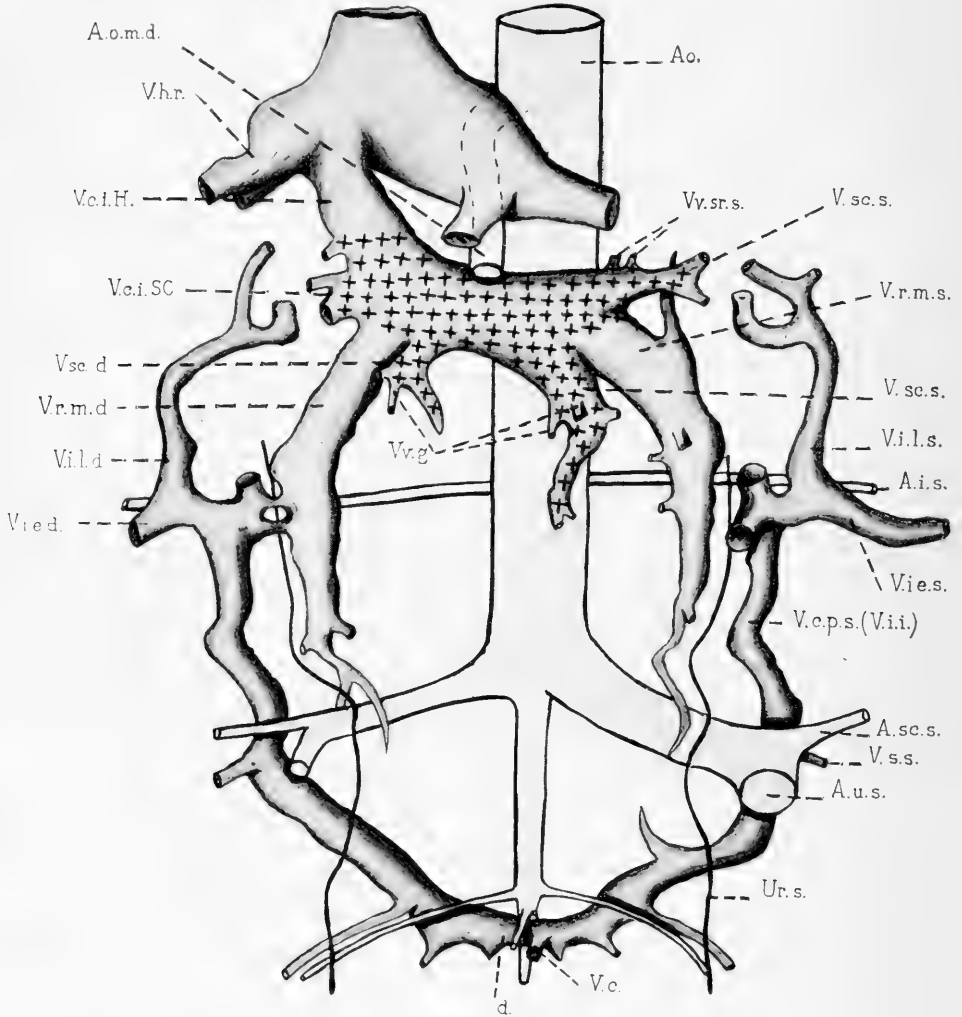


FIG. 7. Reconstruction of the venous system of a sparrow embryo, corresponding to a chick of about 14 days. Ventral view. $\times 30$. (Explanation of lettering on page 284.)

In Fig. 7 (sparrow, corresponding to a chick of 14 days' incubation) the subcardinal portion of the postcava (V. c. i. SC.) is seen to be relatively small, the mesonephros having diminished to an unimportant

organ on each side. Practically all that now remains of the subcardinal system is the previously described anastomosis caudal to the A. omphalomesenterica. From this time on the subcardinal portion of the postcava diminishes in size still more as it approaches the adult stage. In the adult the subcardinal system has diminished to a small part of the postcava just proximal to the bifurcation, including the area into which the genital and suprarenal veins open.

Our attention will now be directed to the development of the genital and suprarenal veins which have been mentioned in the above paragraph. About the 5th day of incubation in the chick the suprarenal bodies are found lying between the aorta and the mesonephros on each side, dorsal to the subcardinal vein and anterior to the large anastomosis. Soon after this the sexual glands appear as elongated bodies situated on the median wall of the mesonephros and medial or ventral to the subcardinals. Both sets of organs give blood to the subcardinals.

As has been mentioned before, the portion of the right subcardinal vein cranial to the point where the postcava joins the former vessel (cranial portion of the right subcardinal, marked *c* in Figs. 5 and 6) atrophies (Fig. 6) and finally disappears (Fig. 7). So far as the writer has been able to determine, the suprarenal body of the right side does not at any period of development give branches to the cranial portion of the subcardinal. In Fig. 7 (sparrow, corresponding to a chick of 14 days' incubation) the subcardinal portion of the postcava itself lies embedded in the ventral side of the suprarenal body and receives branches coming directly from the organ. Thus the right suprarenal vein is really a subcardinal derivative, inasmuch as the stem of the postcava is of subcardinal origin, but it is not a subcardinal derivative in the same sense as the left suprarenal and genital veins.

On the left side, on the other hand, the suprarenal veins are, from the beginning, branches of the anterior end of the subcardinal; and as the anterior end of the left mesonephros gradually disappears the corresponding portion of the subcardinal becomes smaller, and finally in the adult stage the suprarenal veins of the same side form the only portion that persists, and these open into the pars subcardinalis of the postcava. In Fig. 7 the suprarenal veins (*Vv. sr. s*) are seen as branches of the anterior end of the left subcardinal vein, and in Fig. 9 (adult) as branches of the subcardinal portion of the postcava. The development of the suprarenal veins in birds, as described above, seems to agree with the conditions found in mammals as described by Hochstetter.

As has been stated, the sexual glands are at first elongated bodies.

While the glands are in their earlier stages of development they may give blood to the subcardinals through several small branches. As the glands become shorter, approaching the adult condition, some of these small branches disappear, and finally one or two remain on each side which ultimately persist as the spermatic or ovarian veins emptying into the pars subcardinalis of the postcava just cranial to the bifurcation. In Fig. 7 the genital veins (Vv. g.) are seen as branches of the small remaining part of the posterior ends of the subcardinals.

Hochstetter (88, 93) advanced the idea that the spermatic or ovarian veins in birds were formed from the subcardinals (efferent veins of the primitive kidney), though he did not make a positive statement and gave no illustrations. *There certainly can be no doubt that the genital and at least the left suprarenal veins are derived directly from the subcardinals.*

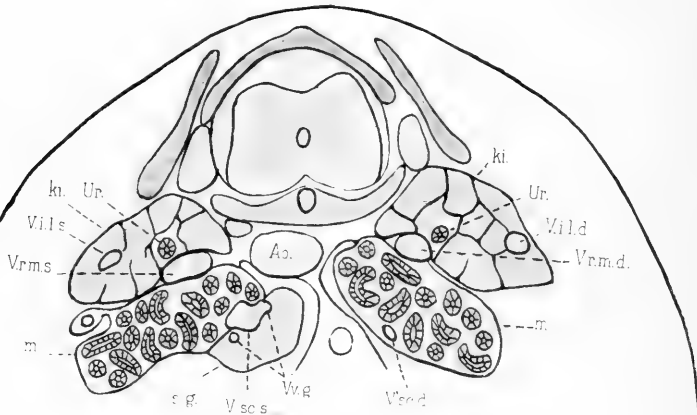


FIG. 8. Outline sketch of a cross-section through a sparrow embryo, corresponding to a chick of 14 days; taken a short distance caudal to the bifurcation of the postcava. Showing relative position of the great renal veins. \times about 20. (*Explanation of lettering on page 284.*)

Fig. 8 shows the adult conditions in the postcaval vein. It is rather difficult to state with certainty to just what extent the subcardinal system persists. The writer has carefully considered the matter and has indicated by crosses a small portion proximal to the bifurcation into which empty the suprarenal (V. sr. s) and the spermatic veins (Vv. g.). *It may be safely stated, however, that the subcardinal system persists at least as a small portion of the postcava proximal to the bifurcation, which portion, as stated above, is marked by crosses. Furthermore the genital and left suprarenal veins are true subcardinal derivatives and empty into the subcardinal portion of the postcava.*

In Fig. 7 a pair of important vessels are shown which have not been present in the preceding illustrations. These are the Vv. renales magnae (V. r. m. d and s), the efferent veins of the permanent kidney. There are also two other smaller vessels which appear for the first time in this figure—the Vv. intervertebrales lumbales (V. i. l. d and s).

Before the permanent kidney appears the anterior ends of the post-cardinal veins have atrophied and disappeared. The kidney begins to develop about the 6th day of incubation and is situated dorsal to the mesonephros and lateral to the aorta and chorda. As soon as the head end develops the V. intervertebralis lumbalis appears as a small vein enclosed among the tubules, which empties into the postcardinal at the same level as the external iliac vein. As the head end of the kidney enlarges this vessel becomes larger and in Fig. 7 (V. i. l. d and s) is seen to be a vein of considerable importance. Moreover, the segmental (vertebral) veins which previously emptied into the anterior end of the postcardinal now open into this new vessel. It functions as the efferent vein of the head end of the kidney (Fig. 9, V. i. l. s.).

After the kidney has attained a considerable size still another vessel, the V. renalis magna, is developed on each side as a branch of the subcardinal system at the level of the large anastomosis; but it is not included in the subcardinal system. This vein runs laterad from the anastomosis till it reaches the dorsal side of the mesonephros, that is, it reaches a position on the median side of the kidney. As the kidney develops the above vein becomes more or less enclosed within its ventral side (Fig. 8) and growing caudad, finally extends to the level of the umbilical artery. While the mesonephros persists it receives a small amount of blood from this organ; but its more important function is to carry blood from the kidney to the postcava: it is the large efferent vein of the kidney. When the great renal veins have reached an advanced stage of development, as in Fig. 7, they anastomose with

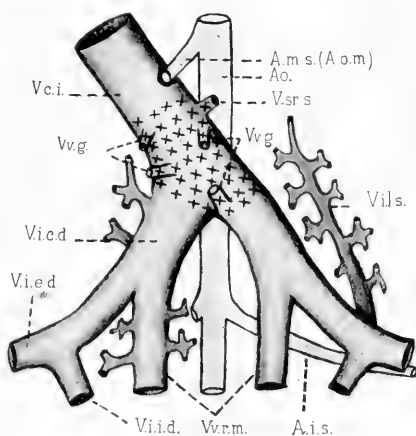


FIG. 9. Region of the bifurcation of the postcava in the adult domestic fowl, showing the part of the postcava which is formed from the subcardinal system, and the relations of the common iliac and great renal veins. The right V. intervertebralis lumbalis is omitted and instead the small efferent renal veins are shown. Ventral view. Natural size. (Explanation of lettering on page 284.)

the postcardinals at the level of the external iliac veins. They approach so near the postcardinals that the walls break through and there then exists a direct channel on each side from the postcardinal to the postcava. Thus the renal portal system is destroyed. It is interesting to note, as Hochstetter has done, that a renal portal system of the permanent kidney also exists before the anastomosis between the great renal veins and the postcardinals; for more or less blood is given to the kidneys by the postcardinals which in turn is carried to the postcava by the great renal veins. But as soon as the above anastomosis takes place this renal portal system is destroyed, as well as that in the mesonephroi.

In Fig. 7, on the right side, the anastomosis between the great renal vein and the postcardinal is shown; the one on the left has not yet taken place. As a general rule they occur about the 14th or 15th day of incubation in the chick and at a corresponding stage of development in the sparrow. After these anastomoses the adult condition is practically reached and it only remains for a few changes in relative position to take place. In Fig. 7 the anastomosis is seen to be very short; but during further development it lengthens out to a considerable extent so that in the adult condition it forms about the distal half of the common iliac vein. What was originally the proximal end of the great renal vein forms the proximal half of the common iliac vein. (Compare Fig. 9).

There remain to be described two important changes which take place in the region of the posterior portion of the postcardinal veins: (1) About the 6th day of incubation in the chick an anastomosis between the two postcardinals is found far back in the tail-region, which lies ventral to the caudal aorta. As the tail-region shortens up in the process of development the anastomosis is gradually pushed forward till it reaches the normal position just caudal to the posterior lobe of the kidney about the 11th day. In the meantime the *V. coccygomesenterica* has developed and on the 8th day it is seen as a small vessel coming from the dorsal surface of the hind gut. It joins either the anastomosis directly or the one or the other postcardinal anterior to the anastomosis; but in the latter case it finally joins the anastomosis itself. In the adult it communicates directly with the hepatic portal system (vide Fig. 7, d, *V. c.*).

(2) The other change takes place in the postcardinal veins in relation to the umbilical arteries. In the early stages of development the postcardinals are found lying ventral to the umbilical arteries (Figs. 4 and 5), which condition is characteristic in reptiles. About the 5th day of incubation in the chick, and at a corresponding stage of development in the sparrow, a new venous channel is found dorsal to the

umbilical artery, which seems to be *a sort of anastomosis between the proximal ends of the neighboring vertebral veins* (Fig. 10, x, sparrow, corresponding to a chick at the end of the 5th day). This dorsal channel increases rapidly in size and by the following day is as large as the ventral channel. The latter channel decreases and, as a general rule, disappears about the 7th day, thus leaving the postcardinal vein on the dorsal side of the umbilical artery. (Compare Figs. 4, 5, 6, 10 and 7.)

These observations were also made by Hochstetter (93) in the chick. In his article on the reptiles

(93, p. 495) he explains the formation of the loop around the umbilical artery in birds on a mechanical basis by saying that the large umbilical artery (in birds) exerts a pressure on the dorsal side of the neighboring portion of the postcardinal vein, which bends the vein downward. The blood then seeks a more direct course which results in the formation of a collateral channel dorsal to the artery, while the ventral portion of the loop then disappears.

There is a possibility that Hochstetter's explanation would suffice in some instances in birds where the loop is very short; but the writer has found cases where the loop is very much extended antero-posteriorly; in one case, indeed, it extended almost from the level of the external iliac veins to the anastomosis, described above, caudal to the posterior lobe of the kidney. Furthermore, McClure (00, 02) has described variations in *Didelphys* where the veins may be dorsal to the artery, or ventral to the artery, or both dorsal and ventral to the artery; and certainly no mechanical principle is adequate to account for such extreme variations, where a similar loop formation is present in the embryo. It seems to the writer that the explanation of the formation of the loop around the umbilical artery is to be sought in some underlying physiological principle.

RÉSUMÉ.

Up to the end of the 5th day of incubation the subcardinal system increases in size and importance; from the 5th day on it decreases up to the adult stage, where it persists only as a small portion of the stem of the postcava and the genital and suprarenal veins.

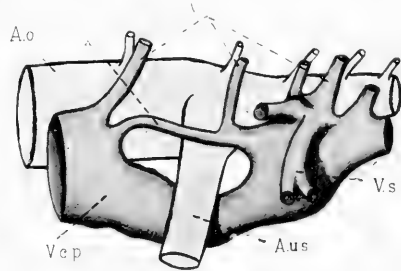


FIG. 10. Reconstruction from a sparrow embryo, corresponding to a chick of 5 days. Showing venous loop around the umbilical artery. Left side. $\times 75$. (Explanation of lettering on page 284.)

The following table shows a comparison of the development of the stem of the postcava in birds with that described by Lewis in mammals:

Rabbit.	Birds.				
V. hepatica revehens communis.	<table border="0" style="display: inline-table; vertical-align: middle;"> <tr> <td style="font-size: 3em; vertical-align: middle;">}</td> <td>Sinus venosus.</td> </tr> <tr> <td style="font-size: 3em; vertical-align: middle;">}</td> <td>Proximal end of ductus venosus.</td> </tr> </table>	}	Sinus venosus.	}	Proximal end of ductus venosus.
}	Sinus venosus.				
}	Proximal end of ductus venosus.				
Hepatic sinusoids.	<table border="0" style="display: inline-table; vertical-align: middle;"> <tr> <td style="font-size: 3em; vertical-align: middle;">}</td> <td>Hepatic sinusoids.</td> </tr> <tr> <td style="font-size: 3em; vertical-align: middle;">}</td> <td>Independent islands in caval mesentery.</td> </tr> </table>	}	Hepatic sinusoids.	}	Independent islands in caval mesentery.
}	Hepatic sinusoids.				
}	Independent islands in caval mesentery.				
Right subcardinal.	<table border="0" style="display: inline-table; vertical-align: middle;"> <tr> <td style="font-size: 3em; vertical-align: middle;">}</td> <td>Right subcardinal and anastomosis between right and left subcardinal.</td> </tr> </table>	}	Right subcardinal and anastomosis between right and left subcardinal.		
}	Right subcardinal and anastomosis between right and left subcardinal.				

Caudal to the bifurcation of the postcava in birds it is difficult to draw a comparison between birds and mammals. The so-called common iliac vein in birds is an independent formation, the proximal end being the original proximal end of the great renal vein; the distal end of the common iliac is formed by an elongation of the anastomosis between the great renal vein and the postcardinal. The external iliac vein in birds is also an independent structure, and the internal iliac is the posterior portion of the original postcardinal.

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ANATOMY OF THE FLOOR OF THE FOURTH VENTRICLE.

(The relations between the surface markings and the underlying structures.)

BY

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WITH 4 PLATES AND 2 TEXT FIGURES.

In the following study I have undertaken to find out how much of surface anatomy can be seen in the floor of the fourth ventricle, and what relation this bears to the underlying structures. This has been done with the end in view that it might lead, not only to a more accurate knowledge concerning the anatomy of the nuclei and the tracts which lie in the ventricular floor, but also might be of immediate practical use to the pathologist in the cutting of material from this region to the best advantage, and in the identification of the extent and situation of morbid processes.

Naturally, this is not the first time that the task of determining the relations between the surface anatomy of the floor of the medulla and the underlying parts has been undertaken. As far back as 1840 Arnold and Stilling were working on the same problem, and later we have the remarkable work of Clarke. But from that time on, following the introduction of new staining methods, the attention of anatomists has been given almost entirely to the study of the finer histology of sections without regard to surface relations. On going back through the literature, one finds everywhere the same descriptions of the floor of the ventricle, and all based on the researches of the previous investigators. In 1896, however, Retzius published his admirable work showing how much more complete the gross description of the brain could be made by a careful study, such as modern anatomy demands. On reading his description of the floor of the fourth ventricle, one first realizes how many structures had been overlooked which can be seen in the ventricular floor, and how far the descriptions commonly given in text-books vary from the conditions actually present. Retzius, however, does not include in his description of the brain the finer internal anatomy, and so makes no attempt to explain the significance of the various

structures which he describes as forming a part of the floor of the fourth ventricle, and their relation to the underlying parts.

Since now we know, after many investigations, so much concerning the finer structure of the oblongata, and also have from Retzius such an accurate description of the surface, what a tempting task is offered in the study of the relation of the one to the other! A more complete knowledge of this relation, it may indeed be hoped, will render the understanding of the structure of this complicated region somewhat easier.

The simple plan was adopted of making a drawing of the floor of the ventricle, and then preparing from the same specimen a series of transverse sections taken at recorded levels. An adult brain was selected which had been hardened in formaline and showed distinctly the various structures in the ventricular floor. Regard was given to the fact that some variation exists in the arrangement of the markings in different brains. A specimen was therefore selected that showed best the more constant arrangement. A drawing of this was then made, the specimen being carefully studied under water and the finer structures brought out with a simple lens. Each part was measured as accurately as possible and reproduced in the drawing enlarged twice. This is shown in Plate I. Photographs and tracings were then made from the drawing to serve as duplicates, for purposes of additional record. The specimen was then cut transversely into measured segments, either 2 or 4 mm. thick, varying according to the complexity of the region, the level of the segments being recorded on a duplicate of the drawing. By reconstructing the specimen after section it was possible to see exactly through what parts the incisions were made, and so a control record of the levels was kept. The segments were then mordanted preparatory to the myelin sheath method, imbedded in celloidin, and cut. During this process there was some warping of the segments, so that in trimming on the microtome the final sections were in some cases not exactly transverse. Such corrections were recorded. The first sections taken from the blocks were kept apart, as corresponding to the recorded levels on the drawing; the deeper ones were preserved as a series for purposes of identification. The sections, thus prepared, were stained by Weigert's myelin sheath method. Some of the more important ones are reproduced in Plates III and IV, the enlargement being twice that used in the drawing of the floor of the ventricle, *i. e. four times natural size*. The levels corresponding to the sections are indicated on Plate II. For accuracy in identification of structures, comparison was made with other series, taken from the collection of the Institute, and with prepa-

rations stained in various ways, including a series of neuroglia fibre specimens prepared by Weigert, and kindly loaned for this purpose.

Before giving the results of the study of these preparations we will briefly review that which has already been found out concerning the anatomy of the ventricular floor.

Stilling, sixty years ago, in describing the floor of the fourth ventricle, divided the caudal half of it, on each side of the median line, into three triangles (*Bau des Nervensystems*, 1842). One of these, the "Ala cinerea," owing to its darker color, stands out prominently, its apex extending forward to the "transverse fibres of the acoustic nerve," and its base resting against the "Calamus scriptorius." This he determines to be the nucleus of the vagus nerve. He observes a small ridge running across the base of this triangle, cutting off a distal segment, and so separating the anterior part, or "Vagus nucleus," from the caudal border of the ventricle. The posterior segment he names "Nucleus of the Accessorius" (*Stilling*, Taf. VII, fig. 9). The other two triangles, separated by the ala cinerea, lie with their apex directed backwards. The median one is his "Hypoglossal nucleus," and the one lateral to the ala cinerea he calls the "Nucleus of the Glossopharyngeus." In the anterior division of the floor of the ventricle, *Arnold* had previous to *Stilling* described the "Eminentia teres," the "Fovea anterior," and "Locus coeruleus." The first of these *Arnold* had identified as the "Nucleus nervi facialis" (*Icon. nerv. cap.* Taf. I, fig. 8). He also describes the "Striae medullares" and suggests their association with the auditory nerves.

That much, then, was found out regarding the floor of the fourth ventricle, without the aid of any imbedding or staining methods, and from sections cut with a razor.

A quarter of a century later *J. Lockhart Clarke* (*Phil. Transact.*, 1868, p. 263), from specimens stained with carmine and cleared in the oil of turpentine, concludes that the triangle lying lateral to the ala cinerea is the "inner nucleus of the auditory nerve." He also makes out the course of the facial nerve with its knee and two arms. He considers its nucleus of origin to be situated beneath the fasciculus teres, in common with that of the abducens. The loose strands of the posterior arm he describes as an association bundle between the facial and the motor nucleus of the trigeminus.

From this time until *Retzius* published his work on the "Menschenhirn," in 1896, we find no important contribution to our knowledge of the floor of the fourth ventricle. *Henle's* work (*Nervenlehre des Menschen*, 1879) should perhaps be mentioned as giving the most careful

review of the subject. It is a curious fact that, as the anatomies become more modern, the descriptions and illustrations of this part of the nervous anatomy correspond less and less to nature, and drift toward misleading multicolored diagrams. Retzius points this out, and produces a page of drawings taken from different sources showing a lamentable lack of faithfulness on the part of the more modern writers. Stimulated by this, Retzius makes a careful study of one hundred specimens, and illustrates the typical forms with drawings and well executed photographs. His description of the floor of the fourth ventricle is so complete that we cannot do better than to follow it more or less in detail:

The ventricular floor, in the majority of cases, is divided by the striae medullares into three regions, namely: The "frontal," the "median" (a region occupied by the striae), and the "caudal." The striae, however, as is well known, present a great individual variation. They may be large, small, or entirely absent. When present they lie parallel, convergent, divergent, transverse, oblique, or longitudinal. Owing to this irregularity, *Retzius* agrees with *His* in recommending, for descriptive purposes, a longitudinal division of the floor,—each side to be divided into a median and lateral area, which is indicated by a more or less well marked groove connecting the superior and inferior (ala cinerea) foveae. This groove is called the "lateral furrow," and the foveae are merely parts of it widened out. Such a groove in a gross way separates the motor and sensory fields of the floor of the ventricle, the former of the two lying mesial. In adults' brains at the caudal tip of the ventricle (calamus scriptorius) there is usually present a small triangular bridge-like structure (obex), extending between the prominent nuclei of the posterior columns of the cord (clavae), and covering in the tip of the ventricle in the median line. Arising from under this and out of the opening of the central canal and extending from the median line along the edge of the clava is the "*Area postrema*," a rounded tongue shaped space with a fine granular surface and brownish color. This area was already known to *Stilling* and *Henle*, but is especially described by *Retzius*. Two other structures come out with this from the region of the central canal, the ala cinerea and, next to the median line, the hypoglossal field or the trigonum hypoglossi. The area postrema is distinguished from the ala cinerea by its color, rougher surface, and by a glistening light colored ridge, which separates the two. This ridge is usually well marked, and extends laterally and anteriorly to the inferior end of the area acustica, in the structure of which it is lost. From its position *Retzius* names this ridge the "*Funiculus*

separans." The ala cinerea bounded by the funiculus separans posteriorly, and arising with it from the median line out of the central canal, extends forward, more or less triangular in shape, wedging itself in between the area acustica and the trigonum hypoglossi. It ends anteriorly with a pointed tip in the region of the striae medullares. Its surface as a whole is depressed, and forms a shallow pit, the floor of which is slightly convex.

Lying median to the ala cinerea is the hypoglossal field, arising out of the central canal by a slender stile or wedge, gradually broadening, and ending in the region of the striae. In the foetus and yet more evident in the adult the trigonum hypoglossi is resolved longitudinally into two fields, of which the one lying on the median side is the narrower. The boundary between them consists, as a rule, of a single or double formation of numerous short oblique furrows and ridges, or a series of wrinkles of the surface of the floor, affording a "feathered" appearance. This is brought out strongly by magnification under water with a simple lens. This peculiar wrinkling occurs also between the lateral division of the hypoglossal field and the ala cinerea, giving the appearance of a "bird feather." Retzius therefore designates this lateral field as the "*Area plumiformis.*" The narrow field, median to the area plumiformis, he calls the "*Area medialis trigoni hypoglossi.*" Near the middle of this field there often is a slight enlargement and elevation—the "*Eminentia medialis trigoni.*"

The area acustica is an irregularly triangular or quadrilateral raised surface with its convex base toward the median line, and extending laterally to the insertion of the tela choroidea inferior, and into the recessus lateralis. Its superior or frontal portion is usually covered by the striae medullares, with the consequent irregular elevations. Its inferior end extends caudally as far as the area postrema, and forms the lateral boundary of the ala cinerea. The acoustic area is more prominent in the foetus, and forms a projection or tubercle, which Schwalbe designated the "Acoustic tubercle." Later Dejerine (*Anatomie des Centres Nerveux*, 1901, Tome Deuxieme, p. 498) has suggested the limiting of this name to the nucleus of termination of the cochlear nerve, which properly corresponds to the tuberculum acusticum of mammals other than man.

Regarding the superior part of the floor of the ventricle, Retzius has found little that is new. He describes a "Fovea mediana"—a depression of the median sulcus slightly frontal to Arnold's eminentia teres. The superior fovea and locus coeruleus in his description do not differ from what we have already learned from Arnold, Stilling, and Clarke.

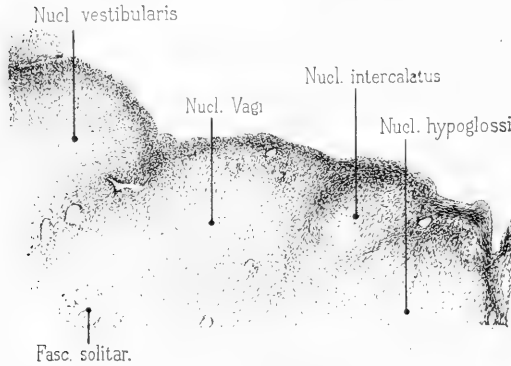
The question that now arises is: what significance have all these structures? *Retzius* makes no attempt himself at explanation. *Dejerine*, who is acquainted with his description, concludes (*op. cit.*, page 501) that the funiculus separans corresponds to the situation of the fasciculus solitarius, and that the area postrema forms the ventricular portion of the nuclei of the posterior columns. In the trigonum hypoglossi he finds only the nucleus of the hypoglossus. *Obersteiner* (*Nervose Centralorgane*, 1901, p. 74) about the same time concludes that the narrow median zone of this field corresponds to the nucleus funiculi teretis. *Miss Sabin's* reconstruction of the medulla (*Model of Medulla, Pons, and Midbrain*, Vol. IX, Johns Hopkins Hospital Reports, and Atlas of the Medulla and Midbrain, Baltimore, 1901) shows the structures beneath the ventricular floor, but the details of their relations with surface markings are not especially treated.

We will now take up in order the study of our series of preparations. Typical sections out of the series have been selected, and drawings of them, four times enlarged, are reproduced in Plates III and IV. The numbers correspond to the levels indicated in Plate II. In the most caudal sections (figs. 1, 2, and 3) the fourth ventricle does not appear. We see, however, the transition from the spinal cord type of fig. 1 to the medulla type of fig. 4. In fig. 1 the posterior longitudinal fissure forms a cleft between the nuclei of the posterior columns of the cord, and extends ventrally to the grey substance surrounding the central canal. In this grey substance antero-laterally there are a few motor cells belonging to the hypoglossal nucleus, which nucleus, however, in sections just above this, between fig. 1 and fig. 2, becomes more distinct as a compact group of cells. In fig. 2 the posterior longitudinal fissure is shorter, owing to the dorsal migration of the central canal. Lying at the bottom of this fissure is an area of loose vascular tissue containing a few myelinated fibres, and extending ventrally as a wedge into the grey substance surrounding the central canal. In this section the grey substance can be seen to be differentiated into a darker and a lighter area. The former lies ventral, and forms the hypoglossal nucleus. The latter lies dorsal to this, and is contiguous with the vascular area in the posterior longitudinal fissure. It forms the beginning of the vagus nucleus. On one side of the section the fasciculus solitarius can be seen lying lateral to the nucleus of the vagus. In fig. 3 the posterior longitudinal fissure has become continuous with the central canal, but is bridged over dorsally by the obex. The obex has a similar histological structure, and in following through the series is apparently continuous with the wedge shaped area described in fig. 2. The vagus and hypoglossal nuclei retain the same relations as in the previous sections.

Fig. 4 shows the floor of the fourth ventricle bounded on each side by the insertion of the tela choroidea inferior, the torn edge of which shows in the sections, situated at a point corresponding to the descending root of the vestibularis. Lateral to it lie the nuclei of the posterior columns. The space between the attachment of the tela and the median line is divided by surface furrows into three areas. The outermost area consists superficially of a loose vascular tissue, similar in structure to the vascular area seen in sections 1 and 2. Here it corresponds to the area postrema of Retzius. Median to this there are two other areas separated by a sharply cut furrow. The one at the median line forms the beginning of the trigonum hypoglossi. The smooth rounded area between this and the area postrema consists of a thickened ependyma overlying the vagus nucleus. By tracing this structure through the sections between 4 and 5 it is found to correspond to the funiculus separans. It appears in the section somewhat broader than in the drawing of the floor of the ventricle (Plates I and II). This is due to the fact that the structure curves caudally towards the median line, and is therefore in fig. 4 cut in an oblique direction. A relation between the funiculus separans and the fasciculus solitarius, as found by *Dejerine*, is not found in any of our sections. It will also be observed in section 4 that the area postrema does not represent an intraventricular part of the nuclei of the posterior columns of the cord, but is a vascular structure overlapping the vagus nucleus, and associated in structure and position with the obex, tela choroidea, and the wedge shaped area seen in fig. 2.

Fig. 5 forms a favorable place for the consideration of the finer surface structures in the floor of the ventricle. The three major areas are distinctly marked out. The area corresponding to the trigonum hypoglossi is subdivided into a median and lateral area. Also at this level there exists the most marked formation of ridges and furrows, which give rise to the feathered appearance as described by Retzius. So here perhaps we can learn what these markings of the floor signify. Sections of this region were studied which had been prepared by various methods. The most information regarding the histology of the markings of the floor, however, was obtained from a neuroglia fibre series prepared by Weigert, and I will take this opportunity to express my thanks for his kindness in loaning them for use in this study. In this neuroglia series one finds directly beneath the ventricular epithelium a compact layer of neuroglia fibres, the ependyma, and it is found to be this that forms the substance of the small wrinkles seen in the floor. They appear in sections as ridges of compact neuroglia fibres,

and from Nissl and myelin sheath preparations are found to be devoid of nerve cells, axis cylinders, and blood vessels. The ependyma extends into the grey matter and median raphe in the form of processes, forming well defined partitions between the dorsal nuclei which Weigert, in his monumental work (*Beiträge zur Kenntnis der Normalen Menschlichen Neuroglia*), describes as "kielstreifen," or the tracks left by embryonal sulci. In adult specimens the place at which a process takes its origin is generally indicated on the surface of the ventricular floor by a more



TEXT FIG. 1. Section showing the distribution of the neuroglia fibres in the floor of the fourth ventricle at a level corresponding to fig. 5, Plate III. The drawing represents the appearance as seen under low magnification.

or less well marked groove (text fig. 1). The size and form of the groove correspond in some degree to the size and compactness of the neuroglia process. That is: when the process is compact and slender the surface groove is usually sharply cut, and when the process is broader and less compact the surface depression is shallower and more rounded out. Owing to this partition formation it is possible with low magnification to make out in glia fibre preparations the definite boundaries of the dorsal nuclei. So we have, in the comparison of these specimens with myelin sheath and Nissl preparations, another means of determining the size and arrangement of the dorsal nuclei.

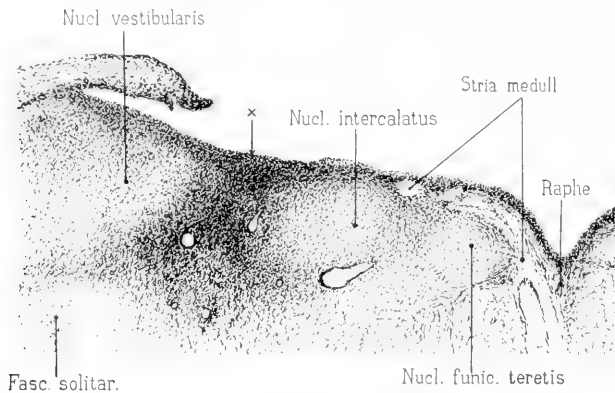
In fig. 5, by comparison with text fig. 1, it is easy thus to determine that the three major areas are occupied by the vestibular, vagus and hypoglossal fields. We further see that the hypoglossal field is subdivided, and that the lateral subdivision (area plumiformis) corresponds to the "nucleus intercalatus" of *Staderini* and *Van Gehuchten* (*Van Gehuchten—Recherches sur l'origine réelle des nerfs crâniens. III. Le nerf glosso-pharyngien et le nerf vague. Journal de Neurologie 1898-1899*), which nucleus forms a dorso-lateral cap over the hypoglossal nucleus. The hypoglossal nucleus, itself, appears in the floor of the ventricle only in the median division of the trigonum. We find that it is the prominence of the hypoglossal nucleus and small development of the nucleus intercalatus that results in the rounded surface elevation called *eminentia medialis trigoni* by *Retzius* (*Eminentia hypoglossi*, Plates I and II).

In the region of fig. 6 we observe adjoining the median line on each side the nucleus funiculi teretis, overlapped by the obliquely cut fibres of the striae medullares. In some of the sections studied, to all appearances many of the fibre bundles of the striae ramified in the nucleus, and seemed to terminate there. It is realized, however, that such histological pictures may be very misleading. It is considered to be far from conclusive evidence regarding the relation between the two structures. The distal and proximal ends of the nucleus are indicated in Plate II. It will be observed that the nucleus corresponds in its position very closely to the area of the striae. It is distinctly separated from the eminentia teres.

There is a large field of grey matter, in fig. 6, bounded by the nucleus funiculi teretis mesially, the descending bundles of the vestibularis laterally, and ventrally by the formatio reticularis and the fasciculus solitarius with its nucleus. Concerning the signification of this field there is at present a divided opinion. The majority of writers consider the entire space to belong to the dorsal vestibular nucleus. There are others, however, who consider the median part of this field to belong to the nucleus of the glosso-pharyngeus. By going through a series it is easy to see that the median part of this field is a continuation of what *Staderini* and *Van Gehuchten* in more caudal sections call the nucleus intercalatus. The area occupied by this nucleus is indicated on Plate II as Nucleus intercalatus. In the region of fig. 6 this nucleus seems to fuse with the dorsal vestibular nucleus, and in myelin sheath and Nissl preparations the two areas have the same structure and no dividing line can be made out. That they, however, are not the same, but, on the contrary, have different functions is supported by the following reasons:

Firstly. If the nucleus intercalatus belonged to the vestibular nucleus the area occupied by the two would be greater than that occupied by the combined nuclei of the glossopharyngeus, vagus and hypoglossus. This would be out of all proportion to the function of the vestibular nerve, as we at present understand it. Secondly. In many human specimens where the striae are absent or only faintly marked, and even better in other mammals (calf and sheep), the naked eye appearance of the floor shows the vestibular nucleus to be separated from the nucleus intercalatus by the lateral furrow which connects the superior and inferior foveae. Thirdly. We have already seen that in neuroglia fibre specimens, processes extend from the ependyma ventrally into the grey matter forming partitions between the dorsal nuclei. In specimens of this region prepared in that manner there exists a neuroglia parti-

tion between the dorsal nucleus of the vestibularis and the nucleus intercalatus. This is indicated in text fig. 2, which represents a neuroglia



TEXT FIG. 2. Neuroglia preparation made in the region corresponding to fig. 6, in Plate IV. The magnification is the same as text fig. 1.

fibre preparation taken from the region under consideration. In sections from other specimens we have observed a distinct notch in the floor at the point indicated in text fig. 2 by a cross. These would correspond to brains with a well marked lateral furrow.

As bearing on this subject, I may further mention a case, reported by Neubürger and Edinger (*Berliner klin. Wochenschr.*, 1898, No. 4), in which there was a congenital absence of one-half of the cerebellum. On the abnormal side the vago-glossopharyngeal and vestibular nuclei were found to be devoid of the network of fine fibres, which presumably forms the origin of their central cerebellar sensory tract. The nucleus intercalatus was not described. I have recently, however, had the opportunity of examining the preparations from this case, and find that the so-called nucleus intercalatus, in its greater part, is normal in appearance, and equally rich in fibre network on both sides. It thus stands out separated in sharp contrast from the pale and transparent field occupied by the vagus and vestibular nuclei.

In fig. 6, overlying laterally the restiform body, there is seen a nuclear structure in the substance of the tela choroidea inferior. This can be traced through the sections between 5 and 6 as a thin nuclear layer or lamella which extends caudally from the nucleus cochlearis, and laterally from the nucleus vestibularis. Whether it is a part of either or both of these we were unable to satisfactorily make out. In Plate II it is represented as belonging to the cochlear area. The cochlear nucleus proper does not make its appearance until we reach the sections lying between figs. 6 and 7.

The frontal ends of the nucleus funiculi teretis and the nucleus intercalatus are cut across in fig. 7. These disappear between figs. 7 and 8. Lateral to the nucleus intercalatus is the vestibular field, and lateral to that is the nucleus cochlearis, and the stipe of the flocculus. In this section the nucleus and most of the fibres of the glossopharyngeus have disappeared.

Fig. 8 represents a section through the nucleus of the nervus abducens forming, together with the genu of the N. facialis, an elevation of the floor (eminencia facialis). On one side can be seen the fibre bundles of the N. abducens leaving the nucleus. A few fibres connecting the nucleus with the superior olive are present. Of the N. facialis three portions can be seen in this section; the loose strands coming from its nucleus, a cross section of the genu, and the nerve trunk in its ventral course of exit. Overlapping the N. facialis and the nucleus abducentis is the distal extremity of a mass of grey matter, which increases in size as we approach the aqueduct of Sylvius. Since as yet we are ignorant concerning its function, this structure will be spoken of as the "*nucleus incertus*." At this level the fibres from the nucleus and trunk of the vestibular nerve and the restiform body are seen passing dorsally in their course to the cerebellum. Some of the more frontal fibres can be seen of the root of entrance of the vestibular nerve.

Fig. 9 is in the trigeminal region, and shows the root of that nerve, the motor nucleus, and the bundle of decussating fibres, the latter seeming to pass into the region of the nucleus lying lateral to the posterior longitudinal fasciculus. The posterior longitudinal fasciculus, except for ependyma, lies at this level exposed in the floor of the ventricle, and corresponds to the broadening of the longitudinal median furrow, situated in the floor of the ventricle proximal to the eminentia facialis (fovea mediana of Retzius). The layer of grey matter seen in previous sections and called nucleus incertus is here little changed. In fig. 10, however, it is much enlarged in width and thickness. Underlying it are the large pigmented cells of the trigeminus (locus coeruleus), and mesially is the posterior longitudinal fasciculus. Lateral to it is the superior root of the trigeminus. The nucleus consists of a network of fine fibres in the meshes of which lie scattered groups of medium sized multipolar nerve cells. In its appearance and position it bears a somewhat similar relation to the trigeminus to that which exists between the nucleus intercalatus and the vago-glossopharyngeus. It is possible that these nuclei, the nucleus incertus and the nucleus intercalatus, may represent central sympathetic centers, which we are led to expect in the floor of the medulla, as analogous to the grey matter surrounding

the central canal of the spinal cord, in which *Onuf* and *Collins* (Experimental researches on the central localization of the sympathetic. *Archiv. Neurol. and Psychopath.*; 1900) have traced secondary degenerations following removal of sympathetic ganglia.

CONCLUSION.

Now, that we have examined our series individually, we are in a position to consider the floor of the ventricle as a whole, and the position and arrangement of the structures of which it consists. The fact that we have the levels of the sections exactly recorded enables us to plot out the areas of the various nuclei and tracts, as far as we were able to identify them in section. Further, as all the drawings were enlarged according to a definite scale, we are enabled to give their exact size in length and width. In Plate II the different areas have in that way been outlined. If we compare this plate with the original drawing (Plate I), we can see the relations of the outlined areas to the superficial structure of the floor. As a résumé, therefore, that which we see in the floor of the fourth ventricle, when looking at our specimen from above, and taking in consideration but one side of the median line, may be described somewhat as follows:

Lying against the median line in the caudal half of the floor is an oval elevation, 5.2×1 mm. This represents the rounded frontal end of the hypoglossal nucleus, and may therefore be called "*eminentia hypoglossi*" (*eminentia medialis trigoni* of Retzius). It varies somewhat in prominence in different specimens according to the development of the structures lateral to it. In the specimen illustrated in Plate I it is less prominent than is usual. The remainder of the hypoglossal nucleus is completely covered by other structures. The entire nucleus measures 12.3×2.2 mm. The intraventricular portion is 7 mm. long, and except at the *eminentia hypoglossi* is overlapped by the nucleus intercalatus and nucleus vagi. The extraventricular portion extends 5.3 mm. caudad to the tip of the calamus scriptorius, and lies ventral to the vagus nucleus and the nucleus of the funiculus gracilis.

Situated at the median line frontal to the *eminentia hypoglossi*, and separated from it by a slight depression, is a somewhat similar, but less prominent, elevation formed by the nucleus funiculi teretis. This measures 5.7×1 mm. The appearance of this structure varies according to the arrangement of the striae, which have their median termination in this region. It is possible that there is an intimate relation between the striae and this nucleus.

Lying lateral to the elevations formed by the nucleus funiculi teretis and the nucleus hypoglossi is the elongated wedge shaped elevation formed by the nucleus intercalatus (area plumiformis), which measures 11 mm. long, and 2.2 mm. in greatest width. The frontal portion forms the body of the structure and is situated in the region of the striae. The tapering caudal extremity extends from this, between the eminentia hypoglossi and the vagus area, as far as the tip of the calamus scriptorius, overlapping a portion of the hypoglossal nucleus. The nucleus intercalatus lies superficial in the floor throughout its entire extent, except in the frontal part, where it is more or less covered by the striae medullares. This nucleus is probably not a part of the vestibular nucleus.

In different parts of the floor of the ventricle can be seen a formation of fine ridges. They are particularly numerous in the region of the nucleus intercalatus, and from their regularity often present the appearance of a "bird feather." They consist of small neuroglia elevations covered by a single layer of epithelium, and are devoid of nerve cells or fibres. They are present in fresh brains, but show more distinctly in hardened specimens. They radiate on the surface of the ventricular floor from regions where neuroglia processes ("Kielstreifen") extend inward as partitions between the dorsal nuclei. It is possible that they serve as a support to these processes.

Lateral to the nucleus intercalatus is the fovea vagi (ala cinerea), which represents the middle one-third of the vago-glossopharyngeal nucleus, and is the only part of this nucleus that lies superficial in the floor of the ventricle. The entire vago-glossopharyngeal nucleus is 13.5 mm. long, and averages 2 mm. in width. Frontal to the fovea vagi, the nucleus lies concealed beneath the vestibular nucleus. The distal one-third extends 2.5 mm. caudad to the tip of the calamus scriptorius, the extraventricular portion lying ventral to the nucleus gracilis, and dorsal to the hypoglossal area. The intraventricular portion of the caudal one-third of the nucleus is covered by a layer of loose vascular tissue, which is continuous with the obex, and which extends into the dorsal region of the central canal. This is the area postrema of *Retzius*. Separating it from the fovea vagi there is usually some thickening of the ependymal neuroglia forming a translucent cord-like elevation, the funiculus separans. The fasciculus solitarius lies lateral and ventral to the vago-glossopharyngeal nucleus throughout its course. It nowhere lies superficial, and bears no apparent relation to the funiculus separans.

All that part of the floor of the ventricle that lies lateral to the anterior fovea (fovea trigemini) and the fovea vagi (ala cinerea) and the

lateral furrow, which connects the two, belongs to the acoustic area. This area consists of a median, or vestibular field, and a lateral, or cochlear field. The vestibular field forms an irregular spindle shaped elevation, 16.1×4.5 mm., extending from the anterior fovea to the nucleus gracilis. Its median border is convex, and is more or less completely separated from the nucleus intercalatus by the lateral furrow. In other mammalians (sheep and calf) this furrow of separation is more distinct than in man. The cochlear field is that portion of the floor that extends into the recessus lateralis.

Lying near the median line, proximal to the striae medullares, and 16 mm. cephalad to the obex, is a rounded elevation, 4 mm. in diameter, formed by the genu of the facial nerve, inclosing the nucleus of the abducens. This we call the "*eminentia abducentis*." Partly overlapping this, and extending forwards to the aqueduct of sylvius, is a longitudinal elevation, averaging 2.7 mm. in width. This is due to a field of grey substance consisting of fine fibres, in the meshes of which lie scattered groups of small and medium sized multipolar nerve cells, which area begins as a thin layer in the region of the eminentia facialis, and gradually becomes thicker as it extends into the region of the mid-brain. Its function is unknown, and we therefore call it the "*nucleus incertus*." In its position it is closely related to the nucleus nervi trigemini, overlapping it throughout its course.

Between the nuclei incerti, in the median line, is a shallow depression of the floor of the ventricle, measuring 5.7×1 mm. which forms the fovea mediana. The posterior longitudinal bundle here lies superficial in the floor covered only by a thin layer of ependyma.

Lateral to the nucleus incertus, and the eminentia facialis is an elongated depression of the floor 3.2 mm. in its greatest width caudally, and gradually narrowing as it extends forward. It is due to the exit at this point of the root of the trigeminal nerve. It may therefore be called "*fovea trigemini*" (anterior fovea).

It may be hoped that familiarity with the facts pointed out in the above description will make more instructive the examination and dissection of material from this region of the brain.

In conclusion I wish to acknowledge my obligation and gratitude to Professor Edinger, at whose suggestion, and under whose guidance this work was done.

DESCRIPTION OF PLATES.

PLATE I.

Drawing showing the floor of the fourth ventricle of an adult human brain, enlarged twice.

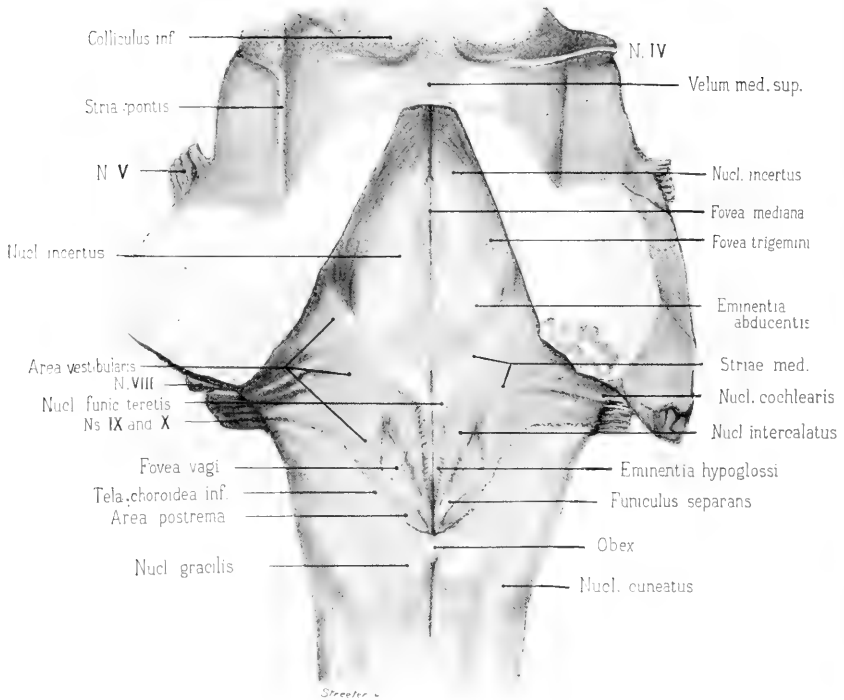
PLATE II.

The same, showing by interrupted cross lines the sections illustrated in Plates III and IV. The size and position of the various nuclei situated in the floor are indicated in outline on the right side. Where one lies beneath another the outline is dotted. Thus one recognizes that the hypoglossal nucleus is covered in greater part by the nucleus of the vagus and the nucleus intercalatus. Antero-laterally the vagus nucleus extends beneath the acoustic field. The fasciculus solitarius is indicated by a lateral sub-division of the vago-glossopharyngeal area and is shaded slightly darker. The nucleus intercalatus and nucleus funiculi teretis, except for the striae medullares, lie superficial throughout their whole length. Together with the nucleus cochlearis is included the thin lamella-like nucleus situated in the tela choroidea inferior, overlapping the corpus restiforme.

PLATES III AND IV.

Frontal sections of the floor of the fourth ventricle, the numbers of which correspond to the interrupted cross-lines of Plate II. These figures represent sections enlarged twice as much as are the surface views on Plates I and II, i. e. four times natural size. Especial care has been taken to represent the furrows and ridges on the edge of the specimens, and the attachment of the tela choroidea inferior.

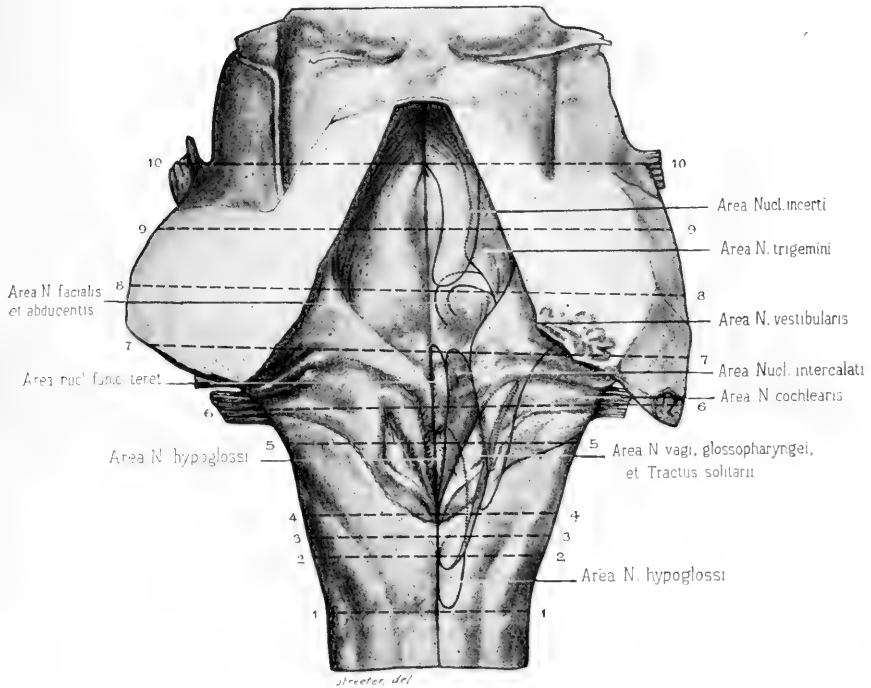
G. L. STREETER



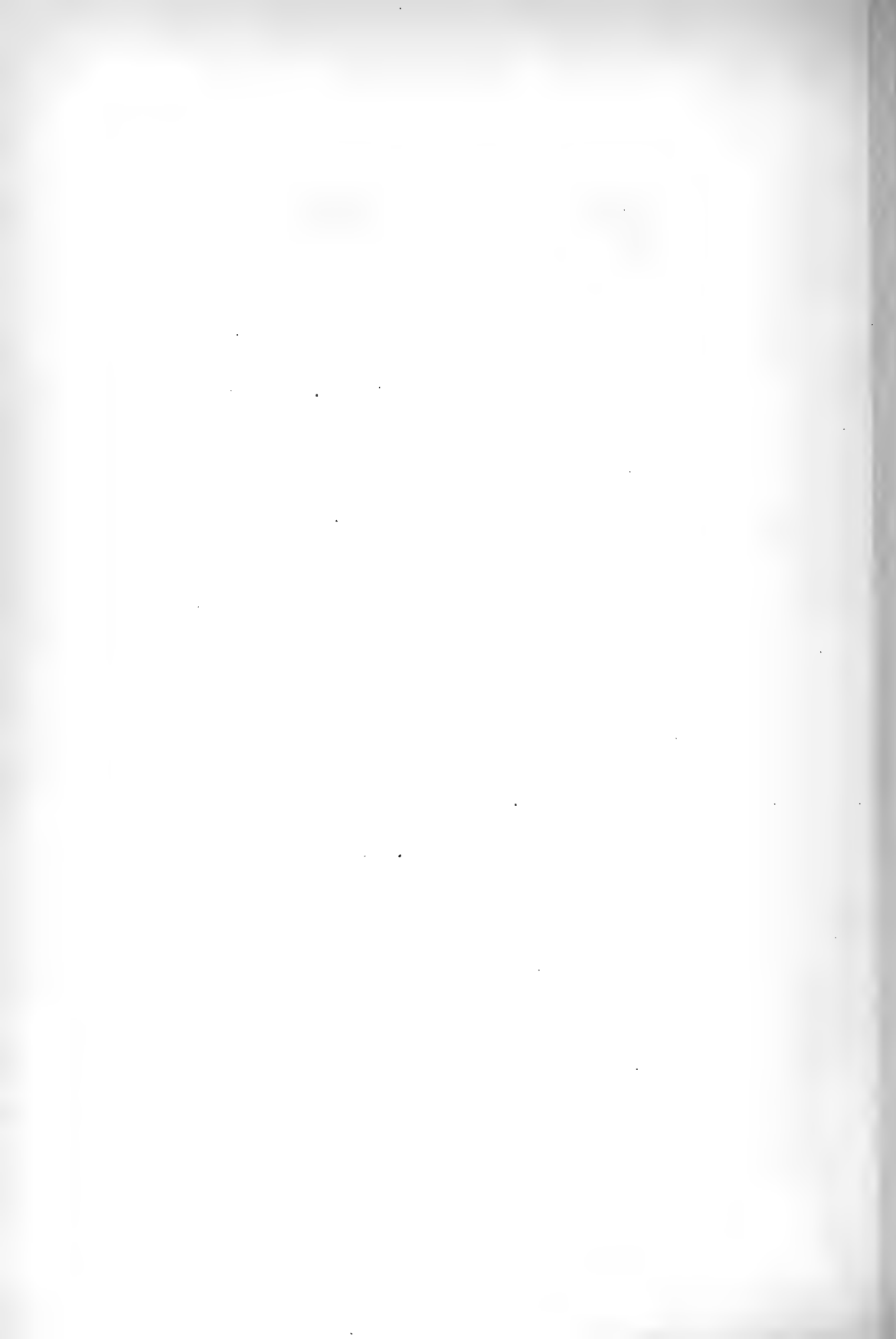
SURFACE MARKINGS OF FLOOR OF FOURTH VENTRICLE

(Man)

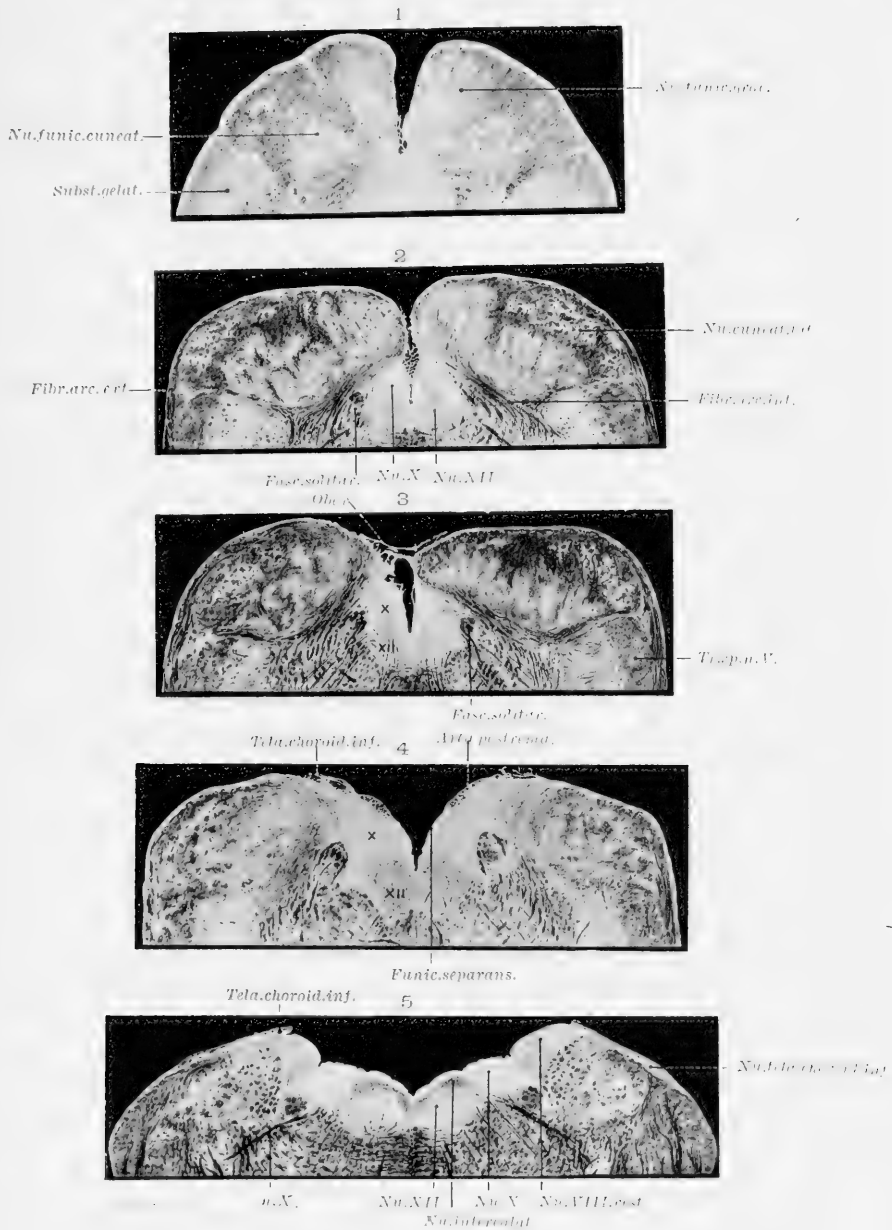
G. L. STREETER



POSITIONS OF NUCLEI AND PLANES OF SECTIONS ILLUSTRATED ON PLATES III AND IV

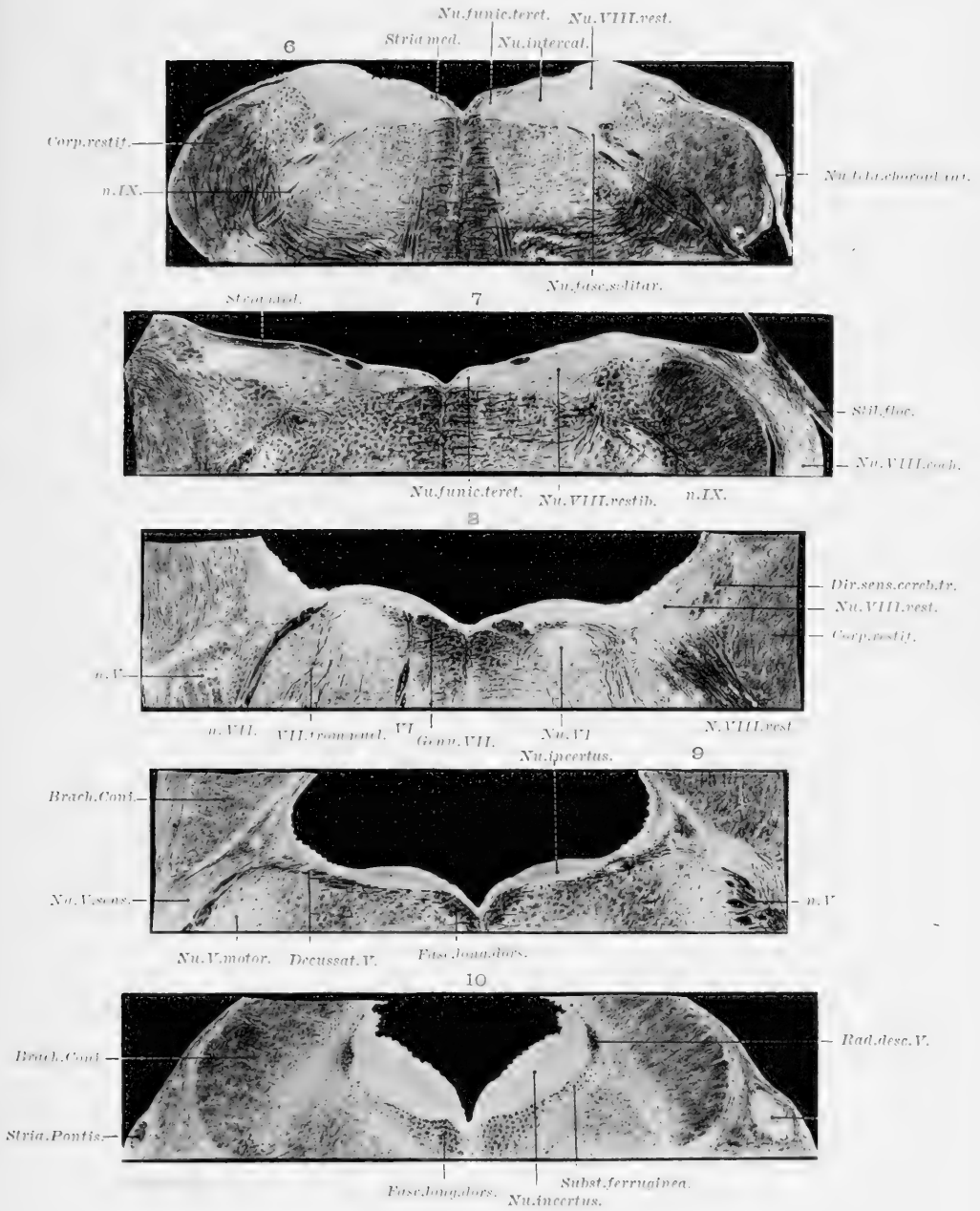


S. L. STREETER





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ON THE CIRCULATION THROUGH THE PULP OF THE
DOG'S SPLEEN.

BY
FRANKLIN P. MALL.

From the Anatomical Laboratory of the Johns Hopkins University.

WITH ONE PLATE AND ONE TEXT FIGURE.

Recent researches upon the blood-vessels of the spleen prove definitely that the arterial capillaries communicate quite freely with the pulp-spaces, but there is still a difference of opinion regarding the presence of distinct channels, independent of the pulp-spaces, connecting the arterial capillaries with the venous sinuses. It seems that the more the subject is investigated the more the two views regarding the circulation through the pulp approach each other. A system of capillaries completely closed does certainly not exist, but the pulp-spaces seem to have among them larger and more direct channels leading from the artery to the vein. These may be likened to larger and more direct holes punched through a sponge, which therefore communicate freely with one another.

A number of reseaches by Thoma and his pupils have brought up the spleen problem anew, and judging by the methods they have employed, these studies will probably lead to a final solution of the question.¹ The works of Sokoloff and of Wicklein deal mainly with the vascular walls in hyperaemia of the spleen and contain many valuable experiments, while those of Thoma deal with the relation of the blood-vessels to the surrounding tissues when injected with either fluid or with granular masses. Thoma says (1899, p. 281): "In den meisten Organen ergeben Injectionen der Blutbahn mit den genannten körnigen und gelösten Farbstoffen keine auffälligen Unterschiede. Die bei der Milzinjection hervortretenden Unterschiede müssen somit als bedeutungsvoll anerkannt werden. Die Injectionen mit körnigen Farbstoffen beweisen, dass die Milzarterien durch die Verbindungsstücke unmittel-

¹ Sokoloff, *Virch. Arch.*, 112; Wicklein, *Ibid.*, 124; Kalenkiewicz, *Inaug. Diss.*, Dorpat, 1892; Golz, *Inaug. Diss.*, Dorpat, 1893; Thoma, *Dorpater Naturfor.-Gesellsch.*, 18; Thoma, *Verhandl. der anat. Gesellsch.*, 1895; and Thoma, *Archiv für Anatomie*, 1899.

bar in die Milzvenenplexus einmünden. Damit ist der Weg gegeben, welchen die zelligen Elemente des Blutes nehmen, wie auch die Erfahrungen bezüglich der venösen Hyperämie bestätigen. Es besteht somit auch in der Milz ein geschlossenes Gefäßsystem. Die Ergebnisse der Injectionen gelöster Farbstoffe beweisen jedoch dass die Wandungen dieses Gefäßsystems in höherem Grade durchlässig sind als die Wandungen anderer Gefäßverzweigungen. Es ist zu schliessen, dass normaler Weise während des Lebens ein Theil des Blutplasmas denselben Weg durch die Spalträume der Milzpulpa strömt, welchen bei der Injection die gelösten Farbstoffe nehmen."

My own work upon the spleen² has led me gradually to conclusions similar to Thoma's. In my preliminary communication, which appeared before Thoma's last paper, the conclusions are almost identical with his regarding the circulation through the pulp. "The microscopic anatomy shows that the ampullae and venous plexus have very porous walls which permit fluids to pass through with ease and granules only with difficulty. In life the plasma constantly flows through the intercellular spaces of the pulp cords, while the blood corpuscles keep within fixed channels." Later on I found it necessary to modify this view somewhat, making the walls of the capillaries of the pulp still more porous. "By studying numerous successful injections of the last third of the ampulla I find that its communication with the vein is not wide but is cut up with bridges of tissue passing across its lumen before it communicates with the vein (1900, p. 34). It appears as if in the neighborhood of the lymph follicles the walls of the ampullae are most porous (p. 35). Experiments show that if the muscle is paralyzed the blood discs enter the pulp-spaces, thus causing an hemorrhagic infarction (p. 36). It seems as if the pulp-spaces are in all cases filled through these openings in the walls of the veins. Yet I am unwilling to accept this explanation until further arguments are made to support it, but am rather inclined to the idea that the pulp is filled with blood passing through the openings in the walls of the ampullae (p. 39)."

I do not quote the instances in which I brought forward arguments in favor of a closed circulation, but only those in which the closed channel was doubted. The reason for this will become apparent when I discuss some new specimens and experiments I have made recently.

Two years ago Weidenreich³ published an extensive and excellent criti-

² Mall, Johns Hopkins Hospital Bulletin, 1898; *Zeit. für Morphol. u. Anthropol.*, Stuttgart, 1900; and Spleen, Reference Handbook of Medical Sciences, New York, 1903.

³ Weidenreich, *Arch. f. mik. Anat.*, LVIII, 1901.

cism of the literature upon the vascular system of the spleen, giving also a valuable experiment which throws light upon the circulation through the pulp. His conclusion regarding the arterial capillary is as follows: "Die arterielle Capillare geht aus der Hülsenarterie hervor und stellt ein dünnwandiges, leicht dehnbares Rohr dar von wechselnder Weite; ihre Wand besteht aus einer äusseren Schicht, welche aus stark in die Länge gezogenen Hüsenzellen und anscheinend auch wirklich durch eine Fortsetzung der Hülse selbst gebildet wird, und einer inneren Endothellage mit spärlichen, grossen Kernen. Diese Capillaren münden entweder unter spitzem Winkel direct in einen Milzsinus ein oder lösen sich durch Auffaserung ihrer Wand in dem Reticulum des Milzparenchyms auf (p. 322)." Apparently Weidenreich has come to a conclusion practically identical with that of W. Müller,⁴ although he made no direct injections (p. 340).

Shortly after Weidenreich, Helly⁵ published two papers upon the spleen with conclusions practically the same as mine and Thoma's. He says: "Die Milz hat ein, überall von einer regelmassigen Endothelschichte ausgekleidetes, daher geschlossenes Gefässsystem mit sehr durchlässigen Wandungen" (Vol. 61, p. 272). Helly repeated Weidenreich's transfusion experiments and confirms him regarding the presence of foreign red blood corpuscles in the spleen pulp. According to Weidenreich these foreign cells passed over into the pulp from the capillary artery, and according to Helly they entered the pulp backward through the capillary vein.

The quotations just given show that the recent authors are of one opinion regarding the large pores in the capillary walls. It appears that these openings are smallest according to Thoma, larger according to Helly, still larger according to Mall, and so large that they communicate most freely with the pulp-spaces according to Weidenreich. The problem is further complicated by W. Müller, Weidenreich and others, who find that both open and closed capillaries occur in the same spleen. When we consider the difficulties and the differences of opinion, it is not hard to understand that there should be different conclusions regarding this question. While I have found numerous direct capillary channels in the distended spleen, I have never seen one in the contracted spleen. Furthermore, I have never been able to follow anything like an endothelial lining from an artery to a vein. So while the interpretations of the results are apparently different in the publications of

⁴ W. Müller, *Feinerer Bau der Milz*, Leipzig, 1865, p. 79.

⁵ Helly, *Arch. f. mik. Anat.*, LIX and LXI, 1902.

Thoma and Weidenreich, they have had in reality the same kind of specimens before them. Weidenreich's single complete capillary, which is extremely difficult to obtain when the spleen is not injected, is Thoma's *Zwischenstück*, quite easily found when hyperaemic spleens are injected with fine granular masses. On the other hand Thoma's extravasations, which are always present, represent the normal course according to Weidenreich. So it seems to me that all of the recent workers practically agree regarding the walls of the capillary vessels of the spleen, and the question formulates itself anew, *How complete is the capillary wall, and is it exactly the same in all portions of the spleen?* With this there is joined a second but most important question, *Do all of the blood corpuscles enter the pulp-space in passing from the artery to the vein?* Both of these questions must be answered by making experiments and injections. To attempt them through simple sections of the spleen, no matter how thin they may be, is practically a waste of time.

For purposes of description I have shown that it is well to divide the spleen into a number of lobules,⁶ which are practically identical in arrangement with those of the liver. Each lobule is about a millimeter in diameter with its artery in the centre and its main veins and trabeculae on the periphery. There are about 80,000 lobules in the dog's spleen. Each lobule is broken up into terminal or histological units, one for each terminal artery or ampulla. Around this there is some spleen pulp which lies within one of the meshes of the venous plexus. This is well shown in Fig. 13 in my paper in the *Zeitschrift für Morphologie und Anthropologie*. The arteries of the lobule are covered with a lymphatic sheath continued from the Malpighian follicle, known as the ellipsoid sheath. This ellipsoid of Schweigger-Seidel⁷ continues to the end of the artery as a small group of round cells (see figure) and marks the beginning of the ampulla. Assuming then that the ampulla communicates with the venous plexus, it may be divided into three parts. The first third, which is the ampulla proper of Thoma; the second third, which contains large side openings, and the third third, which is Thoma's *Zwischenstück*. For the present I shall speak of the ampulla in this way, even if at times it appears to contain neither cavity nor walls. The capillary veins or venous plexus flow together into intra-lobular collecting veins, which in turn empty into the interlobular veins lying within the trabeculae at the periphery of the lobule.

The division of the spleen into lobes and lobules is not new. Kyber⁸

⁶Mall, *Zeit. f. Morphologie u. Anthropologie*, 1900.

⁷Schweigger-Seidel, *Virch. Arch.*, XXIII.

⁸Kyber, *Arch. f. mik. Anat.*, Bd. VI, 547.

used the term lobule in a vague sense (p. 548), corresponding more with my histological unit. This division is also accepted by Hoyer.⁹ Kyber's lobes correspond with the arterial branches which enter the spleen, and form about ten unequal subdivisions of the spleen substance. The lobules I have described are about a millimeter in diameter and can easily be seen on the surface of the organ, or in sections. They are not to be confounded with Kyber's lobules.

That the terminal artery and the ampulla are very porous is shown easily by injecting the artery with any fluid, such as carmine gelatin, which in all cases passes over into the pulp at once, filling all of its spaces and the veins evenly. Such specimens naturally lead one to conclude that the circulation through the spleen is open, and were it not for other facts all anatomists would be willing to accept this conclusion. And when the spleen is evenly injected with carmine gelatin it is impossible to find the end of an artery with any degree of certainty, and it is very exceptional to find one reaching to a vein.

If a spleen, made oedematous by injecting gelatin into either the vein or the artery, or by filling the pulp with blood by ligating the vein for half an hour, is injected through the artery with some fine granular mass like Prussian blue, it is found that at the end of each arterial capillary there are a number of ampullae which communicate with the pulp-spaces, with one another and with the veins. It seems as if the ampullae are only large holes within the spongy pulp. A picture showing this arrangement is given by me in my article in the *Zeitschrift für Morphologie und Anthropologie*, Vol. II, Fig. 12. It must be remembered, however, that in all such specimens a considerable quantity of the Prussian blue has passed over into the smaller pulp-spaces. If the injection is continued until the veins are well filled all the pulp-spaces are also filled with the blue. Free communications between the ampullae and veins have been seen from time to time by numerous investigators from W. Müller to Helly, but no one has ever been able to find them in great number nor free from extravasations. In fact, a recent investigator, who no doubt is strongly inclined towards a closed circulation, states expressly that he could not find a single communication between the artery and the vein.¹⁰

The first third of the ampulla is lined with spindle-shaped cells which are directly continuous with the endothelial cells of the artery. The second third branches and often communicates with neighboring

⁹ Hoyer, *Morph. Arbeiten*, Bd. III, 267.

¹⁰ Von Schumacher, *Arch. f. mik. Anat.*, LV, 1899.

ampullae. The last third of the ampulla is difficult to demonstrate, but under certain conditions it can be injected, as has been shown by Thoma and by me. I find from numerous specimens that its communication with the vein is not wide, but is cut up by bridges of tissue passing across its lumen before it connects with the vein. This cutting up is so extensive that in uninjected specimens it has been impossible for me to find a single ampulla connecting with a vein. In other words, it may be better to state that the ampulla rarely reaches the vein, but is separated from it by a small band of spleen pulp. When the spleen is distended to its maximum and fine granules are injected into the artery they pass directly from the ampulla to the vein, as well as into the surrounding tissue, for they must pass somewhere. This condition is illustrated in Plate I.

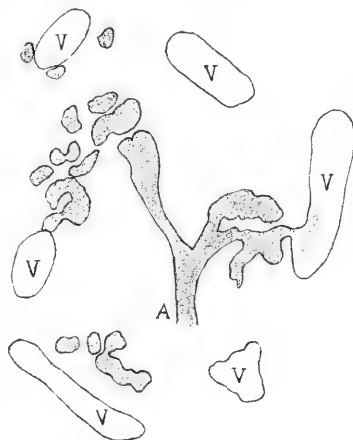
When cinnabar granules and gelatin are injected into the artery for a long time with a pulsating pressure most of the granules are found in the veins, but a great many are also scattered throughout the pulp. According to one's inclination this becomes an argument either for or against an open circulation. When either granules or foreign nucleated blood corpuscles are injected into the circulation of a living animal many of them are found between the cells of the spleen pulp, and they no doubt entered the pulp-spaces through the holes in the walls of the ampullae. Helly believes that the foreign red corpuscles pass from the artery to the veins and then through the "homogeneous membrane of v. Ebner" in the walls of the veins back into the pulp. That this roundabout way is the improbable course I shall show presently.

It is of decided advantage to inject an organ like the spleen with a fluid that will not mix easily with water, and I have tried a variety of mixtures of asphalt, turpentine and granules with great success. Hoyer¹¹ has already used this mixture in the contracted spleen, and what I have found in the oedematous spleen confirms and supplements his results. When the spleen is distended to its maximum with either blood or gelatin the relation of the terminal artery to the pulp is shown beautifully by injecting the turpentine-asphalt solution into the artery. Some granules of carmine should be added to the solution, for they lodge in the fine arterial branches and ampullae, and a few of them pass over into the pulp. It is well in making an artificial oedema of the spleen to inject the gelatin, to which ultramarine blue is added, into the veins. Finally the specimen is hardened in formalin and cut

¹¹ Hoyer, *Internat. Monatschr. f. Anat. u. Physiol.*, 1887; and *Morphol. Arbeiten*, 1894, 276 and 284.

into sections, by the freezing method, 20 μ thick. The specimens are to be mounted in glycerine. In the sections of such specimens the veins are found filled with blue granules, the pulp with gelatin and some blue granules, the terminal arteries with some carmine granules and the ampullae with asphalt and some carmine granules. As there is no mixing of the fluid gelatin and the asphalt in the pulp, the asphalt must take the course of the least resistance from the artery to the vein. With Prussian blue this is often directly through Thoma's *Zwischenstück*; with asphalt the course is always through the pulp-spaces.

In specimens in which little of the asphalt reaches the veins it is found that the asphalt passes out into the pulp-spaces from the ampullae, then piles up, forming clusters like bunches of grapes (Text Fig. 1). Each of these "grapes" fills a pulp-space. As the clusters spread out the globules of asphalt often radiate, leaving intervening pulp-spaces free. Finally all the pulp-spaces are filled with the clusters of globules, then they encircle the veins and are continued into them as fine threads of asphalt. At other times some of the veins are surrounded with asphalt globules without many of them communicating with the veins. Sometimes the injection of the asphalt follows the reticulum in all directions,



TEXT FIG. 1. Outline of the terminal artery, ampulla and venous sinuses in a spleen made hemorrhagic by ligating the vein and then injecting the artery with asphalt and turpentine. The masses of asphalt reach from the artery to the vein and fill the large irregular spaces in the pulp. A, artery; V, vein.

encircles the veins and enters them at many points. When the veins have first been plugged with ultramarine blue the asphalt which may enter the veins at points cannot spread far. When fine carmine granules are injected with the asphalt but few of them enter the veins, most of them lodging in the arteries and ampullae and some of them are scattered throughout the pulp. It appears then that the asphalt may push the aqueous fluid from the pulp-spaces and gradually pile up as does wax when injected into a lung. Or it may follow the reticulum, pushing the watery fluid to the centre of the pulp-spaces, as is again the case when the lung into which wax is injected contains much air. In this case the lung is filled with many small vesicles of wax full of air. The asphalt injections, therefore, give a most decided argument in favor of an open circulation.

Numerous experiments upon the dog's spleen show conclusively that the walls of the venous plexus are very porous. This can be shown well by injecting aqueous Prussian blue into the vein, which gradually passes through its walls at every point. If granules a little larger are injected (cinnabar), it will be found that they also pass through easily, but still larger granules (ultramarine blue) pass through the walls of the veins with greater difficulty. Yet often many of these granules pass through the vein-wall at all points, showing that it is very porous. Around the Malpighian follicles there is always an extensive "extravasation," showing that the openings at this point are very large and numerous. So constant is this "extravasation" found that it is out of the question to consider the openings around the follicles as artificial.

The nature of the wall of the vein has been well demonstrated by Höhl,¹² who gives an excellent picture of it (Fig. 10). It is composed of an extremely dense network of fibrils which withstand the action of pancreatin, and is therefore not elastic in nature. Höhl considers the fibrils as belonging to the reticular group, for they anastomose frequently and are directly continuous with the reticulum of the pulp. The fibrils around the vein were first isolated by Henle¹³ by means of a diluted solution of potassium hydrate, and for this reason v. Ebner¹⁴ considers them as elastic tissue, a conclusion which he supports with the Unna-Tänzer stain for elastic tissue. It is well known that reticulum fibrils as well as white fibrous tissue fibrils do become transparent in diluted solutions of potassium hydrate, but that their sharpness is again brought out in case they are stretched,¹⁵ a condition easily obtained under the cover-glass by slight pressure upon it. Von Schumacher¹⁶ repeated v. Ebner's tests for elastic tissue in the veins of the dog's spleen and sometimes found numerous elastic fibrils encircling them and at other times none at all. These tests have been repeated by Höhl¹⁷ and by Hoyer,¹⁸ who find that all or nearly all of the fibrils are reticular, which may be accompanied by some elastic fibers. In tests made with Weigert's elastic tissue stain I have been unable to find any elastic fibrils accompanying the reticulum fibers encircling the smaller veins. It is well when staining for elastic tissue not to stain too long,

¹² Höhl, *Archiv für Anatomie*, 1897.

¹³ Henle, *Anatomie*, II, 1866.

¹⁴ Von Ebner, *Anat. Anz.*, XV, 1899.

¹⁵ Mall, *Abhandl. d. k. säch. Gesellsch. d. Wiss.*, XIV, 1890.

¹⁶ Von Schumacher, *Arch. f. mik. Anat.*, LV, 1899.

¹⁷ Höhl, *Anat. Anz.*, XVII, 1900.

¹⁸ Hoyer, *Anat. Anz.*, XVII, 1900.

or else reticulum and even white fibers will take on some of the color and make them look like elastic fibers. Höhl has shown, however, that the reticulum fibers of the lymphatic gland, and even those of the spleen pulp, are accompanied in part by elastic fibers, a result which has been confirmed by Thomé¹⁹ and by myself.²⁰ I found that the amount of elastic tissue accompanying the reticulum in lymph nodes varied very much indeed and that often the periphery of the follicle contained many elastic fibrils while the centre had no fibrils at all that would stain with Weigert's stain. This result corresponds well with that of Thomé. In the Malpighian follicle, however, the elastic fibers radiate from the artery and do not extend to the surrounding pulp.

It is apparent from the above that the fibrils around the veins are mostly reticulum, and that elastic fibrils may accompany them. The work of Hoyer, Thomé and myself points clearly towards this conclusion.

A discussion of the homogeneous elastic membrane of v. Ebner between the fibrils encircling the veins and the large spindle-shaped endothelial cells within is more difficult. If this membrane is present it is an additional argument in favor of closed circulation through the pulp and is much in the way of both Weidenreich and Helly in their discussions. Weidenreich finds the membrane present but accepts an open circulation, while Helly, who believes in a closed circulation, sees foreign blood corpuscles and leucocytes passing through it. According to Böhm²¹ these veins have an elastic intima analogous to that of the artery. Von Schumacher found it inconstant in man and absent in the dog. Hoyer was unable to find it at all. Furthermore, in an extensive study upon the elastic tissue of the spleen by Lebrell,²² no mention is made of this elastic membrane. Were it present he certainly should have seen it. Since it is not supposed to be present in the dog's spleen, my failure to find it is not remarkable, and from my experience with the Weigert elastic-tissue stain I am inclined to think that it really does not exist at all.²³ No doubt all stages of the development of reticulum, from the connective-tissue syncytium to the complete reticulum fibril with its accompanying elastic fiber, is found in the lymph follicle, judging by my own experience and by the works of Hoyer and Thomé. Recently Flint²⁴ has followed the development of the basement membranes in the

¹⁹ Thomé, *Jena. Zeit.*, XXXVII, 1902.

²⁰ Mall, *Amer. Jour. Anat.*, I, 1902, p. 361.

²¹ Böhm, *Von Kupffer Festschrift*, 1899.

²² Lebrell, *Internat. Monatschr. f. Anat. u. Physiol.*, XX, 1903.

²³ See also Kyber, *Arch. f. mik. Anat.*, VI, 1870, p. 566.

²⁴ Flint, *Amer. Jour. Anat.*, II, 1902.

submaxillary gland of the pig and found that they arise from a syncytium and are fibrillar (pp. 5 and 10), even if in transverse sections they appear homogeneous. If we could add to such preparations an excessive stain for elastic tissue it is easy to conclude, as v. Ebner did, that these basement membranes are also homogeneous and elastic. Since, however, the elastic membranes are not present in the veins of the dog's spleen they do not stand in the way of an open circulation in this animal.

Recently Weidenreich has asserted that there are numerous lymphatics in the spleen which empty directly into the veins of this organ. This is only another way of expressing what W. Müller stated a number of years ago. It is easy to state that the channels from the pulp to the veins are lymphatics, but in view of the work of Ranvier,²⁵ MacCallum²⁶ and Sabin²⁷ our conception of lymphatics has been greatly sharpened. According to Sabin all of the lymphatic channels arise from four points from the veins, which correspond with the lymph hearts, and then spread all over the whole body. In order to accept Müller's notion it must be shown that lymphatics have an independent origin the spleen, which is very improbable.

Judging by the structure of the vascular system of the spleen-pulp, it is not remarkable that numerous investigators have concluded that the circulation should be directly through the pulp-spaces. That this should be so appears very remarkable when the circulation through other organs and tissues is considered, where the capillary walls are lined by a complete layer of endothelial cells and their lumina are equal. No one admits, however, that such capillaries are within the spleen pulp, but because they are closed elsewhere it is concluded that they must also be closed within the spleen. If the ease with which "extravasations" take place from the capillaries of embryos, when the blood-vessels are injected, is recalled, one is struck with the similarity between them and those of the spleen-pulp. In fact I have frequently observed that in certain portions of the embryo the "extravasation" takes place with greater constancy than elsewhere. Recently this system of irregular capillaries has been more sharply defined by Minot,²⁸ who terms them sinusoids and shows that a sinusoidal circulation is present in many of the organs of the embryo and in some of the organs of the adult. He states that he does not consider it improbable that the circulation through the spleen will prove to be sinusoidal. That

²⁵ Ranvier, *Archiv d'Anatomie*, I, 1897.

²⁶ MacCallum, *Archiv für Anatomie*, 1902.

²⁷ Sabin, *Amer. Jour. Anat.*, I, 1902.

²⁸ Minot, *Proc. Bost. Soc. of Nat. History*, XXIX, 1900.

this is true I think the recent work upon the spleen proves quite conclusively. Since sinusoidal or open circulation exists elsewhere, the old argument that the capillaries of the spleen are closed because the capillaries of the rest of the body are closed, is no longer of any value.

It remains still to be shown that in normal circulation through the spleen the solid elements of the blood are carried through the spleen sinusoids or pulp-spaces. It is well known that in higher animals but relatively few red blood discs are found in the pulp-spaces and that it is practically impossible to obtain natural injections of them. This fact, together with a mythical homogeneous membrane lining the capillary veins, is v. Ebner's strong argument in favor of a closed circulation in the spleen. Von Schumacher, who also believes in this elastic membrane, always finds blood in the pulp with the membrane intact.

In case the blood passes through the pulp-spaces in its normal circulation, it should be possible to retain it in them by making the proper experiment. Sokoloff and Wicklein made numerous experiments which appeared to prove that after ligation of the splenic vein the blood first accumulated in the veins, then the pulp becomes oedematous, after which the blood elements pass over into the pulp. No doubt all of these observations are correct, but it appears to me that their reasoning is wrong, as Weidenreich has shown recently. Sokoloff states that as a rule the normal spleen contains no blood within it, and it is difficult to find it even in the blood-vessels (p. 211). This is due to the contraction of the muscle, which always takes place when the organ is removed and presses the blood out of the spleen (p. 213). "Wie wäre es denkbar, dass bei einer solchen Ueberfüllung der Venen, die Pulpa nach dem Tode ihr Blut in die Venen entleeren sollte. Wenn der Blutstrom unter normalen Verhältnisse aus der Arterie in die Milzpulpa und von da in die Venen sich ergiessen würde, musste hier offenbar die Pulpa mit Blut überladen erscheinen," etc. (p. 215).

In addition to this Sokoloff showed that the walls of the capillary veins are very porous, in fact wanting around the Malpighian follicles, and it was through these pores he thought that the blood passed into the pulp in case the vein was closed long enough.

Wicklein repeated the experiment of Sokoloff and found that if the vein was ligated long enough to produce an extensive infarction of the pulp this infarction would disappear in the course of time in case the ligation was removed. In all cases he ligated the vein for 30 minutes, a time sufficiently long to cause an extensive distention of the pulp with blood, then he removed the ligation and killed the animals in from 4 hours to 21 days, and in all cases found the pulp normal in every respect.

He concludes from these experiments that the blood first passed into the pulp backward through the veins, and then when the ligature was removed the blood passed into the veins again, by what mechanism he does not state.

I have repeated these experiments a number of times and find that in the course of half an hour after ligature of the veins the spleen is distended to its maximum and the pulp is always gorged with blood, as described by Sokoloff and by Wicklein. If now the spleen is removed from the body by cutting its attachments to open all the large vessels, it empties itself at once, and sections show that the pulp is as free from red corpuscles as is the normal spleen. There must, therefore, be some mechanism by which the blood which enters the pulp either from the artery or the vein may be rapidly expelled from the pulp. In case the ligature from the vein is simply removed in the living animal the spleen does not become entirely anaemic, but when it is removed from the body it contracts to its maximum and expresses every drop of blood from its pulp. An extremely instructive experiment is made by keeping the vein ligated until the spleen is blue, but not distended to its maximum. This takes from 10 to 15 minutes. Then the spleen is to be removed from the body, leaving the ligature intact. The contractions begin at once and pump the blood around under the capsule, thereby giving some large hemorrhagic spots in which the pulp is gorged with blood. At other points, however, the spleen is anaemic and practically normal. A portion of the spleen-pulp has been emptied of its blood, and due to the severe contraction it was passed to some other portion of the spleen to make it even more hemorrhagic than before. A double process has taken place, which can be observed with ease; the contraction has forced blood from the pulp into the vein in one portion of the spleen and from the vein into the pulp in another portion. At any rate one thing is definite—when the blood is free in the pulp contraction of the muscle has the power to squeeze it out at once and to force it over into the vein.

Miescher-Rüsch,²⁹ in one of the best among the many excellent papers upon the spleen, states that in the dog the blood is pressed out of the pulp by the muscular contraction, while in the salmon, which has no muscle fibers in the spleen, the blood stays in the pulp-spaces. In the salmon, at any rate, the blood corpuscles must be flowing constantly through the pulp-spaces, forced onward by the arterial pressure.

It is practically impossible to determine with certainty whether the blood circulates through the pulp-spaces of higher animals as it does in

²⁹ Miescher-Rüsch, *Archiv f. Anatomie*, 1881.

fishes unless the muscles of the trabeculae and capsule are paralyzed or are thrown out in some way. Jaschkowitz³⁰ found by cutting the nerves of the spleen that the muscle becomes paralyzed and the pulp fills with blood. I have repeated Jaschkowitz's experiment and have discussed it more fully elsewhere.³¹ It appears to me that in view of the anatomy of the spleen and the effect of contraction of the muscle upon blood in the pulp it is rational to conclude that when the muscle is paralyzed by cutting the nerves the increased amount of blood in the pulp came directly from the arteries rather than back through the veins. The muscle is excluded and we have on one hand high arterial pressure and on the other hand low venous pressure. It appears to me that there is but one way by which this blood got into the pulp-spaces, i. e., through the holes in the ampullae.

In connection with the effect of contraction and relaxation of the muscle of the spleen and its effect upon the blood in the pulp we may consider Roy's³² discovery of its rhythmic contraction. It was found that the contractions of the spleen are very regular, one a minute, and that the change of volume during each contraction may be as much as 18 per cent. In a dog's spleen of average size this is about 5 grams. Since about 5 cc. of blood flows from the veins of the spleen every minute,³³ there should be a variation of the outflow from the vein during this time. Roy concludes that the pulsation of the spleen acts as a pump by which the circulation through the spleen is aided. Without entering upon the discussion of this question it may be noted that this conclusion is doubted by Schäfer and Moore.³⁴ "The spleen volume is extremely responsive to all fluctuations in the general blood-pressure, and the circulation through the organ can be and probably is entirely brought about, as in other organs, by the difference between the arterial and venous pressure." Artificial circulation is carried on easier when the organ is distended, even after death of all the muscles, and the same seems to be the case in the living spleen. W. Müller has shown that it is impossible to inject the arteries of the spleen through the veins unless the spleen is pretty well distended (p. 85), and this should be the case judging by the arrangement of the ampullae. When the pulp is distended the reticulum fibrils pull the ampullae open and when it is, compressed the ampullae will be closed, making of them a kind of valve.

³⁰ Jaschkowitz, *Virch. Arch.*, XI.

³¹ Mall, *Zeit. f. Morphol. u. Anthropol.* II, 1900.

³² Roy, *Journal of Physiol.*, III, 1880-82.

³³ Mall, *l. c.*, p. 36.

³⁴ Schäfer and Moore, *Journal of Physiol.*, XX, 1896, p. 50.

It happens also that forcible distention of the spleen, or contraction of the muscle of a hyperaemic spleen pulls all of the veins open, even after they leave the trabeculae to enter the spleen lobule. So a contraction of the muscle of a hyperaemic spleen will tend to close the ampullae of the arteries and to open the veins. The effect of this of necessity must be to force the blood from the pulp into the veins, which is always the case. When it is once outside of the spleen the valves will prevent its return. And I have found that in certain cases the pressure in the splenic vein may exceed the arterial, a condition which can be brought about only in case the spleen contraction acts as a pump. In one case the pressure in this vein rose to 190 mm. Hg. with the artery closed, i. e., the arterial pressure practically at zero (l. c., p. 37).

Objection may be raised against Jaschkowitz's experiment as an argument in favor of an open circulation, for considerable time elapses between cutting the nerves and the following hyperaemia and infarction. It must still be shown that in the living animal the blood is constantly passing through the pulp, as is the case in the salmon's spleen. The influence of the contraction of the muscle upon the blood in the pulp must be removed in other ways.

In order to bring more evidence to bear upon this question I have made four kinds of successful experiments, which prove conclusively that practically all of the blood corpuscles pass through the pulp of the spleen.

In the first of these the dog was bled to death and the blood whipped. Cannulae were then tied into the splenic artery and vein, after which the anastomoses were tied and the spleen removed. The whipped blood and spleen were then kept at from 3° to 5° C. for 24 hours. Then the blood and spleen were warmed to 37° and the blood was injected into the artery with a pulsating pressure from 80 to 100 mm. Hg. In just one minute the blood began to flow from the vein. In 5 minutes the spleen began to swell a little, which continued slowly until the spleen was quite red and of the appearance it has in the living animal. Now the flow from the vein was at the rate of 5 cc. a minute, about the same as in the living animal. At the end of half an hour the spleen was placed carefully in strong formalin. During the whole time of artificial circulation the arterial blood was red and the venous blood blue, and at no time was there the faintest indication of the contraction of any muscle. Next day frozen sections were made and in all cases it was found that the pulp was filled with blood, extending freely over into the lobular veins, which were gorged. The interlobular veins were not so full, for during the whole experiment the vein was freely open, the

pressure in it being practically zero. That the injection into the pulp is not a backward injection is proved by ligating one of the arteries to the spleen while making the experiment. The veins of the pulp of the region supplied by the closed artery were injected through the venous anastomoses within the lobule, but in this region the pulp-spaces were all empty. It is natural to conclude from this experiment that the blood passed from the ampullae into the pulp-spaces, then through the pores in the walls of the veins to form columns of blood discs which are pushed from the smaller to the larger veins of the spleen.

The muscle of the fresh isolated spleen is easily paralyzed by injecting the artery with normal salt solution or even with ordinary aqueous solutions of gelatin. When fresh spleen is paralyzed in this way it is found by injecting gelatin and cinnabar granules, or by injecting whipped blood, specimens are obtained which are exactly identical with the experiments described above. I thought for a long time that the large number of cinnabar granules found in the lobular veins indicates that the granules pass in great part from the artery directly into the vein and in lesser part from the artery over into the pulp-spaces. But when the experiments are graded it is found that the granules do not enter the veins until the pulp-spaces are first filled. The same is true when artificial circulation is carried on with whipped blood. All the injections, especially those with asphalt and turpentine, confirm this view. In them numerous terminal arteries are found, around which the pulp spaces are injected, forming pictures much like bunches of grapes. From these the injection passes into the veins. Incomplete injections after the veins are plugged with granules are especially valuable for the study of the relation of the arteries to the pulp-spaces. It may be added that in all of these tests the greatest "extravasation" of blood, of granules or of coloring matter is always immediately around the Malpighian follicles, showing that the communication between the ampullae and pulp-spaces are there the freest.

The muscle of the spleen can be paralyzed in the living animal by injecting nitrites into it. In all of my experiments I injected nitrite of soda from one-half per cent to one per cent in strength. The latter solution paralyzes the muscle very quickly. In one experiment the upper, or larger end of the spleen, was washed out with a half per cent solution through the vein with the artery closed for a period of five minutes. At the end of this time the upper part of the spleen was totally paralyzed and flabby. The artery was then opened for 25 minutes, and to show that the circulation through the paralyzed portion was well established the blood was collected from the open vein, which was

9 cc. in 10 minutes. The vein was now closed for 15 minutes and then the animal was killed by cutting the aorta. During the time the vein was closed the spleen became very much distended with blood. The spleen was now cut out, leaving the veins and arteries freely open. During the 5 minutes which followed the normal end of the spleen contracted to a solid mass, the paralyzed end contracted slightly and the zone between contracted markedly. Careful examination showed that there were no clots in any of the veins. Frozen sections, after the spleen had been hardened in formalin, showed that the pulp of the paralyzed end of the spleen was filled with blood, that of the normal end was free from blood, and that in the intermediate zone there was some blood in the veins and some in the pulp. Experiments of this sort only show that the blood which enters the pulp after the vein is closed is not expelled in case the muscle of the spleen is paralyzed.

A better test is made by injecting the nitrite through the artery. This can be done easily by inserting the cannula into one of the anastomoses to the stomach, pointing towards the spleen, and when the fluid is injected the main artery is to be clamped to prevent the fluid from escaping into the aorta. Of course all of the anastomoses are to be tied. If a spleen is injected in this way for ten minutes it is found that the muscle is paralyzed completely. Then by closing the cannula and opening the main artery the normal circulation is re-established. In case the first blood enters the pulp directly it should be found filled with red blood corpuscles. So at the end of one minute the spleen was cut out with one stroke of the scissors, leaving the main arteries and veins open. The paralyzed end of the spleen did not contract. The specimens were placed in strong formalin at once and frozen sections were made a few days later. They showed that the pulp was gorged with blood in the paralyzed portion of the spleen. It was practically impossible to find the line of demarcation between the pulp and the veins. As the end of the spleen which was not paralyzed was approached the pulp was found to contain a much smaller number of red blood corpuscles, but at no point was it full of them. Experiments of this kind show that when the muscle of the spleen is paralyzed with sodium nitrite the blood which enters the artery passes first into the pulp-spaces and remains there, for there is no muscular contraction to expel it.

Probably the most satisfactory experiment is made by paralyzing the muscle of the spleen so quickly that it has no time to contract and empty the pulp-spaces. This can be accomplished by making an interstitial injection with strong formalin and then removing the spleen at once and with one stroke of the scissors. The whole experiment can be performed

in 5 seconds, and it is usually found that the spleen does not show the faintest sign of contracting when it is laid upon a glass plate. When it is simply removed from the body without the injection of formalin it contracts during a period of several minutes and gradually expels all of the blood from the pulp and veins.

In order to make this experiment more definite I used the very hyperaemic spleen, found during active digestion. The animal was placed under the influence of morphine and the hyperaemic spleen drawn gently through an opening made in the abdominal wall. Next ten cubic centimeters of the strongest formalin were rapidly injected into several portions of the spleen with a hypodermic syringe and then the organ was severed from the body with one stroke of the scissors. After the spleen was observed for 5 minutes in order to see that it had been completely paralyzed it was hardened in formalin. The sections which were subsequently made showed that the whole pulp was filled with blood, just as is the case in the salmon's spleen or the dog's spleen when the muscle is paralyzed for a greater length of time. This differs from the rest of the experiments in one most important respect—the blood was caught in position in the pulp of the normal hyperaemic spleen. There can be but one interpretation of this experiment—the blood passes through the pulp-spaces in normal circulation, and due to the rapid fixation and paralysis of the muscle it is held there.

The crucial experiment is made by fixing the spleen in the living animal by injecting formalin directly into the carotid artery. For this purpose the dogs were fed four hours before the experiments in order that their spleens should be very hyperaemic. The cannula was introduced into the carotid artery pointing towards the heart and 2000 cc. of a 10 per cent solution of commercial formalin was injected at a pressure of 200 mm. Hg. This treatment coagulated immediately all of the tissues fixing definitely the chyle in the lacteals throughout their extent as well as all of the blood in the spleen. All of the muscles were immediately and completely paralyzed. The spleen remained very hyperaemic and showed no indication whatever to contract. Frozen sections showed that there are a great mass of red discs in the pulp especially around the Malpighian follicles. The distribution of the blood corresponds in every respect with that of cinnabar granules when injected either into the artery or the vein. At many points the veins are well filled with blood and at others the pulp and veins are so evenly filled with blood that the line between them cannot be seen. In general the spleen is nearly as full of blood as is the case when the vein has been ligated for half an hour. The effect of the formalin upon the

spleen when it is injected into the artery of a live animal must be practically instantaneous, paralyzing the muscle and fixing the blood corpuscles in their natural channels. That the pulp of the spleen is found gorged with blood in this experiment is conclusive evidence in favor of an open circulation.

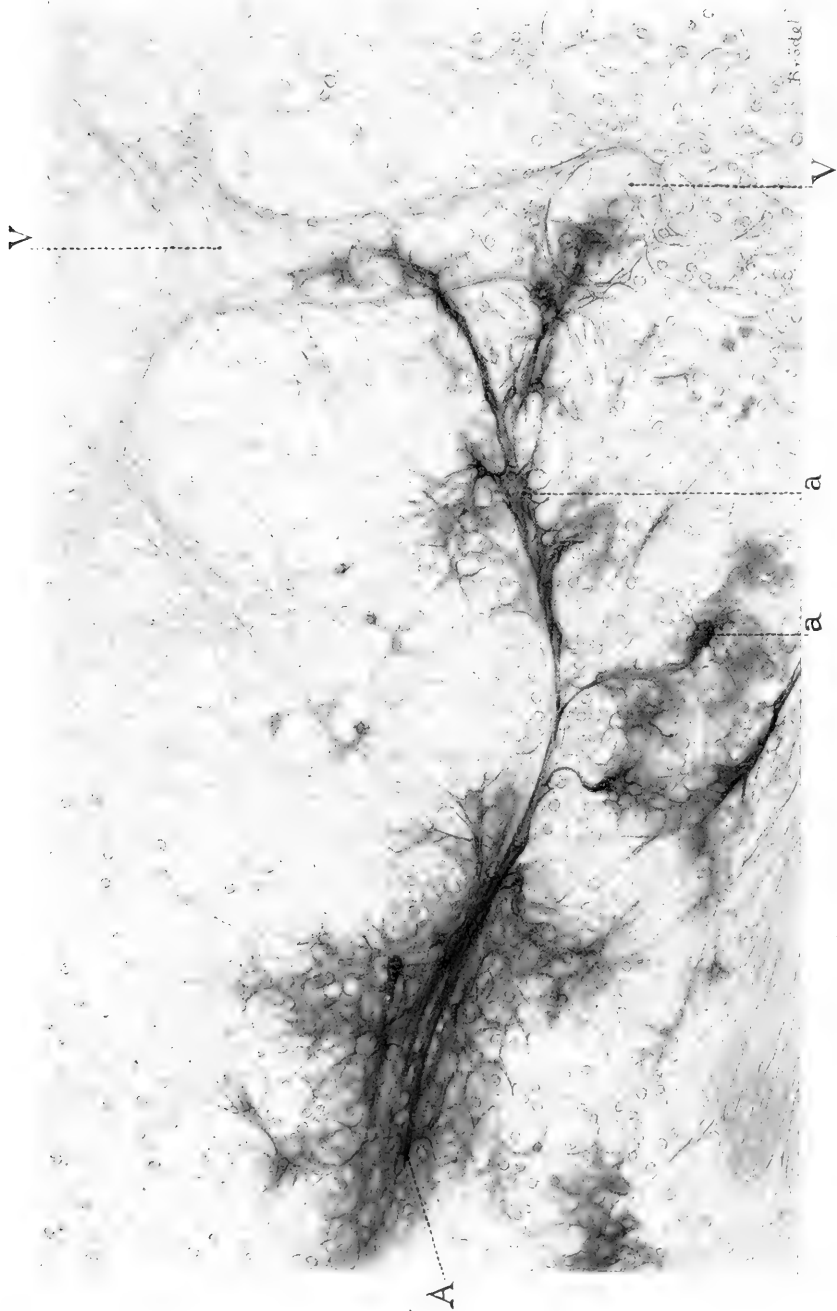
The forces which drive the blood through the pulp are undoubtedly the arterial pressure, the elasticity of the reticulum and the contraction of the muscle of the spleen. Judging from the arrangement of the trabeculae and veins in distended spleens it is very apparent that the contraction of the trabeculae have a decided influence in pulling the veins open. So when the muscle contracts it exerts a pressure upon the pulp more than it does upon the contents of the larger veins; in other words, the arrangement is such that the contraction of the muscle forces the flow of blood from the intralobular veins to the interlobular veins. When the pulp is compressed, however, the elasticity of the reticulum (l. c., p. 29) acts more upon the pulp than upon the capillary veins, again favoring the circulation from the pulp-spaces into the capillary veins. Therefore the anatomical and physiological arrangement is such that the contraction of the muscles of the trabeculae and capsule will press blood from the pulp into the veins without the aid of the arterial pressure. On the other hand it is through the arterial pressure that the pulp-spaces are filled when the spleen is relaxed, for it alone can overcome the elasticity of the reticulum. The arterial pressure itself is sufficient to carry on a complete circulation through the spleen, but the pulp-spaces can be fully emptied only by the contraction of the splenic muscle. The contraction of the splenic muscle has a tendency to close the capillary arteries while on the other hand with the aid of the elastic reticulum the capillary veins are pulled open. Therefore this contraction forces blood in one direction only.

The conclusion to be drawn from this study is that the course of the red blood corpuscles is always through the pulp-spaces in passing from from the artery to the vein. I have been unable to gather any good evidence in favor of some closed capillaries, as suggested by W. Müller, Miescher, Weidenreich and others. Thoma's *Zwischenstück* represents only the more direct pulp-space between the ampulla and the vein, which is best demonstrated when the rest of the pulp-spaces are gorged with blood.

EXPLANATION OF PLATE I.

Section of a spleen made oedematous by injecting chrome yellow suspended in gelatin into the vein. The artery was then injected with an aqueous solution of Prussian blue. The specimen was cut on the freezing microtome, tinged with picric acid mounted in glycerine. Enlarged 250 diameters. *A*, artery; *a*, ampulla; *V*, vein.

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ON THE TRANSITORY OR ARTIFICIAL FISSURES OF THE HUMAN CEREBRUM.

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WITH 1 TABLE.

Nearly a century ago J. F. Meckel¹ discovered the transitory fissures in the cerebrum of human embryos eight or nine weeks old; these he believed to be normal and in no way connected with the permanent fissures. The presence of the transitory fissures was confined by numerous competent anatomists and from time to time their relation to the permanent fissures was discussed. According to Tiedemann they represent the earlier stages of the permanent fissures, and Cunningham states that most of them are obliterated while several "occupy positions which later on are occupied by permanent fissures, and either show direct continuity of existence with these, or at least act as their precursors."

It was gradually shown that the transitory fissures are usually present in embryos of the third and fourth months. To be sure suitable material for study is difficult to obtain and usually the specimens studied were those that had been preserved in alcohol for a considerable time. The influence of alcohol, especially weak alcohol, upon tissues is well known and this naturally led Bischoff in 1868 to suspect that the transitory fissures were artificial, having been produced by the macerating influence of weak alcohol. Furthermore, he found that the fissures were not present in the brains of embryos which had been hardened in chloride of zinc. This view is accepted by Marchand (1891) in his paper on the corpus callosum.

Were it not so difficult to obtain fresh human embryos, this question would have been settled long ago. That these fissures are normal seems to be proved by Ecker, in 1869, who observed their presence in the fresh

¹References to the literature upon this subject will be found in the following papers: Cunningham, *Jour. of Anat. and Phys.*, XXIV, 1890; Hochstetter, *Bibliotheca medica*, Stuttgart, 1898; and Retzius, *Biol. Untersuch.*, X, 1902.

brain of an embryo three months old. Further observation by Hochstetter (1898) shows that they are not present in the fresh brain. Hochstetter examined the brains of two very fresh human embryos and in neither of them was there a trace of a transitory fissure. In other specimens which were well preserved the transitory fissures were only slightly marked, or were not present at all. The observations of Hochstetter are confirmed by Retzius, who had an opportunity to examine the fresh brain of an embryo of the third month. The membranous skull was removed and the specimen hardened in Zenker's solution. After this treatment, it was found that the lateral and mesial surfaces of the brain were perfectly smooth with the exception of a slight depression on the mesial side.

It appears then that when the brains of fresh embryos of the third and fourth months are examined no transitory fissures are found. Furthermore, when fresh specimens are carefully hardened the transitory fissures are insignificant and not numerous, or are not present at all.

About five years ago I noticed that the cerebral vesicles of human embryos hardened in formalin are entirely different from those hardened in alcohol. Not only are the vesicles perfect in form with walls in apposition to the membranes of the skull, but the arrangement of the cells is definite and clear. Specimens hardened in alcohol are sometimes folded and usually macerated, the degree of maceration always being far in excess of that of the rest of the body.

The recent publication of Retzius has induced me to tabulate the condition of the brains in my embryological collection to determine the frequency and degree of transitory fissures in brains hardened in formalin as well as in those hardened in alcohol. The table which I have constructed records the condition of the brains in over fifty specimens. There are about a dozen excellent formalin specimens in the collection not included in the table, for they have not been sectioned and I am unwilling to injure them before they are cut into serial sections. It appears to me that these specimens recorded in the table, together with the observations of Hochstetter and of Retzius, set the transitory fissures aside as artificial products of the effect of weak alcohol upon the brain.

The appended table gives the numbers, the length and the condition of the cerebral vesicles of embryos in my collection in which there are any data relating to the transitory fissures. The specimens have been grouped in months, using for this purpose a rule which has been published recently.² According to this rule the age of an embryo in days

² Mall, Johns Hopkins Hospital Bulletin, 1903.

equals the square root of one hundred times its length from vertex to breech in millimeters. Thus an embryo 30 mm. long is $\sqrt{30 \times 100}$, or 54 days old. Or, to determine the vertex-breech length of an embryo for a given number of days, square the number of days and divide by one hundred. Thus the vertex-breech length of an embryo 30 days old is $\frac{30^2}{100}$ or 9 millimeters. The data upon which this rule rests will be found in my paper on the pathology of early human embryos.³ This formula applies only to embryos up to 100 mm. in length. In embryos from 100 to 220 mm. long from vertex to breech the length in millimeters equals the age in days.

In nearly all instances the embryos were hardened either in alcohol or in formalin. Not only is this recorded in my notes, but it is also indicated by the condition of the tissue in case the specimen has been cut. It is very apparent from all of my specimens, both normal and pathological, that when the embryo is macerated to the least degree the effect is much more marked in the brain than elsewhere. It appears that any dissociating fluid effects the brain first. So in order to tabulate the specimens I have had to express the extent of maceration of the brain in degrees, which in general is two or three degrees more advanced than that of any other organ of the embryo.

The condition of the brain is marked 0 in the table in case its lateral mesial surfaces are perfectly smooth as pictured by Retzius for the fresh brain of a human embryo at the end of the third month. Those brains in which there are slight irregularities of the walls, as is the case when there is some shrinkage with separation of the vesicle, are marked 1. Some of these folds are certainly not true transitory fissures, for in the same embryos there is the same separation of the epithelial cells in the oesophagus and in the intestine. I have, however, included in this group those brains in which the transitory fissures are just beginning. The brain is marked 2 whenever it has the typical transitory fissures as usually described.⁴ In case the infolding is more extended, showing signs of maceration and disintegration of the walls of the brain with loose cells within the ventricle, it is marked 3. When the maceration has gone so far that the vesicles are filled with cells and the brain is nearly solid, it is marked 4. In the specimens marked 1 to 4 the spinal

³ Mall, Johns Hopkins Hospital Reports, IX, 1900.

⁴ The condition of specimens marked 1 equals about those with the least number of fissures as pictured by Retzius on Plate 1 in his great monograph, *Das Menschenhirn*. Those marked 2 represent those figures on this same plate with the greatest number of fissures.

cord is not macerated very much, but when the entire central nervous system is macerated and solid it is marked 5. So we have, in addition to the embryos in which the surfaces of the brain are smooth, those in which the cerebral vesicles are folded and macerated from the simple small fold up to a stage in which the entire central nervous system is converted into a pulpy mass.

It is seen from the table that the condition of the brain varies very much in embryos of the first month as well as in the later months. In four of the embryos the cerebral vesicles are perfect and these are from specimens which were carefully hardened. In the fifth, No. 80, there are no data except that the specimen was hardened in alcohol. One embryo, No. 164, is from an autopsy, and the uterus after it had been cut open was kept on ice for 24 hours before it came into my hands. The entire specimen was then placed in strong formalin. Since all of the sections show that the tissues of the body are macerated it is not difficult to understand why the walls of the cerebral vesicles are also macerated and slightly folded.

The embryos of the second month also show a variety of conditions in the cerebral vesicles. There are six perfect ones and three of these were hardened in formalin. One formalin specimen, No. 106, is pretty well macerated, but the specimen had been in water 24 hours before it came into my hands. In it the brain and spinal cord are practically solid.

In No. 86 there is one small fissure on the medial and one on the lateral side of the cerebral hemisphere. This embryo was brought to the laboratory with the amnion unbroken, and without opening it the entire specimen was placed in formalin. It may be that the slight amount of formalin which entered the embryo first acted as a dissociator, caused the cerebral vesicles to expand quicker than the membranes and these narrow transitory fissures followed. In this specimen the fissures are formed by the epithelial wall of the cerebral vesicle turning in without drawing the pia with it. The pia bridges straight over the transitory fissure and the capillaries to the cerebral vesicle are torn off. It is clearly a case of tearing the cerebral vesicle from the pia, which could only have taken place after the death of the embryo.

During the third month it is said that the transitory fissures make their appearance. Among ten specimens there are two with perfect transitory fissures and three with well marked transitory fissures. There are five specimens without any fissures at all and four of them are formalin specimens. One specimen, No. 95, has well-marked total fissures all around the cerebral vesicle. This specimen came to the laboratory fresh and without opening the ovum it was placed in formalin. This

was the first of the formalin specimens which was cut, and for a long time I considered it conclusive proof in favor of the transitory fissures being normal. Here also the slow penetration of the formalin may have acted more markedly as a dissociator which caused the cerebral vesicles to expand quicker than the membranous walls of the head and thereby produced the slight infolding. In this specimen, as in No. 86, the maceration has caused a separation of the cerebral walls from the pia over the transitory fissures. At other points the cerebral cells turn outward, forming small microscopic protuberances. In both these specimens the microscopic examination shows clearly that the transitory fissures are produced artificially by the unequal expansion of the cerebral vesicles and the membranous wall. The walls of the cerebral vesicles naturally were torn away from the pia along the line of the transitory fissures.

I was fortunate enough to obtain a fresh embryo of the fourth month while tabulating the specimens of my collection. Although the abortion had taken place 24 hours previously, the brain showed no indications of fissures at all; in every respect the specimen was like that of Retzius. After the membranous wall had been removed the brain was placed in formalin, in which it retained its smooth form.

The specimens of the fourth and fifth months are very conclusive. There are nine specimens hardened in formalin and none of them have any transitory fissures. They are present in the four specimens which were hardened in alcohol. A single fresh specimen at the beginning of the fifth month was perfectly smooth on both mesial and lateral surfaces, although the embryo came into my possession 24 hours after the abortion.

It is apparent from the specimens which have been described that fluids which dissociate tissues are more marked in their effect upon the walls of the cerebral vesicles than upon any of the other tissues of the embryo. As the cells of the cerebral vesicles become thicker and the tissues firmer the brain substance is more resistant and does not macerate as easily as before, so that by the fifth month transitory fissures can be no longer produced artificially. Formalin, which in strong solutions causes the brain tissue to swell, is a dissociator in very weak solutions, and therefore occasionally produces transitory fissures. According to the experience of Hochstetter, Retzius and myself, the transitory fissures are not found in fresh brains. The transitory fissures are therefore artificial and are of no morphological significance.

TABLE OF EMBRYOS GIVING THE CONDITION OF THE BRAIN WHEN
HARDENED IN ALCOHOL OR IN FORMALIN.

0, indicates that the surface of the brain is smooth; 1, indicates that there are small folds present; 2, typical transitory fissures; 3, folds very marked with the beginning of maceration; 4, maceration complete and cerebral vesicles nearly solid 5, entire central nervous system solid.

EMBRYOS OF THE FIRST MONTH.

Number of embryo.	V. B. length of embryo in mm.	Condition of the brain.	Hardening fluid.	Remarks.
12	2	0	Alcohol	60 %
164	3½	1	Formalin	On ice 24 hrs., then in formalin.
148	4 ³ / ₆	0	Alcohol	80 %
76	4½	0	Alcohol	Whole ovum in absolute alcohol.
1	4½	5	Salicylic acid.
80	5	0	Alcohol	
116	5	2	Alcohol	
19	5½	5	Alcohol	
2	7	0	Alcohol	Ovum in strong alcohol.
4	7	1	Alcohol	
18	7	2	Alcohol	
113	8	4	Alcohol	

EMBRYOS OF THE SECOND MONTH.

163	9	0	Formalin	
88	10	0	Alcohol	
114	10	3	Alcohol	
109	11	2	Alcohol	
175	13	3	Alcohol	
144	14	0	Formalin	
43	16	0	Alcohol	Embryo within amnion in strong alcohol
106	17	5	Formalin	In water 24 hrs., then in formalin.
9	17½	0	Alcohol	
5	18½	4	Alcohol	
74	19	3	Alcohol	
22	20	2	Alcohol	Whole ovum placed in alcohol.
108	22	4	Alcohol	
57	23	5	Alcohol	
100	27	5	Alcohol	Weak alcohol.
45	28	2	Alcohol	
86	30	1	Formalin	Embryo within amnion in formalin, two fissures.
75	30	3	Alcohol	

EMBRYOS OF THE THIRD MONTH.

206	40	2	Alcohol	Fresh, 24 hrs. after the abortion.
218	42	0		
96	44	0	Formalin	Whole ovum hardened in formalin.
95	46	1	Formalin	
105	48	1	Alcohol	
84	50	0	Alcohol	
169	52	0	Formalin	Whole uterus with ovum hardened in formalin.
151	52	1	Alcohol	
139	55	0	Formalin	
	65	2	Alcohol	
179	70	0	Formalin	

EMBRYOS OF THE FOURTH MONTH.

	80	2	Alcohol	
	90	0	Formalin	
146	95	0	Formalin	
	100	0	Formalin	
	105	0	Formalin	
	110	0	Formalin	
	110	1	Alcohol	
	112	0	Formalin	
138	112	0	Formalin	

EMBRYOS OF THE FIFTH MONTH.

219	115	0		Fresh, 24 hrs. after the abortion.
149	120	1	Alcohol	
170	125	0	Formalin	
48	130	1	Alcohol	
	150	0	Formalin	



CHANGES IN THE NISSL'S SUBSTANCE OF THE GANGLION
AND THE BIPOLAR CELLS OF THE RETINA OF THE
BRANDT CORMORANT *PHALACROCORAX PENICILLI-*
TUS DURING PROLONGED NORMAL STIMULATION.¹

BY

A. J. CARLSON.

*From the Hopkins' Seaside Laboratory and the Physiological
Laboratory of Leland Stanford, Jr., University.*

WITH 1 COLORED PLATE.

Beginning with the work of Hodge numerous researches have been made on the histological and micro-chemical changes in ganglion cells in different states of physiological activity. Both the changes observed as well as their interpretation are in many respects at variance,² which may, in part, be due to the different methods employed, but probably also to the fact that the states of rest, activity and fatigue of the cell as typified by change in structure and chemical reaction are probably separated by imperceptible gradations only. As electrical stimuli were in many cases resorted to bring about the conditions of activity and fatigue of the cells. Nissl³ in 1896 pointed out the invalidity of, without further proof, identifying the changes observed in the cells on such treatment as identical with the changes that may accompany normal physiological functioning. The vertebrate retina seems to offer the best field where conditions of rest, activity and fatigue may without much difficulty be induced by variations in the normal physiological stimulus. The first investigator to study the finer structural differences in the cells of the stimulated or fatigued and of the resting retina was Mann (1894).⁴ He did not confine his observations to the retina, but

¹This work was begun in the fall of 1900 at the suggestion of Prof. F. M. McFarland. It was intended to extend the observations to the retinae of reptiles and fishes, but as other work has intervened the note is recorded in its present form.

²For a recent résumé of the literature the reader is referred to an article by Van Durme: *Etude des différents états fonctionnels de la cellule nerveuse corticale*. *Le Nerveux*, II, 1901, pp. 125-142.

³Nissl: *Die Beziehungen der Nervenzellsubstanzen zu den thätigen, ruhenden and ermüdeten Zellzuständen*. *Neurologisches Centralblatt*, 1896, S. 59.

⁴Mann: *Histological changes induced in sympathetic, motor, and sensory nerve cells by functional activity*. *Journal of Anatomy and Physiology*, 1895, p. 100.

studied also the cells in the sympathetic ganglia, in the spinal cord, in the cerebral cortex and in some of the nuclei of the midbrain. These are his conclusions:

"1. During rest, several chromatic materials are stored up in the nerve cell, and these materials are used up by it during the performance of its function.

"2. Activity is accompanied by an increase in size of the cells, the nuclei and the nucleoli of sympathetic, ordinary motor and sensory ganglion cells.

"3. Fatigue of the nerve cell is accompanied by shriveling of the nucleus and probably also of the cell, and by the formation of a diffuse chromatic material in the nucleus."

Of his observations on the retina he says: "In four dogs which were allowed to run about for twelve hours with one eye covered up while one eye was exposed, and the brains and retinae of which were fixed by injecting HgCl_2 from the aorta, I notice in the retina kept in darkness that the nuclei of the rods are very rich in chromatin, the individual chromatin segments being globular, spherical externally, and faceted where in contact with one another, while in the exposed eye the chromatin segments are greatly shrunken and quite stellate. The nuclei of the ganglion cells of the dark retina are smaller than those in the exposed retina, and in the latter the nuclear hyaloplasm is no longer stained with methyl blue."

This is all he says of his work on the retina. He does not mention any changes in the Nissl's substance in the cells of the ganglionic and the bipolar layer; and the figures (Plate I, figs. 6 and 7) show only the changes in the size and contour and in the amount of chromatin in the nuclei of the rods and cones and the bipolar cells. But in the three general conclusions the cells of the retina are evidently included.

Bach (1895)⁵ repeated Mann's experiments on the retina of dogs with some modification, but was unable to verify the latter's findings on any point. Of the Nissl's substance Bach says: "Weder in der Menge, noch in der Anordnung, der Form der färbbaren Plasmaschollen . . . konnte ich constante, markante principielle Unterschiede zwischen beleuchteten, verdunkelten, normalen Netzhäuten entdecken."

Pergens (1896)⁶ found that in the retina of fishes (fixation in nitric acid and staining with methylene blue or the Ehrlich-Biondi stain)

⁵Bach: Zur feinen Anatomie und Pathologie der Ganglienzellen der Retina. Trans. VIII Internat. Ophthalm. Congress, Edinburgh, 1895. Cited from Birch-Hirschfeld.

⁶Pergens: Action de la lumière sur les éléments nerveux de la rétine. Centralblatt für Physiologie, 1896, X, S. 274.

the nuclei of the cells of the retina exposed to light were smaller in size, and the cell protoplasm of the ganglionic layer contracted, as compared to the resting retina. But he appears not to refer to any changes in the Nissl's substance.

The latest work on the subject is that of Birch-Hirschfeld (1900),⁷ who repeated Mann's experiment on rabbits, dogs and cats with the following results: "1. An den Ganglienzellen ist weder hinsichtlich der Grösse und Form der Zelle noch der Weite des pericellulären Raumes ein durchgreifender Unterschied nachzuweisen. Dagegen verlieren die Chromatinkörper im Protoplasma der Zellen nach mehrstündiger Einwirkung des hellen Tageslichtes ihre scharfe Begrenzung, erscheinen an den Enden abgestumpft und verschmelzen scheinbar zu grösseren Schollen.

Am Kern und Kernkörperchen treten keine typischen Unterschiede hervor.

2. Die Körner der *inneren Körnerschicht* sind im *Dunkelauge* chromatinreicher, von rundlich ovaler Gestalt, im *Hellauge* chromatinärmer, länglich oval.

3. An den *äusseren Körnerschicht* verliert sich die am *Dunkelauge* fast constant nachweisbare Zackung der Chromatinkörper nach längerer Lichteinwirkung."

Comparing these results with those of Mann he says: "Der von Mann beschriebene Chromatinreichtum der ruhenden Netzhautzelle kann, was die inneren und äusseren Körner betrifft, ohne weiters, hinsichtlich der Ganglienzellen, unter der Voraussetzung bestätigt werden, das man in dem an den Zellen des Hellauges bemerkbaren Undeutlichwerden den Beginn eines Chromatinschwundes erkennen will."

Birch-Hirschfeld also studied the effect on the retina of concentrated electrical light, to which the eyes were exposed for from five to fifty minutes. In the retinae of eyes exposed to this light for five minutes there was a marked decrease in the amount of the Nissl's substance, especially in the ganglionic layer, without any constant change in size or shape of the cells or their nuclei. In an eye exposed to the light for five minutes and then left in the dark for an hour before extirpation, the cells of the retina had regained their normal amount of Nissl's substance. Subjecting the eye to the light for from twenty to fifty minutes was followed by more marked changes in the retinal elements. The cell bodies and the nuclei, especially of the ganglionic layer, were increased

⁷ Birch-Hirschfeld: Beitrag zur Kenntniss der Netzhautganglienzellen unter physiologischen und pathologischen Verhältnissen. Archiv für Ophthalmologie, 1900, L, S. 166. A very complete bibliography is appended.

in size or shrunken, the cell body stained diffusely blue with methylene blue and the Nissl's substance had completely disappeared.

The changes in the cells by five minutes exposure to the concentrated electrical light he is inclined to interpret as merely due to heightened physiological activity, as they are completely repaired by a short rest. The complete disappearance of the Nissl's substance together with swelling and shrinkage of the cell bodies and the nuclei consequent on longer exposure of the eyes, he regards as conditions of extreme fatigue or rather pathological.

My own work was confined to the retinae of the Brandt cormorant, *Phalacrocorax penicillatus*, and differed in method from that of Mann, Bach and Birch-Hirschfeld in this particular, that the retinae from two different birds, one having been shut up in a darkroom, the other kept in the daylight, were compared, instead of the retinae from the resting and the stimulated eye of the same animal. The cormorant was chosen because the ganglion cells in the retina of this bird are relatively large and very rich in Nissl's substance. In all, the retinae of fourteen birds were examined, seven in condition of rest and seven in condition of activity or fatigue. To secure prolonged absence of retinal stimulation the birds were placed in a dark room for twenty-four hours, at the end of which time they were decapitated, the anterior halves of the eyeballs and the vitreous humor removed and the eyes immersed in the fixing fluid. The dissections were done as rapidly as possible and by the aid of red light. To secure, if possible, maximal normal fatigue of the retinal elements an equal number of birds were confined in a room lighted with acetylene light during the night and the following day placed in a wire cage in the bright sunlight until 2 p. m., when they were decapitated and the retinae fixed in the same manner. During the night especially, but also during the day, the birds were prone to close the eyelids and assume a position as if resting or sleeping, but this they were prevented from doing, at least for any length of time, because they were constantly watched.

The following fixing solutions were used, always at 38° C.:

Sat. aq. Corrosive sublimate. 97 cc. } 1.	Absolute alcohol 60 cc. } 3.
Glacial acetic. 3 cc. } 1.	Chloroform 30 cc. } 3.
Sat. aq. Picric acid. 95 cc. } 2.	Glacial acetic 10 cc. } 3.
Glacial acetic. 5 cc. } 2.	Alcohol. 95 % 4.

The retinae to be compared were fixed in the same fluid, kept the same lengths of time in the dehydrating alcohols, imbedded in paraffin side by side in the same block so as to be sectioned exactly the same

thickness and stained on the same slide with erythrosin and methylene blue according to Held, 50% alcohol or a weak solution of alum being used for differentiation.

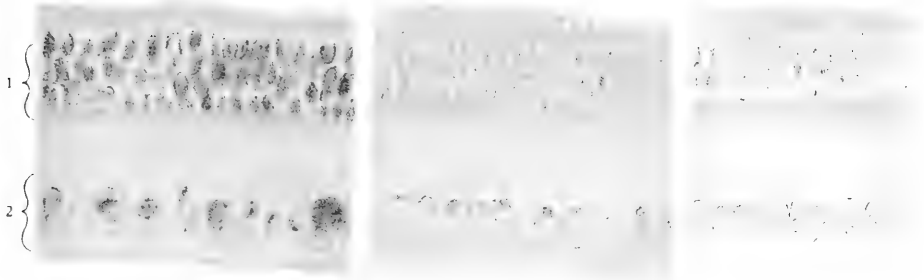
The retinae from the stimulated and the resting eyes thus prepared show a *constant difference in the amount and appearance of the Nissl substance in the cells of the ganglionic and the bipolar cell layer*. The ganglion cells of the stimulated retinae are poorer in Nissl's substance, the Nissl's granules present are less distinct than in the resting retinae, and the protoplasm of the cell bodies take a diffuse blue stain. Any shifting in position of the Nissl's substance cannot be made out. In the resting state the coarsely granular chromophile substance fills the whole cell body, being massed particularly heavy around the periphery. In some cases the cells of the stimulated retinae gave an appearance as if the Nissl's substance first disappeared from the center of the cell (fig. 3 b), but this appearance is probably due to the greater abundance of the substance around the periphery under normal conditions. But though this difference in the Nissl's substance is shown in all the retinae examined, it is by no means equally marked in all the preparations; and in the same preparations all the ganglion or the bipolar cells of the resting retina do not show an equal abundance of Nissl's substance, nor do the cells in stimulated retina show an equal paucity of it. In fact, in nearly all the preparations, cells can be found in the resting retina which have no greater amount of chromophile substance than is possessed by some cells in the stimulated retina, though the difference between the extremes of the two retinae as well as the difference in the blue coloration of the ganglionic layers as viewed under low power is easily discernable in all. Figure 1 a and b are from a preparation showing an average difference in this total effect, while figure 2 a and b are from a preparation that showed the least difference. Figure 3 a and b are cells from the ganglion layers of the preparation represented in figure 1. The difference in the chromophile substance between figure 3 a and 3 b is rather more than shown by the majority of the preparations. Figure 4 a, ganglion cell from a resting retina, and 4 b, ganglion cell from a stimulated retina, may be considered typical of the difference in chromophile substance of the preparations. Apart from this difference in the Nissl's substance, the nervous elements of the resting and the stimulated retinae appear to show no constant variation. In some of the preparations the cell bodies of the ganglion and the bipolar cells appear somewhat smaller in the stimulated retina, and a greater number of cells are slightly shrunken; but the fact, that in the resting retina the cells

vary greatly in size, and a slightly shrunken cell may appear side by side with shells showing no signs of shrinkage, seems to prevent this appearance to be ascribed to cell activity without further consideration. This normal variation in the size of the ganglion cells in the same retina, as well as the multipolar form of the cells, render comparative measurements of them both difficult and of doubtful value.

As regards the changes in the Nissl's substance of the ganglion cells and the bipolar cells during prolonged retinal stimulation these results on the bird retina agree perfectly with those of Birch-Hirschfeld on the mammalian retina, with this difference that my preparations show a much greater difference between the resting and the stimulated retinae than do those of Birch-Hirschfeld. But that is to be expected, because by my method a more prolonged rest as well as a more prolonged stimulation and consequently more pronounced fatigue were assured. In fact, the preparations from the bird retina showing the greatest change seem to resemble closely the mammalian retina exposed to concentrated electrical light for five minutes (compare fig. 3 b, Plate I of this paper with fig. 5 b, Plate X, of Birch-Hirschfeld). This lends additional support to Birch-Hirschfeld's view that the changes brought about in the cells of the retina by five minutes' exposure to concentrated electrical light are not pathological but simply due to the greatly augmented activity of the cells.

In using the expressions, "reduction," "decrease," "disappearance," etc., of the Nissl's substance I have followed the lead of previous investigators. The cell bodies both of the stimulated and the resting retinae stain intensely blue with Held's or Nissl's methylene blue; the difference is brought out in the differentiation process, when the cells of the stimulated retinae lose the stain more readily, the protoplasm taking a diffuse blue stain and the Nissl's bodies appearing partly fused. But yet these bodies are plainly there. The differentiation can be carried to a point where the cells of the stimulated retinae have lost the blue stain completely, the Nissl's bodies in the cells of the resting retinae still retaining some of the stain. This can be accounted for by an actual diminution of the substance; that is, a change from the chromophile to a non-chromophile condition without any intermediate states, in the cells of the stimulated retinae; for, provided the differentiation fluids diffuse with equal rapidity through the resting and the stimulated cells, the cells having the less amount of the chromophile material will be decolorized the sooner. But it could also be explained on the assumption that in prolonged activity of the cell the affinity of a molecule of the Nissl's substance for the stain is *gradually* reduced, to be

A. J. CARLSON.



1 a.

1 b.

2 a.



3 a.

3 b.

2 b.



4 a.

4 b.



regained during the resting state of the cell. But so far there seems to be no decisive evidence in favor of the one or the other explanation.

EXPLANATION OF FIGURES, PLATE I.

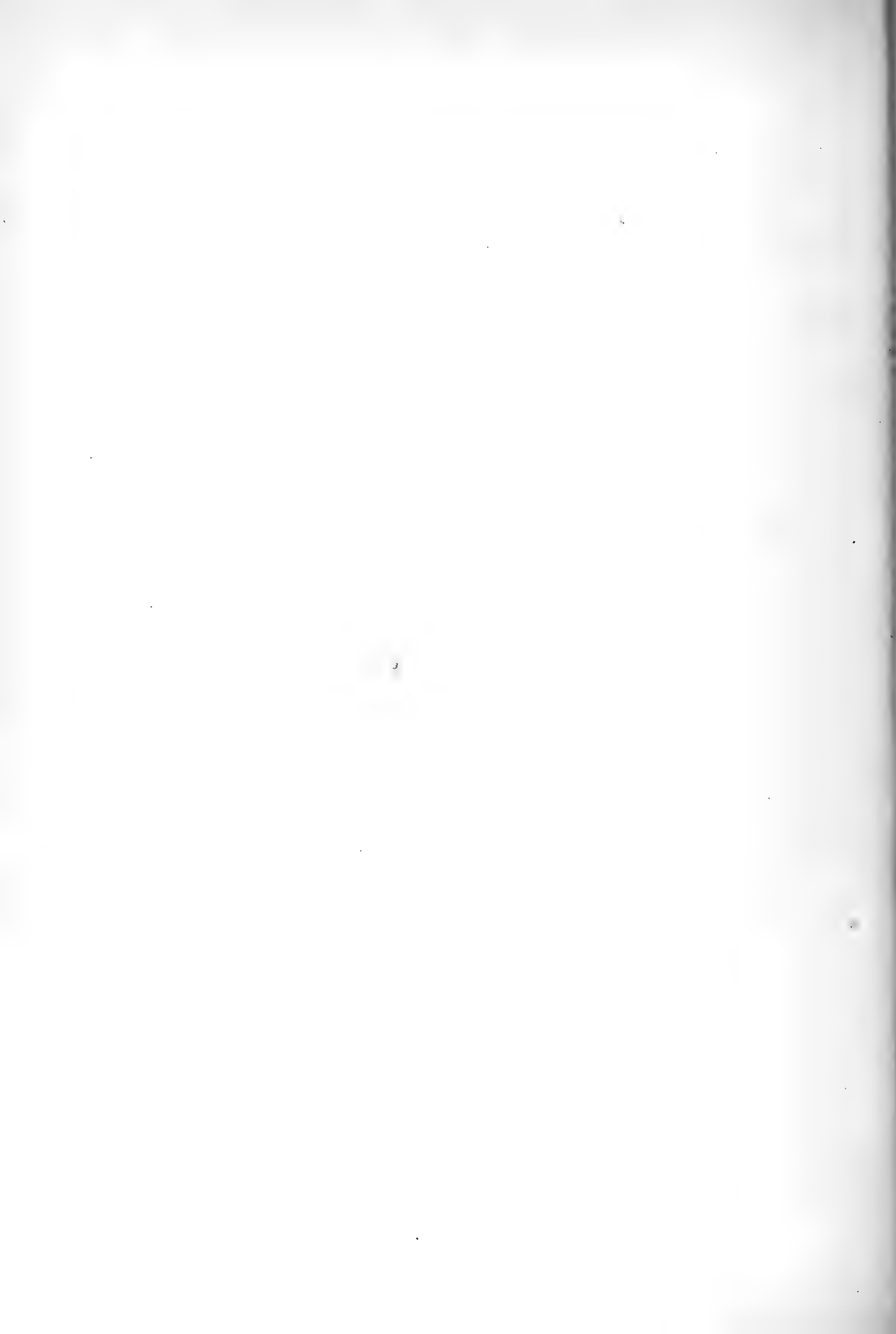
Retina, Brandt cormorant. Stains: erythrosin and methylene blue according to Held. 1. Ganglionic layer. 2. Bipolar cell layer.

FIG. 1. *a.* Bipolar and ganglion cell layers from resting retina. *b.* Same from stimulated retina. Camera, $\frac{2}{3}$ objective.

FIG. 2. *a.* Bipolar and ganglion cell layers from resting retina. *b.* Same from stimulated retina. Camera, $\frac{2}{3}$ objective.

FIG. 3. *a.* Ganglion cell from resting retina. *b.* Same from stimulated retina. $\frac{1}{12}$ oil immersion.

FIG. 4. *a.* Ganglion cell from resting retina. *b.* Same from stimulated retina. $\frac{1}{12}$ oil immersion.



THE HISTOGENESIS OF THE ADRENAL IN THE PIG.

BY

R. H. WHITEHEAD, M. D.

From the Hull Laboratory of Anatomy, University of Chicago.

WITH 6 TEXT FIGURES.

This paper gives the results of a study undertaken with the hope of working out the histogenesis of the adrenal in a mammalian embryo, the pig, without any particular reference to comparative embryology.

The great diversity of views concerning the histogenesis of the adrenal held by investigators of recognized ability is a striking feature of the literature of that organ. From the epoch-making publications of Balfour down to the present time scarcely any two authors seem to be in complete accord. A brief reference to the teachings of some of the leading authorities will serve to show the extent of the confusion:

Balfour,¹ as the result of his study of fish embryos, advanced the opinion that the adrenal in amniota is developed from two anlagen, a mesoblastic and a nervous—the latter being furnished by the sympathetic ganglia situated along the course of the abdominal aorta. According to this view, the cortex of the mature gland is derived from the mesoderm, while the medulla is contributed by the sympathetic ganglia. This hypothesis received considerable support from investigations by some of Balfour's pupils, notably Mitsukuri, and is, perhaps, the most generally accepted of all the views.

Gottschau² noted, as others (M. Braun, Mitsukuri) had done, the nearness of the first trace of the anlage, in the shape of a small cluster of crowded mesenchymal cells, to the inferior vena cava, and believed that it was derived from the mesenchyme. He held that the cortex and the medulla are derived from the same source.

Janosik,³ having observed that the mesothelium in the region of the inferior vena cava and the transverse septum contributes cells to the mesenchyme at the point where the adrenals are formed in mammals,

¹ *The Development of Elasmobranch Fishes*, London, 1878.

² *Arch. f. mikr. Anat. u. Entwickl.*, Leipz., 1883, S. 412-458.

³ *Arch. f. mikr. Anat.*, Bonn, Bd. XXII, 1883, S. 738-745.

concluded that the anlage of the cortex is derived from the peritoneum. Like Gottschau, he holds that the cortex and medulla are derived from the same source.

O. Hertwig⁴ teaches that the cortex is derived from tubules of the Wolffian body, processes from which grow dorsalward and surround portions of the sympathetic ganglia, which in their turn produce the medulla.

Minot⁵ holds that in man the anlage is laid down as a whole by the mesenchyme, the cells composing it afterwards undergoing differentiation into cortex and medulla.

O. Schultze,⁶ while rather avoiding a general discussion of the subject, affirms emphatically that in *Vespertilio murinus* the anlage of the adrenal is laid down *in toto* as a portion of the sympathetic ganglia, to be differentiated subsequently into cortex and medulla.

The citations above have been introduced merely to illustrate the prevalent diversity of opinion. Anything like an adequate review of the literature would be foreign to the purpose of this paper, and a complete bibliography may be found in the publication of Aichel presently to be mentioned; but some of the work which marks the recent revival of interest in the adrenal requires more extended reference.

Minot⁷ accepts the mesenchyme as the source of the adrenal, and points out that the cells from the mesothelium collect near the inferior vena cava and the transverse septum to form the mesenchymal anlage. He believes, however, that this is not a special process, as Janosik thought, but that "the genetic relation of the whole mesenchyma to mesothelium renders it unnecessary to assume a special relation for a single mesenchymal organ." He applies the same criticism to observations indicating the mesothelium of the nephrotomes as the source of the adrenal anlage.

As to the medulla Minot says: "That both the cortex and the medulla of the adult organ are formed in man from the mesenchymal cells, as Gottschau showed was the case in several mammals, is, I think, beyond question." If the sympathetic unites with the mesenchymal anlage, it disappears in the course of development. For: "By a considerable series of observations on the suprarenal capsules of human

⁴Lehrbuch der Entwicklungsgeschichte des Menschen und der Wirbelthiere, Jena, 1897.

⁵Human Embryology, New York, 1897.

⁶Grundriss der Entwicklungsgeschichte des Menschen und der Säugethiere, Leipzig, 1897.

⁷Op. cit., pp. 485-489.

embryos, I have ascertained that there are groups of cells which gradually disappear and take no part in the production of the adult organ. The cells are in clusters in the central portion of the organ and stain very readily, so that they stand out conspicuously in the sections. In appearance they resemble the cells assigned to a sympathetic origin in the rabbit, and I should feel no doubt that they are the same were it not that I fail to find them in embryos of the second month, so that if they are really of sympathetic origin then the union of the two anlagen must take place at a considerably later stage in man than in other mammals. These groups of cells are readily seen in the three-months' embryo, but in the four-months' embryo they are disappearing and many of the clusters are hollow, their cavities being filled with what is apparently a coagulum; by the seventh month the clusters have, so far as I have hitherto observed, entirely disappeared."

J. M. Flint,⁸ in the course of a very careful and exhaustive study of the blood vessels of the adrenal, devotes a chapter to the histogenesis of the organ, his observations being made, for the most part, upon pig embryos. He does not undertake to determine the ultimate source of either the cortex or the medulla, but he states that the cortex is laid down first, and shows that the medulla is developed from cells which

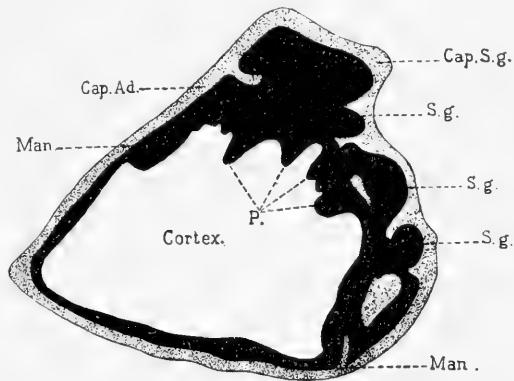


FIG. 1. Diagram of relations of sympathetic ganglia with the adrenal in pig of 35 mm. *Cap. ad.*, capsule of adrenal; *Cap. s. g.*, capsule of sympathetic ganglia; *S. g.*, sympathetic ganglia; *Man.*, mantle layer of cells; *P.*, prolongations from mantle into cortex.

wander in from outside the cortex. He was able to trace these medullary cells in the form of small collections passing more and more deeply through the cortex as the age of the embryo increased, until finally they reached their destination around the central vein. He could follow, not only the masses of cells in their migration, but also the arteries of the medulla, one arteriole for each collection of cells developing *pari passu* therewith. He expresses decided scepticism as to the derivation of these medullary cells from the sympathetic ganglia.

O. Aichel⁹ introduces a new phylogenetic view. From a study of

⁸ Contributions to the Science of Medicine, by the Pupils of W. H. Welch, Baltimore, 1900, pp. 153-231.

⁹ Arch. f. mikr. Anat., Bonn, Bd. LVI, 1900, S. 1-80.

selachians he concludes that the so-called suprarenal bodies, which, since Balfour's work, have generally been considered as derivatives of the sympathetic ganglia, are really derived from retrograding canals of the Wolffian body; and that the interrenal body, the supposed mesoblastic anlage of the adrenal, is laid down by the peritoneal invaginations (Trichter) of the same body. The interrenal body, alone, he says, is the homologue of the adrenal of higher animals. Along with these considerations of phylogeneses he gives a careful study of the early development of the adrenal in rabbits and moles. In the former animal he finds the first evidence of the adrenal anlage in an embryo 6.5 mm. long. It consists of an invagination of the coelomic epithelium on each side of the attachment of the mesentery corresponding to the region of the anterior third of the Wolffian body. He describes and figures such invaginations as running dorsalward to end in small groups of cells which present numerous mitotic figures. These invaginations have nothing to do with the genital ridge, he thinks, but occur too far forward to be connected with that structure. Moreover, the epithelium at the site of the invaginations shows no differentiation, nor does it present any evidence of cell division. These observations lead him to conclude that the invaginations are the remnants of Wolffian body "Trichter," which body, he says, is already undergoing retrogressive changes in this region (anterior third). Accordingly, the anlage of the adrenal cortex in the rabbit is derived from atrophying Wolffian body invaginations.

In the case of the mole, although he had an excellent series of embryos at his disposal, Aichel was unable to find any such coelomic invaginations as those described in the rabbit; the earliest evidence of the adrenal was a small mass of cells undergoing active karyokinesis in the mesenchyme. In the vicinity he could find some cross sections of tubules which he considered remnants of the Wolffian body, but they had no connection with the anlage of the adrenal. Accordingly, it would appear that in the mole the adrenal arises free in the mesenchyme. Nevertheless Aichel thinks that the ultimate source of the anlage is the same as in the rabbit, although he could not demonstrate such an origin in a well-nigh perfect series of embryos.

As to the origin of the medulla of the gland, he states, without giving an account of his observations thereon, that the medulla is derived from the same source as the cortex.

Josef Wiesel¹⁰ employed pig embryos 1 cm., 2 cm., 2.5 cm. and 3 cm.

¹⁰ Ueber die Entwicklung der Nebenniere des Schweines besonders der Marksubstanz. Anat. Hefte, Wiesb., 1901, Bd. XVI, S. 115-150.

long for the study of the cortex. He detected the anlage first in pigs of 2 cm. in the shape of a projection on the medial side of the Wolffian body. Ventral from this projection, he says, the coelomic epithelium is highly developed; it shows, however, no differentiation, being similar to the epithelium of the coelomic cavity in general. This finding, he thinks, warrants the conclusion that the cortex is derived from the coelomic epithelium. Of the medulla Wiesel makes a more thorough study. He traces its origin back to the sympathetic ganglia, and describes the passage of medullary cells in collections through the cortex to the vicinity of the central vein in the way previously described by Flint.

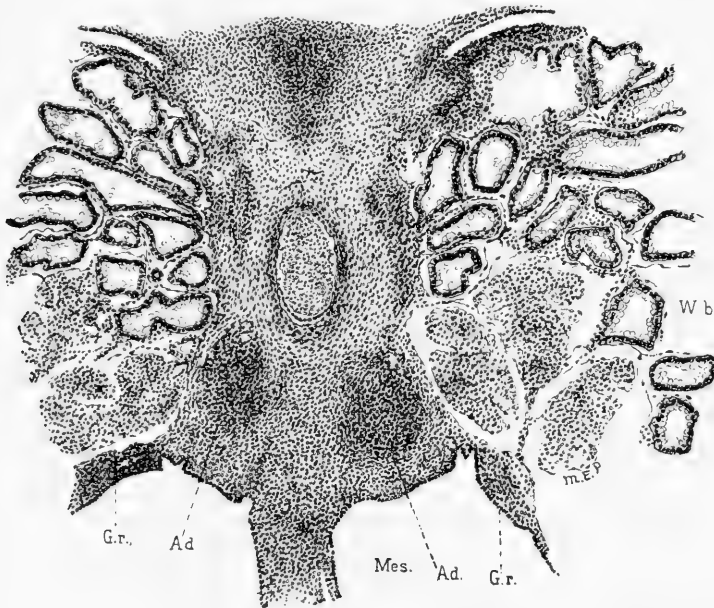


FIG. 2. Pig 13 mm. Leitz obj. 3, oc. 4. *Ad.*, adrenal; *G. r.*, genital ridge, *Mes.*, mesentery; *W. b.*, Wolffian body.

It will be convenient to consider the genesis of the cortex and medulla separately, as they are separated by a considerable interval of time.

THE HISTOGENESIS OF THE CORTEX.

Although the anlage appears at a much earlier stage, it will be convenient to begin the observations in an embryo of 13 mm. and trace it towards its beginning. In such an embryo (Fig. 2) the anlage consists of an ovoid collection of cells situated ventro-lateral from the aorta and dorsal from the angle formed by the junction of the ventral

surface of the Wolffian body with the mesenteric attachment. In the early stages it lies entirely ventral to the glomerular or mesonephric branches of the aorta, but as it increases in size these vessels transfix it. It is clearly differentiated from the neighboring structures, not by any distinct capsule, but by young connective tissue more or less condensed and concentrically arranged. It extends as a column of cells in an antero-posterior direction a distance which roughly corresponds with the anterior one-third of the Wolffian body, falling short, however, of the anterior extremity of that body. In the posterior direction it is limited by the posterior cardinal veins: these veins run forward, one on each side, along the medial aspect of the Wolffian body, and are connected by several cross anastomoses, the last of which about corresponds to the junction of the anterior with the middle one-third of the Wolffian body. At this point the left vein virtually bifurcates, sending one division into the Wolffian body of the same side, while the other crosses the median line to open into the right cardinal; the latter soon bifurcates in its turn, one division entering the Wolffian body of its side, the other joining the primitive inferior vena cava. F. T. Lewis,¹¹ in the course of an interesting account of the development of the inferior vena cava, has suggested that the term "subcardinal" should be applied to the portions of these veins which lie posterior to the anastomoses. Immediately anterior to the most anterior of the anastomoses the caudal extremity of the anlage is encountered. The cells composing it have a moderate amount of finely granular cytoplasm, which possesses considerable affinity for acid dyes; their nuclei are vesicular, and contain a fair amount of nuclear sap and some chromatin granules. At this stage capillaries are beginning to make their appearance in the anlage. Ventral to the anlage and running lateralward on the ventral surface of the Wolffian body is a thickening composed, in the main, of mesenchymal cells and blood vessels; it is continuous with the connective tissue framework of the Wolffian body, and is lined superficially by tall coelomic epithelial cells. In these cells mitotic figures are not infrequent, and in some of them, at least, the plane of cleavage is parallel with the surface. This epithelium, in many situations, is wrinkled or furrowed, and cells are invaginated here and there into the subjacent tissue either singly or in small collections; none of these invaginations, however, directly reach the anlage of the adrenal. The thickening is coextensive in the anterior direction with the adrenal; in the posterior direction it is immediately continuous with the anlage of the genital

¹¹ *Am. Jour. Anat., Balt.*, Vol. I, pp. 229-245.

gland—indeed, there seems to be no reason why it should be regarded as anything distinct from that anlage. Probably it is all incorporated into the genital gland in the process of development. Thus, in the pig of 13 mm. the genital anlage can be traced quite distinctly through at least 35 sections (10 mik. each) anterior to the caudal extremity of the adrenal anlage.

There is no evidence of atrophy in the Wolffian body, signs of which do not appear until a much later stage. This observation is in accord with the statement of MacCallum,¹² that evidences of degeneration in the pig's Wolffian body do not occur until the embryo is about 100 mm. long.

In embryos 12 and 11 mm. long the appearances are quite similar to those just described except as to size.

In the pig of 10 mm. the adrenal anlage is still distinctly visible, and the thickening on the ventral surface of the Wolffian body (at this stage the surface might better be called ventro-medial) is well developed. Ventral to the anlage, in the angle between the Wolffian body and the mesenteric attachment there is a deep furrow lined by the coelomic epithelium, which in some situations produces an appearance suggestive of Aichel's finding in the rabbit of an invagination of the epithelium leading to the anlage. In most sections, however, the two structures are separated clearly by veinlets which emerge from the Wolffian body and run ventral to the adrenal.

In the pig of 8 mm. (Fig. 3) the anlage occupies the space between the aorta and the mesenteric attachment medially, the Wolffian body laterally, the mesonephric arteries dorsally, and the coelomic epithelium ventrally. It does not now extend as an unbroken column of cells as in the previous embryos, but is interrupted at about its middle third.

This interruption seems to be mechanical, being due to a large glomerulus of the Wolffian body, which reaches so far medialward as to leave no space for the adrenal at this point. The propinquity of the anlage

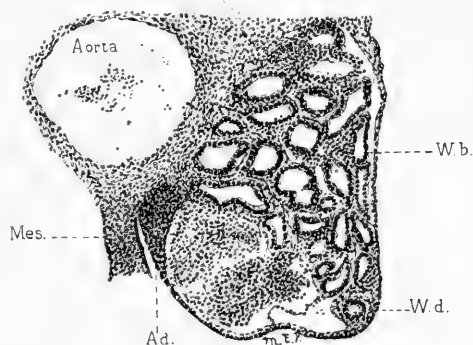


FIG. 3. Pig 8 mm. Leitz obj. 3, oc. 4. *Ad.*, adrenal; *Mes.*, mesentery; *W. b.*, Wolffian body; *W. d.*, Wolffian duct.

¹²J. B. MacCallum: Notes on the Wolffian body of Higher Mammals. *Am. J. Anat., Balt.*, Vol. I, pp. 245-260.

to the coelomic epithelium has increased to such an extent that it is extremely difficult to define any boundary between the two structures (Fig. 4); and the difficulty is not lessened by attempts to draw distinctions between the cells composing them. Mitoses are frequent both in the anlage and in the epithelium. The furrow previously mentioned is still present, but the anlage lies against the lateral wall of the furrow rather than at its bottom. As a result of these findings, it was somewhat confidently expected that younger embryos would reveal an invagination of the coelomic epithelium such as Aichel found in the rabbit; but such was not the case. In embryos of 7 and 6 mm. no evidence of the anlage could be found, except, possibly, a suggestion of thickening at the usual situation. In the hope of finding something more definite, six embryos varying from 8 to 6 mm. were sectioned, but none of them furnished any additional light.

It is clear that one would not be justified in drawing positive conclusions from these findings; but such testimony as they bear would seem to be on the side of those who hold that there is a genetic relation between the coelomic epithelium and the adrenal cortex. One may suppose that the anlage is laid down by invaginations occurring suddenly and hence missed in the embryos sectioned, or by epithelial cells wandering into the mesenchyme. In the latter case, however, we should still have to decide whether the cell-wandering is sufficiently direct and great to constitute a distinctly special process in this region.

THE HISTOGENESIS OF THE MEDULLA.

My observations are entirely in accord with the conclusion of Flint,¹³ that the medulla of the adrenal is developed from certain small cells found in the pig of 35 mm. at the periphery of the cortex just within the capsule. He seems to have shown beyond a doubt that these cells are the ancestors in direct line of the mature medullary cells. The problem left, therefore, is to trace these cells to their source. The results of the present study point to the sympathetic ganglia as that source.

Tracing the relationship between the adrenal and the sympathetic ganglia in the course of their development, we find that in the pig of 13 mm. the ganglia are quite small. They lie dorso-lateral from the aorta nearly opposite to the dorsal border of the Wolffian body, and are connected with the spinal nerves by the splanchnopleural branches. Smaller collections of ganglion cells with many mitotic figures can be

¹³ Op. Cit.

seen running ventralward on each side of the aorta. The latter grow rapidly, so that in the pig of 16 to 18 mm. there are chains of ganglia of considerable size lying between the adrenal and the aorta. Other ganglia lie immediately dorsal to the adrenal. From these ganglia nerve fibres arise, and, accompanied by cells, run lateralward along the dorsal and ventral aspects of the adrenal. Particularly large nerves pass along the medial aspect of the adrenal, some of which lie squarely

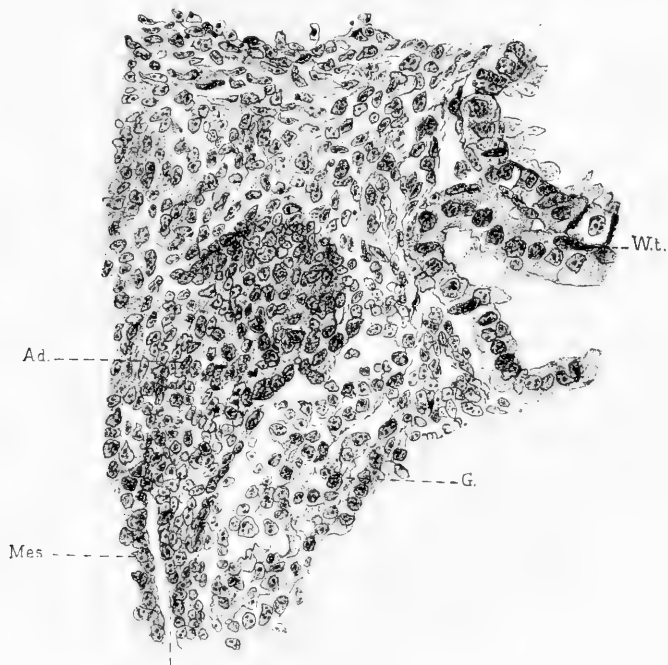


FIG. 4. Pig 8 mm. Leitz obj. 7, oc. 4. *Ad.*, adrenal; *Mes.*, mesentery; *C. c.*, coelomic epithelium; *G.*, glomerulus; *W. t.*, tubules of Wolffian body.

against it, and in some cases even transfix it near its periphery. These nerves are not numerous, and there seems to be no reason to regard them as anything but the nerves to adjacent anlagen which come into close relationship with the adrenal en route to their destination.

In the following successive stages the increase in size both of the adrenal and the ganglia is very rapid; so that in the pig of 25 mm. the space between the adrenal and the aorta is occupied to a great extent by the sympathetic ganglia, and the latter are separated from the adrenal only by its capsule.

In pigs of from 30 to 35 mm. a new element is added to the anlage. Immediately beneath the capsule there are seen collections of small cells, the nuclei of which stain deeply and are surrounded by very scanty cytoplasm. In thick sections (Fig. 5) these are seen to be arranged around the cortical portion in a mantle-like layer, from which offshoots are proceeding inward between the rows of cortical cells. Towards the lateral aspect of the adrenal this mantle becomes very thin, or is even entirely lacking; but along its dorso-medial surface it is thick, and its

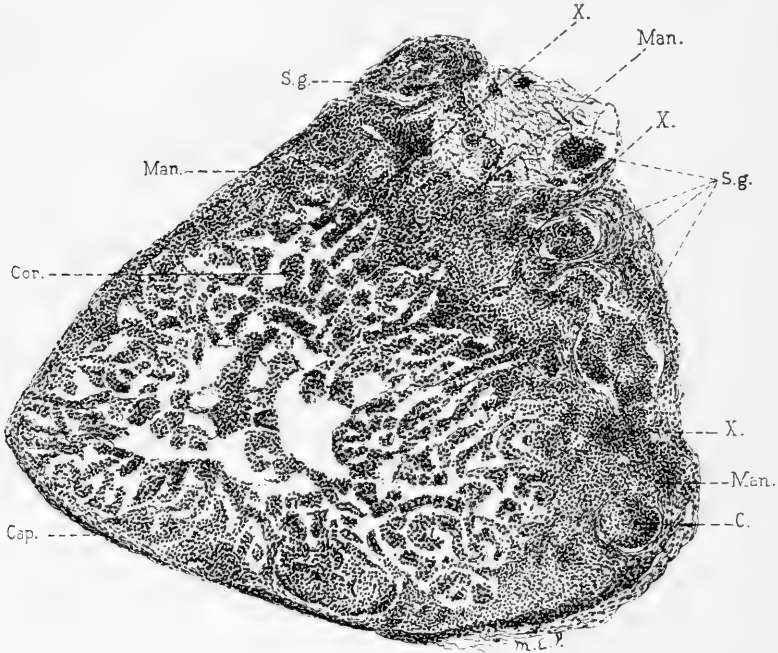


FIG. 5. Pig 35 mm. Leitz obj. 3, oc. 4. *S. g.*, anlagen of sympathetic ganglia; *Man.*, mantle layer of cells; *X.*, columns of cells connecting sympathetic anlagen with mantle; *Cor.*, cortical portion of adrenal; *C.*, isolated portion of cortex; *Cap.*, capsule of adrenal. Section 25 mm. mikrons thick.

prolongations into the cortex are numerous and extensive. In this latter region the capsule of the adrenal adjacent to the ganglia is much broken up, or even wanting over considerable areas; so that in these situations there is nothing between the ganglia and the cortical portion of the adrenal except the mantle of cells previously mentioned. Through the gaps in the capsule cellular strands, often of considerable size, connect the mantle on the inside with the ganglia on the outside. The connection is sometimes so intimate that what is seen in one section as a

distinct ganglion may appear in another as an integral part of the mantle. The anatomical similarity of the cells composing the mantle, the connecting strands, and the ganglia is so great that it is exceedingly difficult to draw any distinctions between them (Fig. 6). One easily gets the impression that strands of cells from the ganglia enter the adrenal along its dorso-medial aspect, and, growing along the lines of least resistance, spread out beneath the capsule and send in prolongations between the cortical rows. The continuity between the mantle and the sympathetic ganglia, and the identity in appearance of the cells composing them seem to offer anatomical evidence quite positive in character.

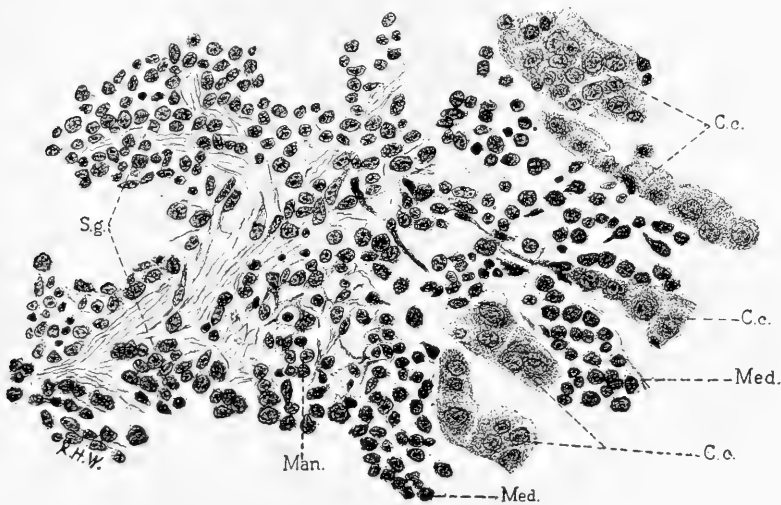


FIG. 6. Pig 35 mm. Section 5 mikrons thick. Leitz obj. 7, oc. 4. *S.g.*, portions of sympathetic ganglia; *Man.*, mantle layer of cells; *C.c.*, portions of cortical columns; *Med.*, collections of medullary cells.

Two objections to this view present themselves: May not the mantle cells be derived from the periphery of the cortex? My preparations afford no foundation for this hypothesis. There is no evidence that karyokinesis is more abundant at the periphery than elsewhere in the cortex, and there is entire absence of transition forms between the cortical cells and those of the mantle. Again, granting that the mantle cells are derived from the sympathetic ganglia, may they not subsequently perish in great part, as has been shown to be the case with many neuroblasts in the substantia gelatinosa of the spinal cord, and as Minot thinks probably occurs in the human adrenal? I think the work of Flint, many of whose preparations he has kindly allowed me to examine, fur-

nishes the answer to this question. It seems to me that he has fully demonstrated that the cells which compose what has been termed in this paper the mantle are the direct progenitors of the medulla.

CONCLUSION.

1. In the pig's adrenal the anlage of the cortex is laid down much earlier than that of the medulla, being first seen at the stage of 8 mm. It is probably derived from the coelomic epithelium.

2. The anlage of the medulla appears first in pigs of 30 to 35 mm., at which time it lies spread out like a mantle along the periphery of the cortex. The findings indicate that it is derived from the anlagen of the sympathetic ganglia.

Since the above was written there has appeared an article by Alfred Kohn,¹⁴ alluding to the existence in various parts of the body of small nodular collections of cells characterized especially by the fact that they assume a brown color when fixed in chromic solutions. Kohn traces the origin of these bodies to the anlagen of the sympathetic ganglia, and proposes therefore to call them paraganglia. He believes that their extracts possess the property of greatly elevating the blood pressure. If these interesting views are correct, they furnish further testimony in favor of the derivation of the adrenal medulla from the sympathetic; for Henle's reaction is a property of the medulla, and it is well known that extracts of the adrenal elevate the blood pressure.

I desire to express my indebtedness to Miss M. E. Poindexter for the accompanying illustrations.

¹⁴Chromophile Cells and Chromophile Organs, reviewed in *Journal of the American Medical Association*, Chicago, 1902, Vol. XXXIX, p. 706.

ON A HITHERTO UNDESCRIBED NUCLEUS LATERAL TO THE FASCICULUS SOLITARIUS.

BY

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WITH 3 TEXT FIGURES.

In the medulla of the dog there is a collection of large nerve cells lateral to the fasciculus solitarius (spinal root of the vago-glossopharyngeus nerve) sufficiently well-defined to merit attention as a separate nucleus. This nucleus has not, to my knowledge, been previously described. The cells are large, round, oval or pear-shaped, of $20-40 \times 40-80 \mu$ in size and stain more deeply with carmine than any of the other cells in the immediate neighborhood. They extend upward from the level of the calamus scriptorius something more than 2 mm. The cells are somewhat scattered, the number in each section (50μ thick) varying from one to eight upon either side. In an occasional section they may be entirely absent. In an unbroken set of serial sections I was able to count 130 cells upon one side and 160 upon the other. At this level the gray substance partially surrounding the fasciculus solitarius does not apparently extend to its lateral aspect, but the section is somewhat lighter here owing to a less compact matt of myelinated fibres. The large cells of this nucleus are scattered about in this network of fibres, some lying quite close to the

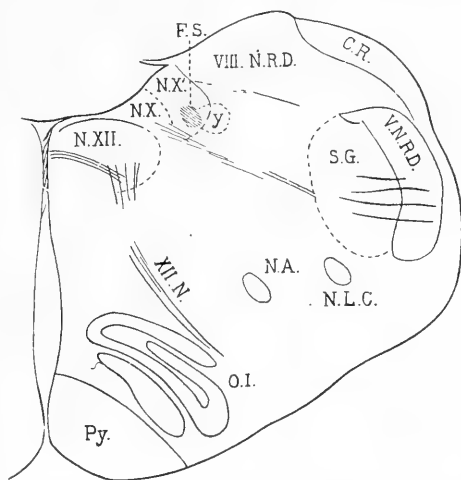


FIG. 1. Outline of cross-section through medulla oblongata of the dog. N. XII., nucleus hypoglossi; N. X., nucleus N. vagi; N. XI., nucleus alae cineraceae; N. A., nucleus ambiguus; N. L. C., nucleus lateralis; O. I., nucleus olivaris inf.; Py., pyramid; V. N. R. D., radix descendens nervi trigemini; S. G., substantia gelatinosa; C. R., corpus restiforme; VIII. N. R. D., radix descendens nervi vestibuli; XII. N., nervus hypoglossus; F. S., fasc. solitarius; y., nucleus described in this paper.

border of the fasciculus, while others are separated from it by a distance varying from 0.2 to 0.7 microns. These nerve cells are apparently quite distinct from those scattered among the descending root bundles of the acusticus, which at this level pass down quite near the fasciculus solitarius. The cells of this nucleus are much larger, of different shape, and stain more deeply with carmine than the cells among the descending root bundles of the acusticus. The cells of Deiter's nucleus first appear in the cross-section of the medulla at a

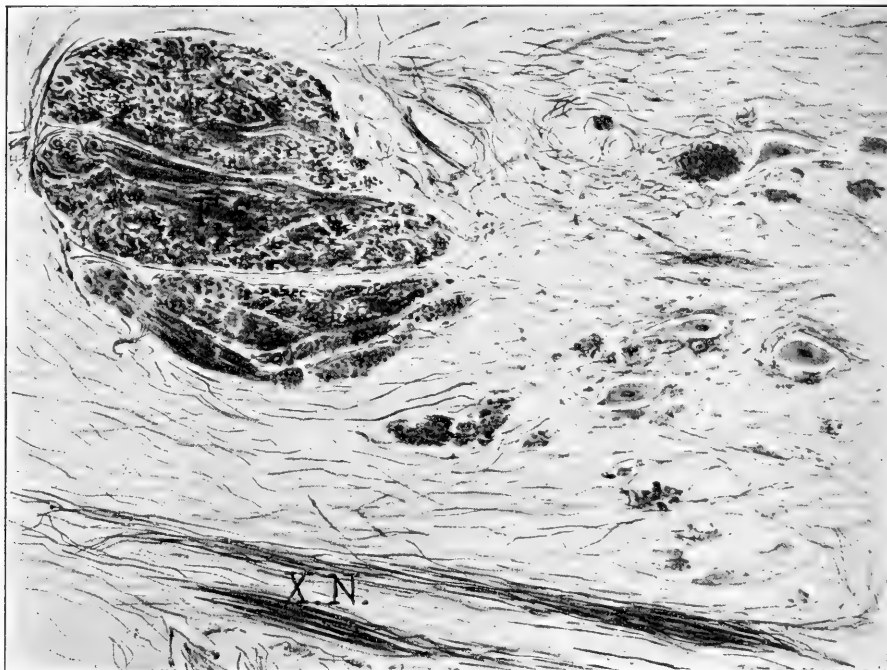


FIG. 2. Fasciculus solitarius and nucleus "y" in the dog. (Drawing made from photograph.) F. S., fasc. solitarius; X. N., bundles of the outgoing vagus. Four cells of nucleus "y" to the right of the fasc. solitarius.

considerably higher level and are separated from these cells by too great a distance for them to be looked upon as an extension downward of Deiter's nucleus.

In examining sections from three human medullas (in two of which the series was complete) I find in all a small, round, compact collection of cells, lateral to the fasciculus solitarius, in nearly the same relative position as the cells just described in the dog. In man this clump of cells is first met at a level somewhat higher than that described above

in the dog, that is, about 5 to 6 mm. above the calamus scriptorius. The cells are considerably smaller, being of about the same size as those cells scattered among the descending root bundles of the acusticus; they are arranged in a more compact nest, and apparently have fewer processes than those in the dog. While in man the number of cells in each section is much greater, the extent of the nucleus from below upward is much less, being in man only about 5 mm. in one case, and 1.5 mm. in another in which its upward extension was not so continuous.

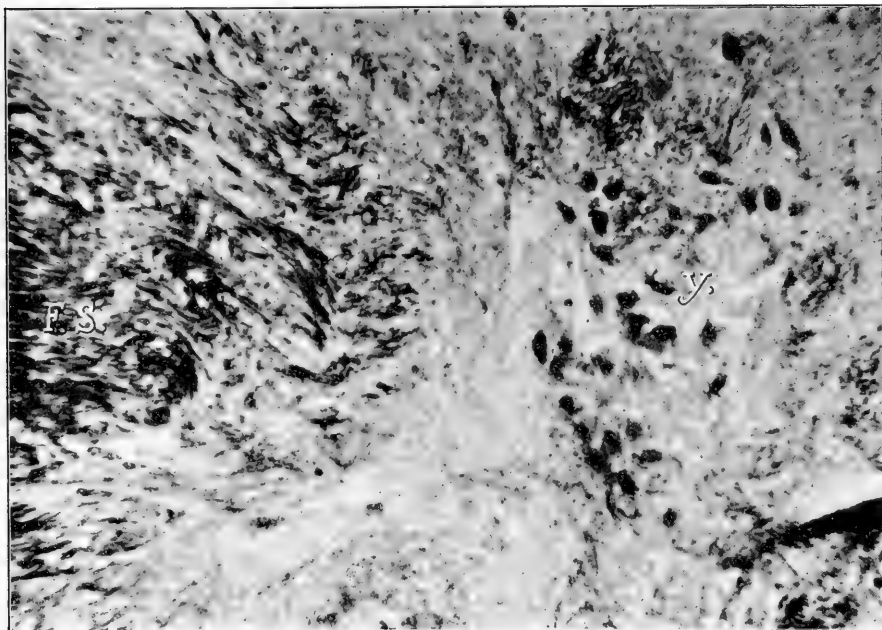


FIG. 3. Fasciculus solitarius and nucleus "y" in man. (Reproduced from photograph.) F. S., fasc. solitarius; y., group of cells lateral to fasc. solitarius.

In the absence of more exact data it is probable that this collection of cells upon the lateral aspect of the fasciculus solitarius in man is the homologue of the large cells found practically in the same location in the dog. What are the relations of this nucleus, if any, to the vagus or glossopharyngeus can only be determined by further research. In man small clumps of nerve cells are found at various levels in the gray substance surrounding the fasciculus solitarius, but so far as I have observed, they are, with this one exception, of very inconsid-

erable extent, although the cells grouped in this way resemble more the cells of this nucleus and the cells scattered throughout the bundles of the descending root of the acoustic than the very small cells generally looked upon as the terminal nucleus of the fibres of the fasciculus solitarius in the gray substance surrounding that bundle.

V. Kölliker¹ probably refers to these clumps of cells when he says: "In dieser Gegend ist dann auch die den *Fasc. solitarius* umgebende graue Substanz besonders entwickelt und tritt oft wie in besonderen Nestern auf."

Many writers speak of cells and gray substance as if they were quite interchangeable terms, which sometimes renders their meaning doubtful.

V. Bechterew² refers to the nucleus described by Mayser in the guinea-pig as *lateral* to the fasciculus solitarius, but this is shown in Forel's³ illustration *mesial* to the fasciculus solitarius.

¹ Gewebelehre, 6th Ed., Vol. II, p. 243.

² Leitungsbahnen in Gehirn und Rückenmark. 2nd German Ed., p. 155.

³ Forel: Über das Verhältniss der experimentellen Atrophie- und Degenerationsmethoden zur Anatomie und Histologie des Centralnervensystems. Festschrift für Nägeli und Kölliker. Zurich, 1891.

THE SPERM CENTROSOME AND ASTER OF ALLOLOBOPHORA FOETIDA.

BY

KATHARINE FOOT AND E. C. STROBELL,

Woods Holl, Mass.

WITH 1 PLATE.

During the past few years evidence has accumulated which assigns to the egg attraction-sphere a position where it threatens to usurp all the functions heretofore claimed for the male attraction-sphere. This promotion of the egg centrosome and aster with its satellites the cytasters, seems to have been at the expense of the male centrosome, until even Boveri can suggest as a possible hypothesis "Anstatt wie bisher zu sagen das Spermatozoon führt ein Centrosoma ins Ei ein, müsste es heissen: das Spermatozoon bewirkt im Ei die Bildung eines Centrosoma, aus dessen Teilung alle folgenden hervorgehen." (Das Problem der Befruchtung. Theodor Boveri, Jena, 1902.)

The egg of *Allolobophora* furnishes evidence which indicates that the centrosome of its male attraction-sphere is part of the spermatozoön itself, this evidence supporting the interpretation of Boveri and others, who maintain that the sperm centrosome is carried into the egg by the spermatozoön.

In 1902¹ we demonstrated the constant presence of three granules in the spermatozoön of *Allolobophora*; one between the spine and head, one between the head and middle-piece, and one between the middle-piece and tail. Photographs of spermatozoa showing these granules can be seen in the above-mentioned article.

It has been our aim to determine whether either granule at each end of the middle-piece forms the morphological center of the male attraction-sphere, or whether the entire middle-piece must be regarded as the morphological centre. In every case in which we have found the middle-piece attached to the head, and its relation to the aster-rays could be therefore accurately demonstrated (photos. 1-8), it is certain that the

¹The Spermatozoa of *Allolobophora foetida*. The American Journal of Anatomy, Vol. I, No. 3, 1902.

posterior granule of the middle-piece functions morphologically as a centrosome. The morphological value of this fact is, however, challenged by Van der Stricht's interesting results in his study of the egg of the bat, where he finds the rays of the sperm aster focussed around the *anterior* granule of the middle-piece. "Un spermaster se forme tout autour d'un corpuscle central, le spermocentre, attenant à l'extrémité antérieure de la pièce de réunion de la queue du spermatozoïde."²

The origin of the sperm centrosome in *Allolobophora* has been very difficult to determine, as preparations showing the exact stage of development necessary to decide this point are rarely found. The middle-piece must be not only intact, but it must be still attached to the head of the spermatozoön; for after it is separated from the head its position within the sphere (photo. 9) is most erratic. Its length may be at any angle in relation to the head of the spermatozoön, and frequently the whole middle-piece is entirely out of the centre of the sphere. This is the stage of the male attraction-sphere usually found; and this fact made it impossible to assign to either of the granules of the middle-piece the morphological value which now seems warranted by our recent preparations.

It is probable that this displacement of the middle-piece in the sphere is due to the mechanical effect of the fixatives. The fixatives and the subsequent technique shrink these eggs, in many cases, one-third of their diameter, and this fact indicates that we may expect a displacement of the structures, unless we assume that the forces act equally on all the constituent parts. In a former paper³ we have shown photographs of different cytological configurations produced in these eggs by the various fixatives, and the displacement of cytological constituents has been demonstrated by many investigators. We have nearly a thousand photographs systematized in such a way as to facilitate a comparative study of the effect of the different fixatives at definite stages of the egg's development; but the inconstancy of the reactions of the egg to the fixative under conditions apparently the same, makes the problem too complicated to justify hasty conclusions.

Photos. 1 to 8 show the middle-piece intact and still attached to the head of the spermatozoön, while the sphere is formed around the *posterior* end of the middle-piece. In photos. 1, 4, 6, and 8, the posterior granule itself is clearly seen. That these granules are larger than those in the spermatozoön before it enters the egg—though perhaps due in part to

² Van der Stricht, O. Le spermatozoïde dans l'oeuf de chauve-souris (*V. noctula*). Verhand. d. Anat. Gesell., 1902.

³ Photographs of the egg of *Allolobophora foetida*. Journ. Morph., Vol. XVI, No. 3, 1900.

fixation—is in keeping with the fact that the spermatozoön increases in size as soon as it enters the egg, the head becoming longer and broader, before it begins to contract into the short thick rod of later stages. This separation of the head and middle-piece appears to be caused by the contraction of the head rather than by the migration of the middle-piece and sphere. The separation of the contracted rod from the middle-piece (photo. 9) is no greater than the contraction of the head would necessitate.

In photograph 9, although the middle-piece is separated from the head, its posterior end—the one farthest from the head—is almost exactly in the centre of the sphere.

Photograph 10 shows the male attraction-sphere and a cross-section through the posterior end of the middle-piece, with the tail of the spermatozoön still attached to the posterior granule. The artificial appearance of the tail in this section (probably due to the fixative) would make us hesitate to interpret this structure as the tail of the spermatozoön, if we had not often found the tail persisting until this stage, in eggs killed in other fixatives. Photographs of some of these preparations were shown in an earlier paper.⁴ Photo. 3 also shows an indication of the persistence of the tail; the middle-piece being still attached to both head and tail, its posterior granule forming the center of the sphere.

In photo. 7, part of the head of the spermatozoön and its middle-piece are clearly defined, and the rays of the aster focus at the posterior end of the middle-piece. The posterior granule of the middle-piece is obliterated by over-staining.

The demonstration of the morphological value of this granule encourages us to hope that we shall find preparations showing that the acrosome forms the focal point for the first rays of the fertilization-cone, thus warranting our assumption of a morphological value to this centrosome-like granule, and supporting our interpretation of the morphological similarity of the male attraction-sphere and the fertilization-cone.

Although we are forced to the conclusion that these preparations indicate that a definite part of the spermatozoön itself forms the centrosome of the male attraction-sphere, *Allolobophora* fails to offer any evidence that this centrosome gives rise to one or both of the cleavage centrosomes. At a later stage the entire middle-piece disintegrates into several granules⁵ and disappears completely, and there is no proof that the granule which persists the longest is the posterior granule of the middle-piece.

⁴Photographs of the egg of *Allolobophora foetida*. Journ. Morph., Vol. XVI, No. 3, 1900.

⁵Photographs of the egg of *Allolobophora foetida*. Journ. Morph., Vol. XVI, No. 3, 1900.

We might assume this if one of the granules could be traced to the cleavage stage, but at the telophase of the second maturation-division, both egg and sperm-attraction spheres, with their centrosomes, disappear. Until improved technique enables us to trace the centrosome through these stages, the evidence given by *Allolobophora* still points to the *de novo* origin of the cleavage centrosomes.

EXPLANATION OF PLATE I.

The photographs of this plate were taken by the method described in full in Zeit. f. wiss. Mik., Bd. XVIII, 1901. "A new method of focussing in photomicrography."—Foot and Strobell.

In order to economize space only a small part of each section is shown in the photographs.

All the sections were stained with iron hæmatoxylin, in most cases with an after stain of dilute Bismark brown.

PHOTO. 1. Section (3μ) of oöcyte, second order, showing the male attraction-sphere with the posterior granule of the middle-piece forming the center of the sphere. The middle-piece of the spermatozoön is intact and still attached to the head, part of which appears in this section, the rest of the head showing in four neighboring sections. Fixative Perenyi's fluid. $\times 1000$.

PHOTO. 2. Section ($2\frac{1}{2}\mu$) of oöcyte, second order, showing the male attraction-sphere with the posterior end of the middle-piece nearly in the center of the sphere. The middle-piece of the spermatozoön is intact and still attached to the head, part of which shows in this section. The rest of the head in three neighboring sections. Fixative Hermann's fluid. $\times 1000$.

PHOTO. 3. Section (3) of oöcyte, second order, showing male attraction-sphere with posterior end of middle-piece in the center of the sphere. The middle-piece is intact and still attached to both the tail and head of the spermatozoön. The rest of the head is in the next section. Fixative corrosive sublimate. $\times 1040$.

PHOTO. 4. Section (3μ) of oöcyte, second order, showing male attraction-sphere with the posterior granule of the middle-piece demonstrated in the center of the sphere. The middle-piece of the spermatozoön is intact, and is still attached to the head, a part of which appears in this section. The rest of the head is in the next section. Fixative Perenyi's fluid. $\times 1000$.

PHOTO. 5. Section (3μ) of oöcyte, second order, showing male attraction-sphere with posterior end of middle-piece in the center of the sphere. The middle-piece of the spermatozoön is intact and still attached to the head, a part of which appears in this section. The rest of the head in the two following sections. Fixative corrosive sublimate. $\times 1000$.

PHOTO. 6. Section (3μ) of oöcyte, second order, showing male attraction-sphere with the posterior granule of the middle-piece demonstrated in the center of the sphere. The middle-piece of the spermatozoön is intact and still attached to the head, a part of which appears in this section; the rest of the head in three neighboring sections. Fixative corrosive sublimate. $\times 1000$.

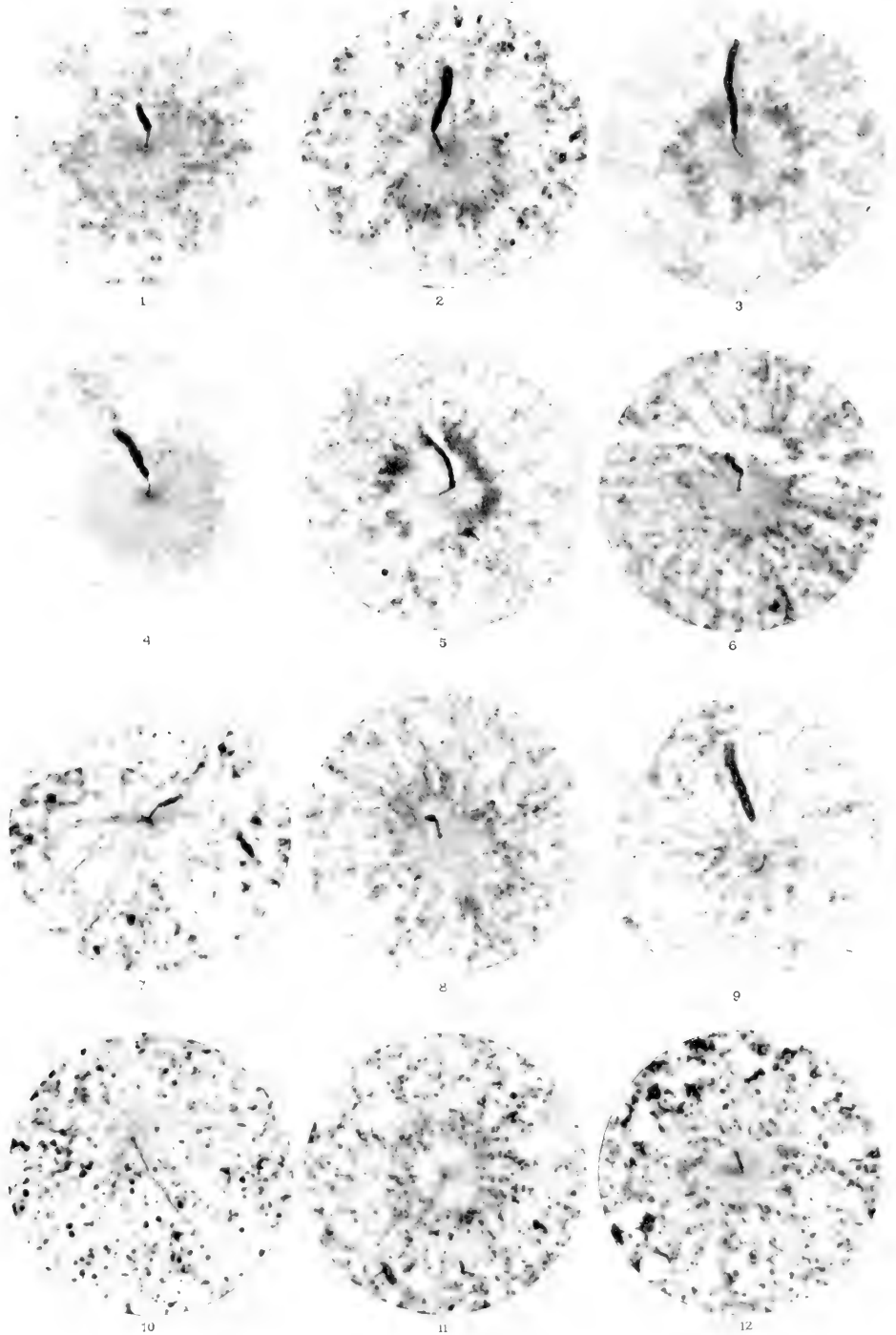


PHOTO. 7. Section ($2\frac{1}{2}\mu$) of oöcyte, second order, showing male attraction-sphere with posterior end of middle-piece in the center of the sphere (overstaining has obliterated the granule). The middle-piece is intact and still attached to the head, part of which appears in this section. The rest of the head is in two neighboring sections. Fixative chromo-acetic. $\times 1000$.

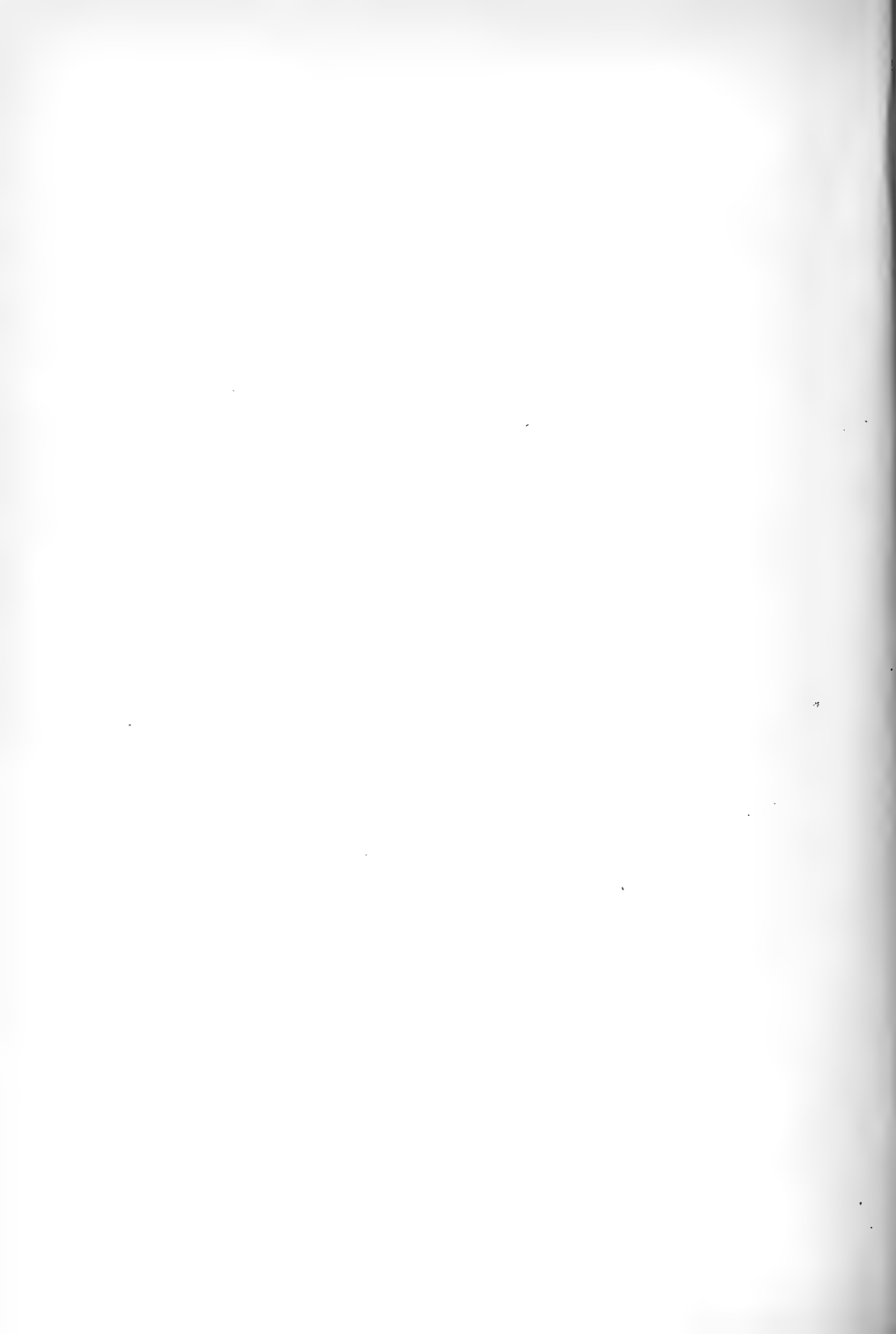
PHOTO. 8. Section (3μ) oöcyte, second order, showing male attraction-sphere with posterior granule of middle-piece in the center of the sphere. The middle-piece is intact, and still attached to the head, part of which appears in this section. The rest of the head is in three neighboring sections. Fixative corrosive sublimate. $\times 1040$.

PHOTO. 9. Section ($2\frac{1}{2}\mu$) of oöcyte, second order, showing male attraction-sphere with posterior end of middle-piece in the center of the sphere. The middle-piece is intact, but separated from the head, part of which shows in this section. The rest of the head is in the next section. Fixative corrosive sublimate. $\times 1000$.

PHOTO. 10. Section (3μ) of polysperm oöcyte, second order, showing one of the male attraction-spheres and part of the tail of the spermatozoön attached to a granule, which must be the posterior granule of the middle-piece. Fixative Hermann's fluid. $\times 1000$.

PHOTO. 11. Section (2μ) of oöcyte, second order, showing male attraction-sphere with one end of middle-piece in center of the sphere. The rest of the middle-piece shows in the next section as a tiny rod with the opposite end near the periphery of the sphere. Fixative Flemming's fluid without acetic acid, $\times 1000$.

PHOTO. 12. Section (2μ) of oöcyte, second order, showing male attraction-sphere with middle-piece, one end of which is in the center of the sphere. The end at periphery of sphere is nearest the head of spermatozoön, which is in neighboring sections. Fixative Flemming's fluid, without acetic acid. $\times 1000$.



A CONTRIBUTION TO THE ANATOMY AND DEVELOPMENT
OF THE VENOUS SYSTEM OF *DIDELPHYS MARSUPI-*
ALIS (L).¹—PART I, ANATOMY.

BY

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WITH 5 COLORED PLATES AND 11 TEXT FIGURES.

It has been found necessary to publish this paper in two parts. The first part deals with the anatomy of the venous system of *Didelphys marsupialis*, while the second part, which appears later, will deal with the development of the veins.

In 1900 the writer² published a preliminary article entitled "The Variations of the Venous System in *Didelphys virginiana*," in which was described a set of variations that occurred in connection with the mode of origin of the postcaval vein. These variations were so unusual in character and occurred with such regularity in all of the opossums examined that a further investigation was deemed necessary. This investigation is now completed and after the examination of one hundred and one (101) opossums the writer can reiterate the statement made in the preliminary article, that the mode of origin of the postcava is so variable in *Didelphys marsupialis*, that it is impossible to assign any one mode of origin for this vessel that may be regarded as typical of the species.

It is astonishing how little has been published upon the anatomy of the venous system of marsupials when one considers the unique character of their postcaval vein. Previous to 1893 the writer has, with Hochstetter, 93, been able to find in the literature but one reference to the postcaval vein (Owen, 66), in which it has been described as occu-

¹On the basis of priority of nomenclature the specific name *marsupialis* has been substituted for *virginiana*. All of the opossums made use of were captured in the neighborhood of Princeton, New Jersey.

²The writer wishes to express his thanks to Stephen S. Palmer of New York, for his generosity in supplying the funds necessary to cover the cost of the Plates in this article. Also to his assistant C. F. Silvester thanks are due for his valuable assistance in connection with the preparation of the material used in the investigation.

pying a position ventral to the abdominal aorta, a position which is unusual in mammals.

Previous to 1893, so far as known to the writer, only the following have contributed to the anatomy of the venous system of the marsupials: Martin, 36, Owen, 35, 36, 39-47 and 66, Forbes, 81, and Cunningham, 82. From 1893 up to the present time, Hochstetter, 93, Beddard, 95, Parsons, 96, Windle and Parsons, 98, and the writer, 00, 01 and 02. Of all the above-mentioned investigators Hochstetter was the first to give an accurate and comprehensive description of the anatomy of the postcaval vein for a large number of marsupials.

In dealing with the anatomy of the venous system of *Didelphys* it will be the purpose of this paper not to enter into a detailed description of all the veins, but rather to give an account of the general arrangement and principal variations of the caval veins and their chief tributaries, in order that the description may serve as a basis for comparison with the veins of other mammals. In addition to this, the main features of the heart will be discussed and a general comparison drawn between the venous system of *Didelphys* and that of other marsupials.

THE HEART.

The heart of *Didelphys* presents only a few characters in which it differs from that of other mammals, and will be considered under the following topics: (1) *The fetal structures*; (2) *the auriculoventricular valves*; (3) *the pulmonary veins*, and (4) *the coronary veins*.

1. *The Fetal Structures*.—A fossa ovalis, annulus ovalis and ductus arteriosus are wanting in *Didelphys* as in all other adult marsupials³ as hitherto described by Owen, 66, Cunningham, 82, Röse, 90, Parsons, 96, and Parsons and Windle, 98. Röse has explained the absence of the fossa and annulus ovalis in the heart of the adult marsupial on the ground that in the embryo the two auricles communicate with each other, as in birds and monotremes, by means of a number of small openings which are secondarily formed, and which close up early in correlation with the abbreviated intrauterine life of these animals.

2. *The Right Auriculoventricular Valve*.—The right auriculoventricular valve of *Didelphys* consists of one medial or septal and two lateral membranous cusps which are continuous at their bases round the auriculoventricular orifice. The left lateral cusp is the largest, the septal next, while the right lateral is quite small and is only with diffi-

³ With the possible exception of *Perameles* in which an allantoic placenta is present.

culty to be distinguished from the left lateral cusp. The two lateral cusps are attached by means of chordæ tendineæ to three muscoli papillares which spring from the septal wall; the medial or septal cusp is, for the most part, attached directly to the septal wall by chordæ tendineæ; a few of the latter may, however, be inserted into the smallest of the muscoli papillares which springs from the right side of the septum.

The right auriculoventricular valve of marsupials has been described by a number of investigators, and it appears from their descriptions that a considerable difference exists not only as to the number of membranous cusps, but also as to the number of muscoli papillares that may be present. These differences are clearly brought out in the following table, which explains itself.

*The Right Auriculoventricular Valve of Marsupials.*⁴

Family—MACROPODIDÆ.	No. of cusps.	No. of muscoli papillares.
<i>Macropus (spec.)</i> (OWEN, 66.)	Not given.	3
<i>Macropus rufus.</i> (WINDLE AND PARSONS, 98.)	4	2
<i>Dendrolagus bennetti.</i> (BEDDARD, 95.)	Not given.	4
<i>Petrogale xanthopus.</i> (PARSONS, 96.)	4	2
<i>Petrogale penicillata.</i> (BEDDARD, 95)	Not given.	3
Family—PHALANGERIDÆ.		
<i>Phascolarctos fuscus.</i> (MARTIN, 36.)	Not given.	3
<i>Phascolarctos cinereus.</i> (FORBES, 81.)	Not given.	2 or 3
<i>Phalangista vulpina.</i> (CUNNINGHAM, 82.)	4	4
<i>Phalangista maculata.</i> (CUNNINGHAM, 82.)	4	2
<i>Phascolomys wombat.</i> (OWEN, 36.)	Not given.	3
<i>Phascolomys wombat.</i> (RÖSE, 90.)	3	One large, one medium-sized and several small.

⁴ Where the number of cusps is not mentioned by the author, in all probability, the usual number, three, was observed.

In the above table as well as in the following pages of this article the writer, in order to avoid confusion, has followed the nomenclature adopted by the authors referred to.

Family—DASYURIDÆ.	No. of Cusps.	No. of muscoli papillares.
<i>Thylacinus cynocephalus</i> . (CUNNINGHAM, 82.)	5	Two groups.
<i>Thylacinus cynocephalus</i> . (RÖSE, 90.)	3	One large, one medium-sized and several small
<i>Dasyurus viverrinus</i> . (CUNNINGHAM, 82.)	2	3
<i>Phascogale calura</i> . (CUNNINGHAM, 82)	Not given.	2
Family—DIDELPHYIDÆ.		
<i>Didelphys marsupialis</i> . (McCLURE.)	3	3

From the above table, which is supposed to represent the normal conditions, it is seen that the number of cusps that may enter into the formation of the right auriculoventricular valve of marsupials ranges between two and five, and that in one instance (*Thylacinus*) there appears to be a marked difference of opinion as to the number of cusps present. The question naturally arises: Do those cases in which less or more than three cusps have been observed represent the normal conditions, or do they indicate that the observers have interpreted differently as to what really constitutes a cusp? It is well known that considerable variation exists among the higher mammals so far as their valve structure is concerned. In some mammals there is scarcely any division into a right and left lateral cusp, so that one would not be far from the mark in describing their valves as consisting of one lateral and one septal cusp. In other mammals the three cusps may be quite distinct and in some instances an extra or supernumerary cusp may be present, being formed, probably, as the result of an extra notching of the free border of one of the lateral cusps. In view of the above statements it appears to the writer that the membranous valves of marsupials must be classed with those of the higher mammals, a classification already adopted by authors of recent text-books (Beddard, 02, and Wiedersheim, 02), although they have given no reasons for so doing.

Before closing this topic it may be stated that the semi-lunar valves of the aorta and pulmonary artery, as well as the mitral or bi-cuspid valves of *Didelphys* and other marsupials, thus far described, agree in their structure with those of the higher mammals.

3. *The Pulmonary Veins*.—There is little to be said concerning the pulmonary veins of *Didelphys* except that they usually unite to form a V. pulmonalis communis before opening into the left auricle. In a few cases in which a V. pulmonalis communis was not present the veins always opened into the auricle close together.

As a general rule the pulmonary veins of marsupials probably present as wide a range in their method of termination as these veins do in the higher mammals. They may open into the auricle by means of a *V. pulmonalis communis* as in *Didelphys*, close together as in *Petrogale* (Parsons, 96), or in separate groups as in *Thylacinus* and the wombat (Röse, 90). Owen, 66, as opposed to Röse, states that in the wombat they may open close together or by a single trunk.

4. *The Coronary Veins.*—The coronary veins of *Didelphys* consist of a dorsal (posterior) and a ventral (anterior) group. The dorsal group consists of one large and several small veins, which, for the most part, lie upon the surface of the left ventricle and open into the left precava near its point of termination in the right auricle. The ventral group also consists of one large and several small veins. The small veins open directly into the right auricle. The large vein (*V. cordis magna*, *V. c. m.* in Text Fig. I), which lies in the ventral (anterior) interventricular furrow, does not, as in most mammals, on reaching the auriculoventricular groove deviate to the left and open into the left precava, but pursues a course somewhat similar to that of a coronary vein in birds, by passing dorsad between the root of the pulmonary artery (*A. p.*) and the left auricle and then deviating to the right over the dorsal surfaces of the roots of the pulmonary artery (*A. p.*) and aorta (*Ao.*) to open into the atrium of the right precava (*prc. d.*).⁵

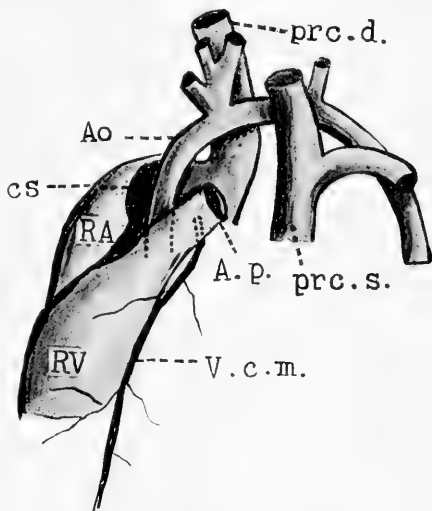


FIG. I. Diagram of vessels at base of heart. *Didelphys marsupialis*. Showing course of *V. cordis magna*. Ventral view. *Ao.*, aorta; *A. p.*, pulmonary artery; *CS.*, crescentic notch; *prc. d.*, right precava; *prc. s.*, left precava; *RA.*, right auricle; *RV.*, right ventricle; *V. c. m.*, *V. cordis magna*.

Cunningham was the first, so far as known to the writer, to notice the unusual course of this vein in marsupials (*Thylacinus*), and regarded its peculiarity as one of the two distinctive characters of the

⁵In birds (*Buteo borealis* and *Somateria mollissima*) the vein in question pursues the same course as in *Didelphys* with the exception that it does not lie dorsal to the root of the aorta, as the vein opens further to the left into the sinus common to the openings of the postcava and the right precava.

marsupial heart, the other being the absence of the fossa and annulus ovalis.

There is one more topic in connection with the structure of the heart that is worthy of mention, since it has been erroneously described by Owen, 66, as a constant marsupial character. I refer to the so-called bifurcated right auricular appendix. It has been described as a prominent feature of the heart by Owen in *Macropus* and *Phascotomys*; by Cunningham, 82, in *Phalangista vulpina* and *P. maculata* and by Parsons, 96, in *Petrogale*. It has been found by Cunningham to be only slightly indicated in *Phascogale* and by the writer in *Didelphys* (C S., Text Fig. I), and to be wanting by Cunningham in *Dasyurus* and *Thylacinus*. The investigations of Cunningham have entirely disproved the claims of Owen as to the constancy of this character for the heart of marsupials, since he found it wanting in *Dasyurus* and *Thylacinus*.

A bifurcated right auricular appendix apparently possesses no great significance beyond the circumstance that it represents an instance in which the free margin of the appendix has become notched or invaginated as the result of its proximity to the root of the aorta. Such a notching is not uncommonly met with in the hearts of the higher mammals, as, for example, in *Arctomys monax*,⁶ in which a well-defined bifurcated right auricular appendix may be present.

THE VEINS OF THE HEAD AND NECK. (*Text Fig. II.*)

There are two precaval veins in *Didelphys*, and this is the rule in all marsupials with the possible exception of *Belideus breviceps*, which has been described by Forbes, 81, as possessing only one. In *Didelphys* each precava (pre.) begins opposite the first rib and is formed through the union of three veins, the V. subclavia (V. s.), the V. jugularis communis (V. j. c.), and a vein which I have designated as the V. costo-vertebralis (V. cv.). The tributaries of the precaval veins are as follows: (1) A V. mammaria interna (V. mam.) which opens into the ventral surface of each precava near its union with the subclavian vein; (2) the V. azygos (V. a.), which opens into the left precava about opposite the head of the third rib, and (3) the posterior group of coronary veins which also open into the left precava, about opposite the head of the fifth rib. The right and left precaval veins open into the right auricle along its antero- and posterodorsal walls, respectively;

⁶ Princeton Morphological Museum, No. 487.

follows the course of the ascending cervical artery and opens into the dorsal surface of the common jugular near its union with the subclavian vein.

The internal jugular vein (V. j. i.) presents no unusual conditions except that it is an exceedingly small vessel as compared with the size of the external jugular (V. j. e.).⁷

The external jugular vein (V. j. e.) begins near the angle of the lower jaw and is formed, on each side, through the union of three veins: The V. maxillaris externa (V. m. e.), the V. maxillaris interna (V. m. i.) and a vein which may be designated as the V. submaxillaris (V. s. max.). The external and internal maxillary veins often unite to form a V. maxillaris communis before joining the submaxillary vein.

The external jugular vein (V. j. e.), along most of its course, lies quite superficially and instead of passing into the thoracic cavity on the dorsal side of the clavicle, as is usually the case in mammals, it forms about it, on each side, a complete venous ring so that one part of the external jugular lies ventral (v.) and another dorsal (do.) to the clavicle (cl.).⁸ Hochstetter, 96, has described the presence of a somewhat similar venous ring in *Ornithorhynchus* and states that the portion of the ring which lies dorsal to the clavicle is much larger than the ventral and forms the main trunk of the external jugular. In *Didelphys* there is not much difference in size between the dorsal and ventral portions of the ring, as, in the majority of cases observed, they were found to be subequal in size.

The formation of such a venous ring about the clavicle, so far as the writer knows, has not been hitherto described for *Didelphys* nor for any marsupial. In a specimen of *Petrogale* recently examined by the writer no indication of such an annulus was present, so that in all probability this feature is not of common occurrence among the marsupials.

Of the veins opening into each external jugular the following are the most important: Beginning craniad, (1) one or two veins which return blood from the postauricular region (V. a. p.); (2) the V. transversa

⁷ This is also the case in *Petrogale* (Beddard, 95, and the writer).

⁸ As a matter of fact two venous rings are formed about the clavicle in *Didelphys*; the one mentioned above, which is formed exclusively by the external jugular vein and another (X.), much larger, which is formed through a confluence of the cephalic vein (V. cep.) with the axillary (V. ax.) and external jugular (V. j. e.) veins. The last mentioned or outer ring (X.) is not uncommon in mammals. It is a prominent feature in the three-toed sloth (*Bradypus tridactylus*) and is sometimes met with in man (Nuhn).

scapulæ (V. t. s.); (3) the V. cephalica (V. cep.), which arises on the radial side of the hand and forearm (this vein also opens into the axillary vein); (4) two veins which may open separately or by a common trunk into the dorsal portion (do.) of the venous ring, one of which (b.) returns blood from the superficial muscles on the ventral surface of the neck, while the other (c.), besides uniting with the internal maxillary vein, collects blood from the side of the larynx.

In addition to the above mentioned tributaries, the external jugular veins anastomose with each other across the middle line of the neck. This anastomosis may be accomplished in one of two ways: Either by means of two vessels which run between the dorsal and ventral portions of the venous rings of opposite sides and fuse in the middle line of the neck (V. an.), or by means of a single vessel which extends between the ventral portions of the two venous rings as in Text Fig. IV (V. an.).

The affluent veins of each external jugular are, as mentioned above, the V. submaxillaris (V. s. max.), the V. maxillaris externa (V. m. e.) and the V. maxillaris interna (V. m. i.). The submaxillary veins are quite large and anastomose with each other on the dorsal surfaces of the geniohyoid muscles. Each submaxillary vein receives the following tributaries: Veins from the tongue and the floor of the mouth; the V. submentalis (V. s. ment.) and small veins from the submaxillary and sublingual glands (a.).

The external maxillary vein collects blood from the face and the internal maxillary from the regions supplied by the internal maxillary artery.

THE VEINS OF THE VERTEBRAL CANAL AND THE DEEP LYING VEINS OF THE CERVICAL AND THORACIC REGIONS.⁹ (*Text Fig. III.*)

Text Fig. III is a diagram of the veins of the vertebral canal and the deep-lying system of veins of the cervical and thoracic (first five intercostal spaces) regions. These two regions need a special description, since the relations which exist here among the veins are quite unusual.

The Vv. columnæ vertebrales (Vv. c. ve.) consist of two large venous sinuses which lie ventral to the spinal cord and extend, on each side, within and along the entire length of the vertebral or spinal canal. In the region of the first thoracic vertebra they anastomose at one point dorsal to the spinal cord.

⁹This deep-lying system of veins was largely studied by means of corrosions.

The V. costovertebralis (V. cv.), previously mentioned as one of the tributaries of the precava, is most intimately connected with this deep-lying system of veins and may, therefore, be considered at this point.

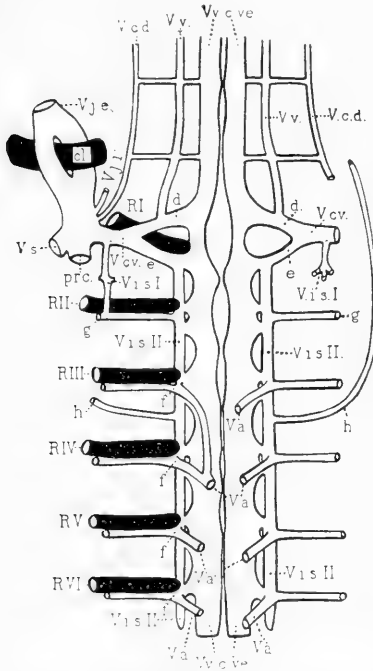


FIG. III. Diagram of the veins of the vertebral canal and the deep-lying veins of the cervical and thoracic regions of *Didelphys marsupialis*. Ventral view. d. and e. tributaries of the V. costovertebralis which lie cranial and caudal, respectively, to the first rib; cl., clavicle; f., anastomosis between the azygos and intercostal veins and the veins of the vertebral canal; g., tributary of the deep superior intercostal vein; h., tributary of the deep inferior intercostal vein; pr.c., precava; R. I-R. VI., the first six ribs; V.a., intercostal branches of azygos vein; V.c.d., V. cervicalis descendens; V.cv., V. costovertebralis; V.i.s.I., superficial V. intercostalis suprema; V.i.s.II., deep V. intercostalis suprema; V.j.e., V. jugularis externa; V.j.i., V. jugularis interna; V.v., V. vertebralis; Vv.c.ve., Vv. columnæ vertebrales.

correspond to the last cervical and first intercostal veins, respectively.

3. The V. vertebralis (V. v.) lies in the vertebral canal with the vertebral artery and opens into the large tributary of the V. costovertebralis which lies just cranial to the first rib (d.). It anastomoses, by means of segmentally arranged vessels, on its medial side, with the

The tributaries of the V. costovertebralis (V. cv.) are, on each side, as follows: (1) A small superficial V. intercostalis suprema (V. i. s. I); (2) two large veins, one of which lies just cranial (d.) and the other caudal (e.) to the first rib (R. I); (3) the V. vertebralis (V. v.), and (4) a deep-lying V. intercostalis suprema (V. i. s. II).

1. The superficial V. intercostalis suprema (V. i. s. I) commonly opens into the V. costovertebralis, but may, instead, open into the precava. It lies superficially, collects blood from the first intercostal space and usually anastomoses directly with the second intercostal vein (g., right side).

2. The largest tributaries of the V. costovertebralis consist of two large veins, one of which lies just cranial (d.) and the other caudal (e.) to the first rib. Both of these veins connect directly with the Vv. columnæ vertebrales (Vv. c. ve.). The vein cranial to the rib is sometimes the larger of the two, though, as a rule, they are subequal in size. These two vessels occupy a position in the cervical and thoracic regions directly in the line of the segmental vessels and appear to

Vv. columnæ vertebrales (Vv. c. ve.), and, on its lateral side, with the descending cervical vein (V. c. d.).

4. The deep V. intercostalis suprema (V. i. s. II) is a comparatively short vessel which runs, on each side, parallel to the vertebral column and extends between the second and sixth to seventh ribs *dorsal to their necks*. This vein opens into the vein, previously mentioned, that lies caudal to the first rib (e.) and collects blood from the second to sixth intercostal spaces. It anastomoses in this region with the intercostal branches of the azygos (f.) and, opposite the head of each rib, by means of a large anastomosis with the Vv. columnæ vertebrales. It also receives two important tributaries: (1) The vein of the second intercostal space (g.), which usually opens into it without previously anastomosing with the azygos branches, and (2) a vein (h.) which collects blood from the deep muscles on the back of the neck and joins the deep superior intercostal vein (V. i. s. II) about opposite the third intercostal space.¹⁰

In comparing the veins of *Didelphys*, as represented by the V. costo-vertebralis and its tributaries, with the vertebral system of veins in the sauropsida, especially birds, one cannot help being impressed by the similarity that exists between the two. In *Didelphys* the vertebral and deep superior intercostal veins occupy the same relative positions with respect to the vertebral column and connect with the jugular and subclavian veins to form the precava, as do the anterior and posterior vertebral veins in birds. In birds, there being no azygos vein, all of the intercostal veins open directly into a posterior vertebral vein. In *Didelphys*, also, some of the veins of the cranial intercostal spaces may open directly into the deep superior intercostal without previously anastomosing with any of the azygos branches (see under Azygos Veins).

THE VENA AZYGOS AND ITS TRIBUTARIES.¹¹ (See Text Figs. III and IV.)

There is, as a rule, but one azygos vein in *Didelphys* and this is situated on the left side. The azygos vein increases slightly in size from behind forward. Its caudal end invariably joins the postcava about opposite the second lumbar vertebra, while its cranial end, after curving round the left side of the aorta, joins the left precava about

¹⁰ In *Didelphys* a branch of an intercostal artery accompanies this vein. Cunningham (82) has described the course of this artery in *Thylacinus* and *Dasyurus* but did not mention the vein.

¹¹ The azygos system was dissected in twenty-six opossums.

opposite the head of the third rib. Between its point of union with the postcava and the middle of the tenth thoracic vertebra the azygos lies dorsal to the aorta and, in consequence of this position, the left intercostal arteries in this region pass dorsad on the left side of the vein.

Between the tenth thoracic vertebra and its point of union with the left precava the azygos vein occupies a position dorsolateral to the aorta, and the left intercostal arteries pass dorsad on the right side of the vein.

The manner in which the caudal end of the azygos vein joins the postcava was found to be quite variable. It may join the postcava to the left, which is the usual method, or to the right of the aorta; or it may bifurcate into two branches on the ventral circumference of the aorta, one of which joins the postcava to the right and the other to the left of the aorta. In the latter case the aorta is encircled by a venous ring formed by the azygos and postcausal veins.

On account of the numerous variations which occur in the cranial part of the thoracic region it is difficult to establish what might be called a typical arrangement of the tributaries of the azygos vein. The arrangement, however, which comes nearest to being typical is represented by Text Fig. IV. Here all of the intercostal spaces on both

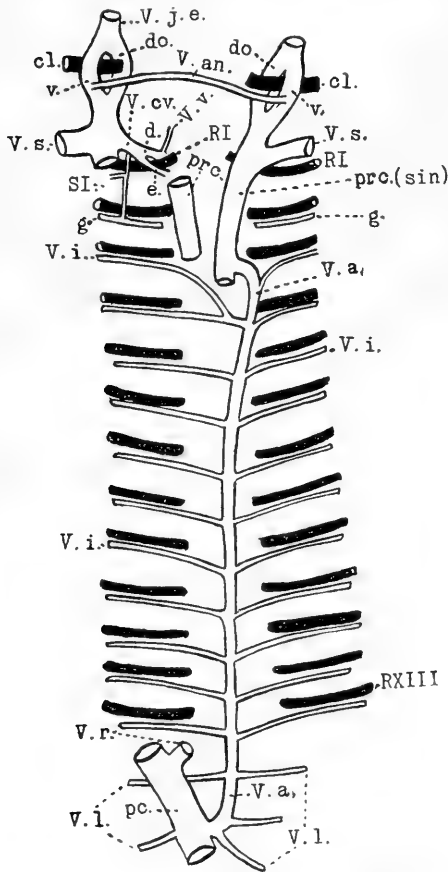


FIG. IV. A diagram representing the usual arrangement of the azygos branches in *Didelphys marsupialis*. Ventral view.
cl., clavicle; d. and e., tributaries of the V. costovertebralis; do., dorsal portion of venous ring about clavicle; g., second intercostal vein; pc., postcava; prc., precava; R., rib; S., intercostal space; v., ventral portion of venous ring about clavicle; V. a., V. azygos; V. an., V. anastomotica; V. cv., V. costovertebralis; V. i., V. intercostalis; V. j. e., V. jugularis externa; V. l., V. lumbalis; V. r., V. renalis; V. s., V. subclavia; V. v., V. vertebralis.

sides, except the first two, are drained by the azygos system; also the blood from the lumbar region, on the left side, as far caudad as the

third, and, on the right side, as far caudad as the second lumbar vertebra, is collected by the tributaries of this vein. The blood from the rest of the lumbar region is collected by the lumbar veins which open into the postcava. The blood from the first intercostal space is collected, on both sides, by the superficial superior intercostal vein (V. i. s. I, Text Fig. III), which opens into the V. costovertebralis; that from the second intercostal space by a vein which opens directly into the deep superior intercostal (g. and V. i. s. II, in Text Fig. III) without previously anastomosing with any of the azygos branches.

The intercostal tributaries of the azygos anastomose with the Vv. columnæ vertebrales in the caudal part of the thorax, and, in the cranial part, with the deep superior intercostal (V. i. s. II), which, as mentioned above, is one of the tributaries of the V. costovertebralis (Text Fig. III, f.).

The relation of the azygos tributaries to the first four intercostal spaces was found to be quite variable and this was especially the case on the right side. In five opossums (three males and two females) the most cranial tributary of the azygos, on the right side, collected blood from the fourth instead of from the third intercostal space, as is usually the case, and the veins of the second and third intercostal spaces opened directly into the deep superior intercostal vein without anastomosing with the azygos. The blood from the first intercostal space was collected by the superficial superior intercostal vein. On the left side the arrangement of the veins was similar to that represented in Text Fig. IV.

Two instances were met with in which tributaries of the azygos collected blood from all of the intercostal spaces, on both sides, with the exception of the first and anastomosed with the tributaries of the Vv. costovertebrales which lie caudal to the first ribs (e.).

In thirty per cent of the opossums examined a small right azygos vein was present which opened into the right precava about opposite the head of the second rib. In every instance the vein was a small and insignificant vessel and its tributaries were confined to the first five intercostal spaces of the right side. In the eight animals in which it was found it collected blood in three, from the second intercostal space; in one, from the second and third intercostal spaces; in one from the third intercostal space; in two, from the third and fourth intercostal spaces, and finally, in one, from the third, fourth and fifth intercostal spaces. When the right azygos received tributaries from the third, fourth or fifth intercostal spaces, the tributaries of the left azygos which usually collect blood from these spaces were wanting.

The general character of the azygos veins of marsupials other than *Didelphys* has been described by a number of investigators as indicated below.

Marsupials in which Two Azygos Veins are Present which Open into the Right and Left Precaval Veins, Respectively.

Family—MACROPODIDÆ.

Macropus (spec.?) (OWEN, 66); *Halmaturus bennetti* (left azygos longer, BEDDARD, 95); *Petrogale (spec.?)* (right azygos longer, McCLURE).

Family—PHALANGERIDÆ.

Left azygos longer in *Phascalartos cinereus*, *Phascalomys wombat*, *Cuscus*, *Phalangista* and *Belideus*¹² (FORBES, 81).

Marsupials in which a single azygos vein is present on the right side.

Family—MACROPODIDÆ.

Petrogale xanthopus (PARSONS, 96); *Petrogale penicillata*, *Macropus rufus* and *Dendrolagus bennetti* (BEDDARD, 95).

Family—DASYURIDÆ.

Thylacinus cynocephalus (CUNNINGHAM, 82).

Marsupials in which a single azygos vein is present on the left side.

Family—PHALANGERIDÆ.

Phalangista maculata and *Phalangista vulpina* (CUNNINGHAM, 82); *Phalangista vulpina* (CUNNINGHAM, 82) and *Phascalartos fuscus* (MARTIN, 36).

Family—DASYURIDÆ.

Dasyurus viverrinus (CUNNINGHAM, 82, and BEDDARD, 95); *Phascogale calura* (CUNNINGHAM, 82).

Family—DIDELPHYIDÆ.

Didelphys cancrivora and *azarae* (BEDDARD, 95) and *Didelphys (virginiana) marsupialis* (McCLURE).

It is evident from the foregoing table that, with the exception of *Thylacinus* and *Halmaturus*, a right azygos vein prevails in the Macropodidæ and a left in the Phalangeridæ, Dasyuridæ and Didelphyidæ.

Beddard, 95, states that he found considerable variation among several individuals of *Halmaturus*, and the writer is inclined to believe that a single azygos vein is the rule in marsupials and that when two are present the case may be regarded as a variation.

¹² It is difficult to reconcile Forbes' two statements that in *Belideus* there is only one precava and that the azygos veins in the same animal open into the right and left precaval veins, respectively.

A connection between the azygos vein and the postcava is apparently not of constant occurrence in the marsupials. Beddard, 95, found such a connection invariably occurring in *Didelphys azaræ*. In *Phalangista*, however, he found it occurring in only one of several individuals examined and, in this case, on account of its large size, it practically took the place of the postcava. In *Didelphys* the writer has never observed any diminution in size of the postcava on account of its connection with the azygos vein.

There is very little in the literature that refers to the manner in which the blood is collected from the intercostal spaces in marsupials.

Forbes, 81, states that when two azygos veins are present the smaller vein collects blood from the first few intercostal spaces (*Cuscus*, *Belideus*, *Phascolomys* and *Phalangista*). According to Cunningham, 82, the azygos tributaries collect blood in *Thylacinus* from the intercostal spaces of both sides with the exception of the first three; the intercostal veins of these three spaces join, on each side, to form a single vessel which opens into the precava. In *Cuscus*, *Phalangista vulpina*, *Phascogale* and *Dasyurus* the single left azygos vein collects blood from all of the intercostal spaces on the left side and from all on the right side except the first three; these, as in *Thylacinus*, return their blood through a single vessel that opens into right precava (Cunningham). In *Petrogale xanthopus* the azygos vein receives all of the intercostal veins from both sides of the thorax (Parsons, 96).

In a specimen of *Petrogale* recently dissected by the writer, although the vessels in this region were poorly injected, the blood from all of the intercostal spaces on the right side appeared to be collected by tributaries of the right azygos. On the left side the intercostal veins from all the intercostal spaces except the first two or three also opened into the right azygos; the veins from the first two or three spaces joined, as on the left side in *Thylacinus*, to form a single vessel which opened into the left precava. The small left azygos vein, which was present in addition to the left superior intercostal, was not injected, so that its connections could not be traced. A V. costovertebralis which has been described above as a constant tributary of the precava in *Didelphys* was wanting on both sides in *Petrogale*.

It is evident from what has been stated above that there is little agreement between *Didelphys* and other marsupials so far as the veins of the first three or four intercostal spaces are concerned. Some of these differences can undoubtedly be explained on the ground that they are individual variations. The most interesting and fundamental difference, however, is the circumstance that in *Didelphys* the most

cranial of the intercostal spaces are, in part, drained by a deep-lying vein similar in its relations to the posterior vertebral vein of the sauropsida instead of by tributaries of the azygos, or by a more superficially situated superior intercostal vein, as is commonly the case in marsupials.

THE POSTCAVAL VEIN AND ITS TRIBUTARIES.

For convenience of description the postcaval vein of *Didelphys* will be described under the following divisions: (1) The *prehepatic* division; (2) the *hepatic* division; (3) the *renal* division; (4) the *postrenal* division.

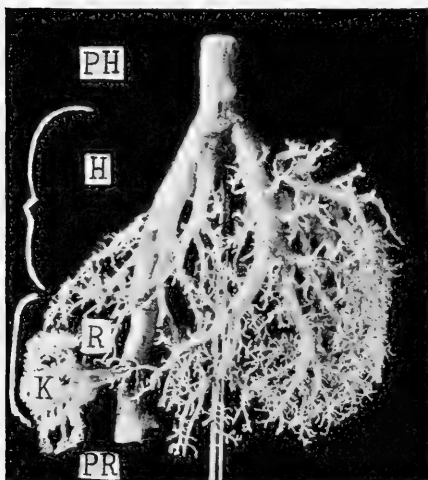


FIG. V. Photograph of a corrosion of the cranial end of the postcava and hepatic and renal veins of *Didelphys marsupialis*. Ventral view. Princeton Morphological Museum, No. 153.

H., hepatic division of the postcava; K., veins of right kidney; PH., prehepatic division of the postcava; PR., postrenal division of the postcava (only a very small portion of this division is shown in the photograph); R., renal division of postcava.

The first three divisions do not present any unusual characters and can be briefly considered; the fourth or *postrenal* division, however, is most variable in character and will be dealt with at length.

1. The *prehepatic* division of the postcava is that portion of the vein which extends between the right auricle and the most cranial of the hepatic veins (PH., Text Fig. V).

The only tributaries which this division receives are the Vv. phrenicæ, which collect blood from the diaphragm and open into the postcava in its passage through the diaphragm. These veins are not shown in the photograph.

Owen, 66, has stated that when the posterior extremities are smaller or not larger than the anterior ones, as in the ursine

dasyure and wombat, the postcava is somewhat less than the left precava and they appear to terminate by separate apertures in the auricle; but in the kangaroo the proportions of the two veins are reversed, and the postcava more obviously receives the left precava before it terminates. In comparing the conditions in *Petrogale* with those in *Didelphys* the writer is unable to draw any such distinctions as those indicated by

Owen, and finds that in both animals the left precava opens into the auricle in common with the postcava.

2. The *hepatic* division of the postcava (H., Text Fig. V), which lies within the liver, includes that portion of the vein into which hepatic veins open. The hepatic veins open into the postcava by means of three large and two or three small branches. The small branches return the blood from the caudate lobe of the liver.

3. The *renal* division of the postcava (R., Text Fig. V), includes that section of the vein which lies between the most caudal of the hepatic veins and a point just behind the most caudal of the two renal veins, so as to include that portion of the postcava into which the renal veins open.

The right suprarenal body is firmly attached to the dorsal surface of the postcava in this region, and its cranial end is embedded in the caudate lobe of the liver. The only direct tributaries which the renal division receives are the V. suprarenalis dextra, which opens into the dorsal surface of the postcava, and the Vv. renales.

The right renal vein usually opens into the postcava cranial to the left and about opposite the first lumbar vertebra. The left renal vein, which lies just caudal to the Truncus cœliacomesentericus, opens into the postcava about opposite the second lumbar vertebra. The left suprarenal body lies upon the left renal vein into which its vein opens.

Multiple renal veins, especially on the right side, were frequently met with and, in a few cases, the right renal artery was found to cross the postcava on its ventral instead of its dorsal surface.

The first three divisions of the postcava, with the exception of that portion into which the renal veins open, occupy a position, as in other mammals, on the right side of the body ventrolateral to the aorta and at no point come in contact with the latter. At the level of the renal veins, however, the postcava bends mediad so as to reach the ventral surface of the aorta and occupies this position with respect to the aorta as far caudad as the Vv. iliacæ externæ.

4. The *postrenal* division of the postcava (PR.) consists of that portion of the vein which lies caudal to the renal veins (V. r.). (See Text Figs. V and IX and Fig. 23, Plate V.) Its tributaries consist of two or three pairs of Vv. lumbales, the Vv. spermaticæ internæ and the Vv. iliacæ. The caudal end of the azygos vein also joins this division of the postcava. Each pair of lumbar veins may open into the postcava either as single vessels or by means of a common trunk. The internal spermatic veins (V. sp. i.) open into the postcava slightly caudad of a point midway between the renal and external iliac veins, the vein of the right side being slightly cranial to the left.

In all marsupials hitherto examined, with the possible exception of *Petaurus taguanoides* (Hochstetter, 93), the postrenal division of the postcava lies ventral to the aorta and, in this respect, forms an exception to the conditions met with in other mammals in which a single postcava is normally present. This unique position assumed by the postcava in marsupials was apparently first observed by Owen in 1866 in the wombat and kangaroo, although it is due to Hochstetter's more recent investigations that it may be regarded as characteristic of the marsupials in general.

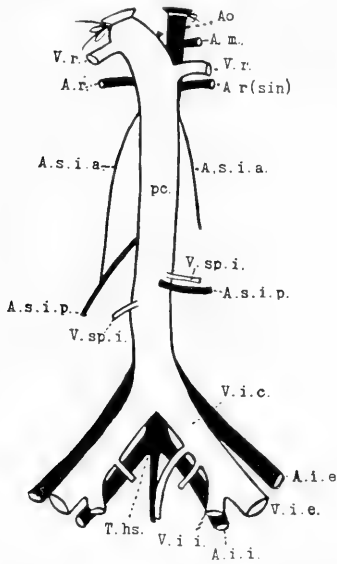


FIG. VI. Postrenal division of the postcava of *Petrogale* (spec.?). Ventral view.

A.i.e., A. iliaca externa; A.i.i., A. iliaca interna; A.m., A. mesenterica; Ao., aorta; A.r., A. renalis; A.s.i.a., A. spermatica interna anterior; A.s.i.p., A. spermatica interna posterior; pc., postcava; T.hs., Truncus hypogastricosacralis; V.i.e., V. iliaca externa; V.i.i., V. iliaca interna; V.r., V. renalis; V.sp.i., V. spermatica interna.

renalis (A. r.) the postcava was situated in the middle line and ventral to the aorta (Ao.). In *Petrogale* the Vv. spermaticæ internæ (V. sp. i.) opened into the postcava, as in *Didelphys*, slightly caudad of a point midway between the Vv. renales (V. r.) and the Vv. iliacæ communes (V. i. c.). In the wombat, however, the spermatic veins opened into the postcava slightly caudad of the renal veins.¹³ Whether this connection,

¹³In the wombat the spermatic arteries also arose in the neighborhood of the kidneys.

In its position, ventral to the aorta, the postrenal division of the postcava of *Didelphys marsupialis* agrees with that of other marsupials. It differs from these, however, in one particular feature, namely, in the variable manner in which its posterior tributaries (Vv. iliacæ) unite to form the postcava.

In order to understand these remarkable variations in *Didelphys* it will be necessary first to consider the anatomy of the postrenal division of the postcava in other marsupials where, so far as known to the writer, its mode of origin is uniform.

In a wombat (*Phascolomys mitchelli*) and a wallaby [*Petrogale* (spec.?)] recently dissected by the writer the postcava was formed, in each animal, through a union of the Vv. iliacæ communes (V. i. c. in Text Fig. VI), which took place ventral to the arteries. Also, in each animal, between the Truncus hypogastricosacralis (T. hs.) and the A.

so far craniad, is the usual method in the wombat can only be determined through further investigation. At any rate in *Didelphys* and other marsupials thus far examined, including the wombat (Hochstetter, 93), the internal spermatic veins open into the postcava at about the same level as that figured for *Petrogale*.

In the wombat the renal and spermatic veins anastomose with each other, on both sides, by means of a vessel which follows the ureter.¹⁴ In *Didelphys* a similar anastomosis was met with, and in well injected animals the anastomotic vessel could be distinctly traced caudad of the spermatic veins as far as the neck of the bladder. Hochstetter, 93, with the exception of its extension to the bladder, was the first to observe the presence of this anastomosis in marsupials. He has also figured the same as occurring in an edentate, *Dasypus novemcinctus* (93, Taf. 23, Fig. 25).

The above description of the postcaval vein in *Petrogale* and *Phascologomys*, with the possible exception of the spermatic veins, agrees in all essential details with the findings of Hochstetter and others who have examined this vein in a number of marsupials.

Following is a list of marsupials, known to the writer, in which the postrenal division of the postcava has been described, and in which it has been found to be similar in all respects to that of *Petrogale*:

Family—MACROPODIDÆ.

Halmaturus giganteus (OWEN and HOCHSTETTER); *Halmaturus bennetti* and *Hyppiprymnus* (spec.?) (HOCHSTETTER); *Macropus rufus* (WINDLE and PARSONS) and *Petrogale penicillata* (WINDLE and PARSONS).

Family—PHALANGERIDÆ.

Phascologomys wombat (OWEN and HOCHSTETTER); *Phalangerista vulpina*, *Belideus ariel* and *Cuscus* (HOCHSTETTER).

Family—DASYURIDÆ.

Phascogale penicillata (HOCHSTETTER).

Family—DIDELPHYIDÆ.

Didelphys lanigera and *Didelphys pusilla* (HOCHSTETTER).

From what has been stated above it is evident that the postcaval vein is formed in a variety of marsupials in a definite and uniform manner and that its variations when occurring represent, as in other mammals, exceptions to the general rule. In *Didelphys marsupialis*, however, the

¹⁴This anastomosis is undoubtedly present in *Petrogale*; the vessels, however, were not injected in the animal examined by the writer.

case is quite different. Here instead of occurring as exceptions the variations appear to be the rule, so that it is actually impossible in this animal to assign any one mode of origin for the postcava that may be regarded as characteristic of the species. This opinion was first advanced by the writer in a preliminary article in 1900, but on the basis of less extensive observations.

For descriptive purposes the various modes of origin of the postcava in *Didelphys marsupialis* have been classified by the writer under three *Types* as follows:

Type I.—Those cases in which the Vv. iliaca internæ unite with the Vv. iliaca externæ to form the postcava,¹⁵ *ventral* to the Aa. iliaca communes or *ventral* to the aorta.

Type II.—Those cases in which the Vv. iliaca internæ unite with the Vv. iliaca externæ to form the postcava, *dorsal* to the Aa. iliaca communes or *dorsal* to the aorta.

Type III.—Those cases in which the Vv. iliaca internæ unite with the Vv. iliaca externæ to form the postcava, both *dorsal* and *ventral* to the Aa. iliaca communes or both *dorsal* and *ventral* to the aorta.

So many variations of this last Type were met with that a further subdivision of Type III was found necessary, as follows:

Type III, A.—Includes those cases in which the principal union between the Vv. iliaca internæ and externæ takes place *ventral* to the arteries in question.

Type III, B.—Includes those cases in which the principal union between the Vv. iliaca internæ and externæ takes place *dorsal* to the arteries in question.

Type III, C.—Includes those cases in which the above mentioned *dorsal* and *ventral* unions are about *subequally* developed.

One hundred and one (101) opossums were examined and, in all but two, the different variations presented by their postcaval veins could be classed under the above mentioned three Types. In these two individuals, however, the postcava neither in its position, with respect to the aorta, nor in its mode of formation, conformed to the marsupial type but rather to the type of postcava which is characteristic of the higher mammals.

The following table shows the distribution of the above mentioned Types among ninety-nine individuals (34 males and 65 females):

¹⁵ When the postcava is bifurcated, in this as well as in the following Types, it is the common iliac veins that are formed instead of the postcava.

Type.	♀	♂	Total.
Type I.....	11	18	29
Type II.....	9	18	27
Type III.....			
A.....	3	5	8
B.....	9	15	24
C.....	2	9	11
Total.....	34	65	99

With the exception of eleven individuals which were about half-grown, the above observations were made upon adults. The variations observed in the half-grown opossums were in all respects similar to those of the adult, and I may state here that the Type of postcava which will be found in the adult is already indicated in the embryo at the time of its birth. Of the three main Types of variations the third easily predominates, while there is not much difference between the first and second. The table, likewise, does not show any marked distribution of the Types among either sex, so I think it may be stated with certainty that no relation exists between sex or age and any particular Type of postcava.

From a study of their development the writer is now able to account for these variations by showing that they are modifications of a "ground plan" arrangement which is common to the veins in the embryo. This question has already been dealt with in a preliminary paper, 02, and will be more fully treated in a subsequent paper on the development of the veins.

THE VARIATIONS IN THE MODE OF ORIGIN OF THE POSTCAVA IN
Didelphys Marsupialis.

Type I.—Includes those cases in which the Vv. iliaca internæ unite with the Vv. iliaca externæ to form the postcava, *ventral* to the Aa. iliaca communes or *ventral* to the aorta.

Twenty-nine examples of this Type were met with distributed among eleven males and eighteen females.

See Figs. 1, 2, 3 and 4 (ventral views) and Fig. 5 (dorsal view), Plate I.

The representatives of Type I more closely approach the conditions

found in *Petrogale* and other marsupials than those of any of the other Types. In each case the affluent veins of the postcava unite to form the latter on the ventral surfaces of the arteries, but the manner in which the union takes place is not the same. In *Petrogale*, etc., two Vv. iliaca communes unite to form the postcava (Text. Fig. VI), while in *Didelphys* it is usually formed through the union of a V. iliaca interna communis with one (Fig. 4) or both (Figs. 2 and 3) of the Vv. iliaca externae.

It is worthy of notice in this connection that in *Petrogale*, etc., a Truncus hypogastricosacralis¹⁶ and two Vv. iliaca communes are the rule, while in Type I the reverse conditions usually prevail, namely, a V. hypogastricosacralis and two Aa. iliaca communes.

One of the most interesting as well as remarkable features of this and all of the other Types is the number of variations that occur within the Type. Figs. 1, 2, 3 and 4 represent the most common of the variations that were met with under Type I, but by no means include them all.¹⁷

Type II.—Includes those cases in which the Vv. iliaca internae unite with the Vv. iliaca externae to form the postcava, *dorsal* to the Aa. iliaca communes or *dorsal* to the aorta.

Twenty-seven examples of this Type were met with distributed among nine males and eighteen females.

See Figs. 6, 7, 8, 9 and 10 (ventral views), Plate II.

Two principal sets of variations were met with within this Type:

First, in which the internal iliac veins join both the right and left external iliac veins to form common iliac veins. In this set of variations the internal iliac veins may (Figs. 6 and 7) or may not (Fig. 8) anastomose with each other ventral to the A. sacralis media before joining the external iliac veins. The internal iliac veins may also, at the point where they join the external iliac veins, be subequal (Figs. 6 and 8) or very unequal (Fig. 7) in calibre. In the latter case (Fig. 7) the blood from the internal iliac veins is returned to the postcava chiefly through the right common iliac vein.

Second, as in Figs. 9 and 10, in which the internal iliac veins anastomose with each other ventral to the A. sacralis media and then open by

¹⁶In the wombat dissected by the writer, two common iliac arteries instead of a Truncus hypogastricosacralis were present.

¹⁷In a few individuals examined (Fig. 3) the spermatic artery (A.s.i.p.) arose by a single trunk from the right side of the aorta and soon divided into three branches. Two of these ran to the ovaries in the usual manner. The third, however, extended caudad on the ventral surface of the postcava and then divided, on each side, into two branches which ran respectively to the psoas muscle (ps.) and the bladder (bl.) The last mentioned branch followed the ureter.

means of a single vessel (*V. iliaca interna communis*) into either the left (Fig. 9) or into the right (Fig. 10) external iliac vein. In the adult, an extraordinary similarity exists between the postcava in *Echidna aculeata* and Type II in *Didelphys*. Compare Hochstetter's Fig. 16 (96, Taf. 28) of this vein in *Echidna* with my Fig. 6 of *Didelphys*.

Type III.—This Type is a combination of Types I and II, since it includes those cases in which the *Vv. iliacæ internæ* unite with the *Vv. iliacæ externæ* to form the postcava, both *dorsal* and *ventral* to the *Aa. iliacæ communes* or both *dorsal* and *ventral* to the aorta.

Including the three subdivisions, A, B and C, forty-three examples of this Type were met with distributed among fourteen males and twenty-nine females.

As shown by the above table, the representatives of this Type constitute about 43 per cent of the variations observed, which is almost twice that of either of the other Types. Considering the composite character of Type III, however, it is evident that this predominance possesses no particular significance beyond the fact that the veins that lie *dorsal* and *ventral* to the umbilical arteries in the embryo, both possess a marked tendency to persist in the adult.

Type III, A.—Includes those cases in which the *principal* union between the *Vv. iliacæ internæ* and *externæ* takes place *ventral* to the arteries in question.

Eight examples of Type III, A, were met with distributed among three males and five females.

See Figs. 11, 12 and 13 (dorsal views) and Fig. 14 (ventral view of Fig. 13), Plate III.

Two sets of variations within this Type were met with:

First, as in Figs. 11 and 12 (dorsal), in which the internal iliac veins anastomose with the external iliac veins ventral to the arteries, as in Type I (Fig. 1), and, in addition to this, by means of a *single small vessel* which lies *dorsal* to the left common iliac artery. In one individual the caudal vein opened into this dorsal anastomosis (Fig. 12, dorsal view).

Second, as in Figs. 13 and 14, in which the internal iliac veins anastomose ventral to the *A. sacralis media* (Fig. 14) and then join the external iliac veins to form the postcava by means of *four vessels*, two of which, the largest, lie ventral (Fig. 14), while the other two lie dorsal (Fig. 13) to the common iliac arteries.

Type III, B, includes those cases in which the principal

union between the Vv. iliaca internæ and externæ takes place *dorsal* to the arteries in question.

Twenty-four examples of Type III, B, were met with distributed among nine males and fifteen females.

See Figs. 15, 16, 17, 18, 19, 20, 21, and 22 (ventral views), Plate IV.

Three sets of variations were met with within this Type:

First, as in Figs. 15, 16, 17, 18, and 19, in which the internal iliac veins unite with the external iliac veins to form the postcava (in this case the common iliac veins), by means of *three* vessels, two of which, the largest, lie dorsal, and one, the smallest, lies ventral to the common iliac arteries.

In Figs. 15 and 16 the internal iliac veins do not anastomose ventral to the A. sacralis media, and the small vessel which lies ventral to the common iliac artery extends between the right (Fig. 15) or left (Fig. 16) internal iliac vein and the common iliac vein of the opposite side. In Fig. 17 the postcava is formed in essentially the same manner as in Figs. 15 and 16, with the exception that the small vessel which lies ventral to the common iliac artery extends, in Fig. 17, between the iliac veins of the same instead of opposite sides. This is a most interesting variation since it represents the persistence, on one side, of the venous ring through which the umbilical artery passes in the embryo (McClure, 02). In Fig. 18 the internal iliac veins anastomose ventral to the A. sacralis media, but in every other respect this variation is similar to that represented by Fig. 16. In Fig. 19 the conditions are the same as in Fig. 18 except that in Fig. 19 the small vessel which lies ventral to the common iliac artery has changed its position with respect to the iliac veins as the result of a fusion of the common iliac veins.

Second, as in Fig. 20, in which the internal iliac veins anastomose ventral to the A. sacralis media and then unite with the external iliac veins to form the postcava by means of *three* vessels, two of which, one large and one small, lie dorsal, while one, quite large, lies ventral to the common iliac arteries. This variation differs from the first set only in the circumstance that the single vessel which lies ventral to the common iliac artery is as large as the largest of the two vessels which lie dorsal to this artery.

Third, as in Figs. 21 and 22, in which the internal iliac veins anastomose ventral to the A. sacralis media and then join the external iliac veins to form the postcava (or common iliac veins) by means of *two* vessels. The larger of these two vessels, which lies dorsal to the common iliac artery, may join the right (Fig. 21) or left (Fig. 22) external iliac vein, while the smaller vessel, which lies ventral to the common iliac artery, then joins the external iliac vein of the opposite side.

Type III, C, includes those cases in which the above mentioned dorsal and ventral union are *subequally* developed.

Eleven examples of this Type were met with distributed among two males and nine females.

See Figs. 23, 24 (ventral views) and 25 (dorsal view), Plate V.

Two sets of variations were met with within this Type:

First, as in Figs. 23 and 24, in which the two internal iliac veins anastomose ventral to the A. sacralis media and join the external iliacs by means of two vessels, subequal in size, which lie respectively dorsal and ventral to the common iliac arteries of opposite sides. In Fig. 23 the ventral vessel joins the right, while in Fig. 24 it joins the left external iliac vein.

Second, as in Fig. 25 (dorsal view), in which the two internal iliac veins, without previously anastomosing ventral to the A. sacralis media, join the external iliac vein of the right side by means of two vessels, subequal in size, which lie, respectively, dorsal and ventral to the common iliac artery of the right side.

TWO POSTCAVAL VARIATIONS WHICH CANNOT BE CLASSED UNDER THE ABOVE THREE TYPES.

In addition to the variations already described in connection with the three Types, two others were met with which differ so widely from them in certain fundamental characters that they need a special description.

The main features which characterize these two cases and distinguish them from the variations described under the three Types are twofold: (1) All of the posterior tributaries of the postcava unite to form this vessel, as in the higher mammals, dorsal to the arteries; (2) the postcava lies to the left of the aorta instead of upon its ventral surface as in the other cases (Text Figs. VII and VIII).

The position of the ureters in these two cases was normal in every respect.

The postcava in these two abnormalities resembles in every detail that of a higher mammal in which the left instead of the right postcardinal vein persists caudal to the kidneys.¹⁵

The two abnormalities differ from each other only in the manner in which the internal iliac veins (V. i. i.) unite with the external iliacs

¹⁵The conditions represented by Text Fig. VII are identical to those found in the cat when the left instead of the right postcardinal vein persists as the caudal end of the postcava.

(V. i. e.). In Text Fig. VII the internal iliac veins (V. i. i.), after anastomosing with each other ventral to the A. sacralis media (A. s. m.), join the external iliac of the left side (V. i. e.) by means of a common internal iliac vein. In Text Fig. VIII the postcava is partially bifurcated and each internal iliac vein (V. i. i.) unites with the external iliac (V. i. e.) of its own side to form a common iliac vein (V. i. c.) without previously anastomosing with the vein of the opposite side, ventral to the A. sacralis media.

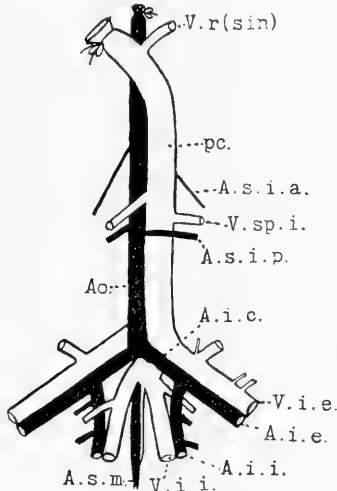


FIG. VII.

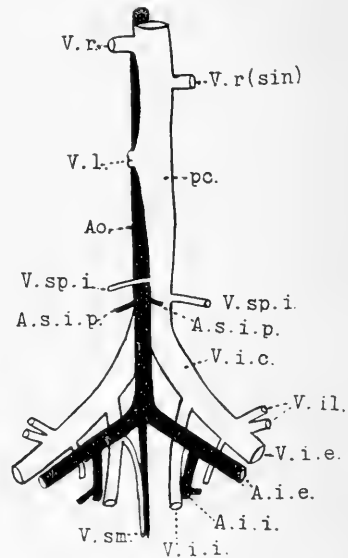


FIG. VIII.

FIGS. VII and VIII. Two abnormalities of the postrenal division of the postcava of *Didelphys marsupialis*. Ventral views.

A. i. c., A. iliaca communis; A. i. e., A. iliaca externa; A. i. i., A. iliaca interna; Ao., Aorta; A. s. i. a., A. spermatica interna anterior; A. s. i. p., A. spermatica interna posterior; A. s. m., A. sacralis media; pc., postcava; V. i. c., V. iliaca communis; V. i. e., V. iliaca externa; V. i. i., V. iliaca interna; V. il., V. iliolumbalis; V. r., V. renalis; V. s. m., V. sacralis media; V. sp. i., V. spermatica interna.

In view of the circumstance that variations in the mode of origin of the postcava are not exceptional but are the rule in *Didelphys*, and that these two particular cases differ fundamentally from the usual Types of variation, they must be regarded as the only genuine abnormalities that were met with among the one hundred and one opossums examined.

An explanation of the development of these two abnormalities will be deferred until the second part of this paper. It appears to the writer as worthy of mention, however, that the morphological explanation of these two abnormalities may be the same as that which accounts for the

presence of a postcava in *Petaurus taguanoides* which is similar to that of a higher mammal, as well as for the presence of an allantoic placenta in *Perameles*.

In addition to the above, another abnormality was met with which, although relating to the arterial system, is quite as remarkable.

As is well known, the posterior mesenteric artery is wanting in all marsupials which have thus far been examined, its place being taken by a branch of the anterior mesenteric artery (*Petrogale*) or by a branch of the A. cœliacomesenterica (*Didelphys*) as the case may be. Among the one hundred and one opossums examined by the writer one was met with in which a large posterior mesenteric artery was present, which took the place of the usual posterior mesenteric branch of the A. cœliacomesenterica. In this animal the posterior mesenteric artery (A. m. p.) was given off from the caudal end of the aorta and passed ventrad through a foramen (F.) in the postcaval vein (Text Fig. IX). In its point of origin from the aorta as well as in its distribution to the intestines this artery agreed in all respects with the posterior mesenteric arteries of other mammals. In addition to its branches to the intestines it also gave off as branches, after passing through the foramen, the two posterior internal spermatic arteries (A. s. i. p.) which were distributed to the ovaries in the usual manner.¹⁹

Owen, 66, has stated that the absence of the posterior mesenteric artery in marsupials is probably related to the simplicity of the mesenteric

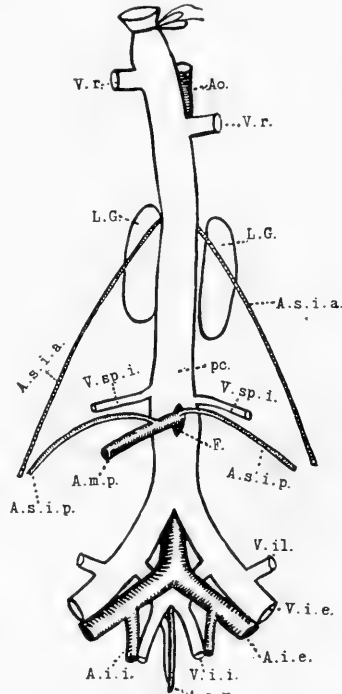


FIG. IX. Postrenal division of postcava of *Didelphys marsupialis* in which a foramen is present through which a posterior mesenteric artery passes.

A. i. e., A. iliaca externa; A. m. p., A. mesenterica posterior; Ao., Aorta; A. s. i. a., A. spermatica interna anterior; A. s. i. p., A. spermatica interna posterior; F., foramen; L. G., lymph gland; pc., postcava; V. i. e., V. iliaca externa; V. i. i., V. iliaca interna; V. il., V. iliolumbalis; V. r., V. renalis; V. sp. i., V. spermatica interna.

¹⁹ In a preliminary paper, oo, the writer mentioned the circumstance that two pairs of internal spermatic arteries may spring from the aorta in *Didelphys*. It may be stated here that these two pairs of arteries occur with great regularity in *Didelphys* and that they were also present in the specimen of *Petrogale* recently dissected by the

in any of the opossums examined. When the postcava was bifurcated as far cranial as the internal spermatic veins one or both of the posterior internal spermatic arteries passed ventrad between the two veins (Figs. 2, 6, 7, 8, 17 and 21, Plates I, II and IV).

In five opossums (3 males and 2 females) the postcava was only partially bifurcated caudad of the internal spermatic veins, as in Figs. 18 and 25, Plates IV and V).

In nine opossums (1 male and 8 females), as in Figs. 10 and 15, Plates II and IV), a foramen was present in the postcava at the level of the internal spermatic veins through which the posterior internal spermatic arteries passed, and the fusion between the caudal ends of the postcaval veins was incomplete. In one case a posterior mesenteric artery passed through the foramen instead of the spermatic arteries (Text Fig. IX).

In seven opossums (2 males and 5 females) there were no indications of a previous bifurcation except for the presence of a foramen in the postcava, which was situated at the level of the internal spermatic veins, and through which one or both of the posterior internal spermatic arteries passed (Figs. 16 and 20, Plate IV).

In the specimen of *Petrogale* examined by the writer the left posterior internal spermatic artery (A. s. i. p.) also passed through a foramen in the postcava which, as in *Didelphys*, was situated at the level of the internal spermatic veins (V. sp. i.) (Text Fig. VI).

THE RELATIONS WHICH EXIST BETWEEN THE DIFFERENT TYPES OF VARIATIONS AND THE PRESENCE OF A BIFURCATED POSTCAVA.

As shown by the table, the postcava in the adult was most frequently bifurcated or presented indications of a previous bifurcation, in those animals in which the internal iliac veins make their principal union with the external iliacs to form the postcava by means of vessels which lie dorsal to the common iliac arteries. Thus under Type II, in which the union between the internal and external iliac veins takes place exclusively dorsal to the arteries, twenty cases were met with, and under Type III, B, in which the anastomosis ventral to the arteries is insignificant in character, twelve cases were met with in which the postcava was either bifurcated or presented some indication of a previous bifurcation. Under Type III, C, in which the vessel which lies ventral does not exceed in size that which lies dorsal to the iliac arteries, six cases were met with in which the postcaval veins were incompletely fused caudal to the internal spermatic veins.

Under Types I and III, A, in which the postcava is formed either

entirely or for the most part by vessels which unite ventral to the common iliac arteries, only four cases were met with in which it was bifurcated or presented indications of an incomplete fusion.

It appears from the above statistics that we have grounds for assuming that the presence of a double postcava in the adult *Didelphys* is in some way related to the manner in which the internal iliac veins unite with the external iliacs to form the postcava, since ninety per cent (90%) of the observed cases in which the postcava was bifurcated or presented indications of a previous bifurcation, occurred under Types II, III, B, and III, C, in which the anastomosis between the iliac veins ventral to the iliac arteries is either wanting, or does not exceed in size that which is situated *dorsal* to the iliac arteries.

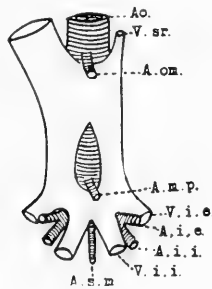


FIG. X.

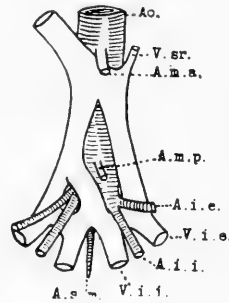


FIG. XI.

FIG. X. Postcava of *Echidna* embryo No. 44. Ventral view. After Hochstetter.
 FIG. XI. Postcava of *Echidna* embryo No. 45. Ventral view. After Hochstetter.
 A. i. e., A. iliaca externa; A. i. i., A. iliaca interna; A. m. a., A. mesenterica anterior;
 A. m. p., A. mesenterica posterior; Ao., Aorta; A. om., A. omphalomesenterica; V. i. e.,
 V. iliaca externa; V. i. i., V. iliaca interna; V. sr., V. suprarenalis.

If this relationship can be definitely established for *Didelphys*, through further investigation, it would seem to account for the presence of the bifurcated postcava in the adult of *Echidna aculeata*, since this condition in *Echidna* is reached through exactly the same venous transformations as those which have apparently produced the bifurcated condition in *Didelphys*, as can be seen from the following brief account of the development of the postcava in *Echidna*.

Hochstetter, 96, who has studied the development of the postcaval vein in *Echidna aculeata*, finds that, at an early stage, it consists, caudal to the liver, of an unpaired and a paired portion. In a young embryo (No. 44, Text Fig. X), the unpaired portion extends from the liver, on the right side of the A. omphalomesenterica (A. o. m.), to a point somewhat caudad of this artery. From this point the two postcaval veins

(paired portion) extend caudad, at first lying ventral to and then on either side of the aorta, and caudal to the A. mesenterica posterior (A. m. p.) anastomose with each other ventral to the aorta. The two internal iliac veins (V. i. i.) which, as Hochstetter says, must be regarded as continuations of the postcaval veins now open into this anastomosis ventral to the common iliac arteries.

In the older embryo (No. 45, Text Fig. XI), the unpaired portion of the postcava possesses the same relations as in embryo No. 44. In the paired portion, however, important changes have taken place. Here the anastomosis between the two postcaval veins caudal to the posterior mesenteric artery (A. m. p.) no longer exists, and the postcava is now formed as in Type III, B, of *Didelphys* (Fig. 18, Plate IV), in which the internal iliac veins (V. i. i.) anastomose ventral to the A. sacralis media (A. s. m.) and unite with the external iliacs (V. i. e.) to form the postcava by means of three vessels two of which lie dorsal and one ventral to the iliac arteries. The transformation of this stage into the adult condition takes place through the atrophy of the vessel which lies ventral to the iliac arteries. The result is that a postcava is formed in *Echidna* similar to that of Type II in *Didelphys*, in which the internal iliac veins join the external iliacs dorsal to the common iliac arteries, which is also the Type in *Didelphys* in which the postcava was found to be most frequently bifurcated.

THE V. PUDENDOVESICALIS.

The V. pudendovesicalis (V. p. v. in Figs. 1, 8 and 23, Plates I, II and V) of *Didelphys*, which returns blood from the bladder and external genital organs, apparently has no regular method of opening into the iliac veins. The remarkable variations presented by these veins will not be further considered here, however, as they have already been fully described by the writer in a former paper (McClure, oo, p. 457) to which the reader is referred.

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EXPLANATION OF PLATES.

All of the Figures on Plates I to V are life sized drawings of the caudal end of the postcava of *Didelphys marsupialis* and illustrate the variable manner in which the postcava is formed in this animal. With the exception of Fig. 23 only that portion of the postcava is represented which lies caudal to the Vv. spermaticae internae. In Fig. 23 the entire “postrenal division” of the postcava is represented. The names of all the vessels are indicated on three Figures (Fig. 1, Type I; Fig. 8, Type II, and Fig. 23, Type III, C, which can be used in identifying the vessels in the other Figs. Fig. 3 is only partially lettered).

The following abbreviations apply to the lettering on Figs. 1, 3, 8 and 23: (d and s refer to dextra and sinistra, respectively).

A. i. c., A. iliaca communis.

A. i. e., A. iliaca externa.

A. i. i., A. iliaca interna.

Ao., Aorta.

A. s. i. a., A. spermatica interna anterior.

- A. s. i. p., A. spermatica interna posterior.
 A. s. m., A. sacralis media.
 bl., Accessory branch of the A. spermatica interna posterior to the bladder.
 Pc., Postcava.
 P. R., Postrenal Division of Postcava.
 ps., Accessory branch of the A. spermatica interna posterior to the psoas muscle.
 V. i. c., V. iliaca communis.
 V. i. e., V. iliaca externa.
 V. i. i., V. iliaca interna.
 V. i. i. c., V. iliaca interna communis.
 V. i. l., V. iliolumbalis.
 V. p. v., V. pudendovesicalis.
 V. r., V. renalis.
 V. s. m., V. sacralis media.
 V. sp. i., V. spermatica interna.

PLATE I.—TYPE I.

- FIG. 1. Ventral view (♂).
 FIG. 2. Ventral view (♀). Postcava bifurcated caudad of V. spermatica interna sinistra.
 FIG. 3. Ventral view (♀). An accessory branch of the A. spermatica interna posterior (A. s. i. p.) is represented in this Fig. which supplies the psoas muscle (ps.) and bladder (bl.).
 FIG. 4. Ventral view (♂). An anastomosis is present on the right side between the V. spermatica interna and the V. pudendovesicalis.
 FIG. 5. Dorsal view (♀).

PLATE II.—TYPE II.

- FIG. 6. Ventral view (♂). Postcava bifurcated caudad of Vv. spermaticae. Postcava formed here as in *Echidna aculeata*.
 FIG. 7. Ventral view (♀). Postcava bifurcated caudad of Vv. spermaticae internae.
 FIG. 8. Ventral view (♂). Postcava bifurcated caudad of Vv. spermaticae internae.
 FIG. 9. Ventral view (♀).
 FIG. 10. Ventral view (♂). Foramen in postcava through which the Aa. spermaticae internae posteriores pass. Postcava partially bifurcated at its caudal end. On account of the variable character of the V. pudendovesicalis this vein which is connected, on the right side, with the V. iliaca externa and the V. iliaca interna communis has not been regarded as entering into the formation of the postcava.

PLATE III.—TYPE III, A.

- FIG. 11. Dorsal view (♀).
 FIG. 12. Dorsal view (♂).
 FIG. 13. Dorsal view of Fig. 14.
 FIG. 14. Ventral view (♂).

PLATE IV.—TYPE III, B.

- FIG. 15. Ventral view (♀). Aa. spermaticae internae posteriores pass through a foramen in postcava.
 FIG. 16. Ventral view (♀). Aa. spermaticae internae posteriores pass through foramen in postcava.
 FIG. 17. Ventral view (♀). Postcava bifurcated caudad of Vv. spermaticae internae. Remains of venous ring through which the umbilical artery passes in the embryo.
 FIG. 18. Ventral view (♀). Postcava partially bifurcated at its caudal end.
 FIG. 19. Ventral view (♂).
 FIG. 20. Ventral view (♂). Foramen in postcava through which the Aa. spermaticae internae posteriores pass.
 FIG. 21. Ventral view (♀). Postcava bifurcated.
 FIG. 22. Ventral view (♂).

PLATE V.—TYPE III, C.

- FIG. 23. Ventral view (♀). Postrenal division of postcava; also showing the two pairs of internal spermatic arteries (A. s. i. a. and A. s. i. p.).
 FIG. 24. Ventral view (♂).
 FIG. 25. Dorsal view (♀). Postcava partially bifurcated caudad of the Vv. spermaticae internae.

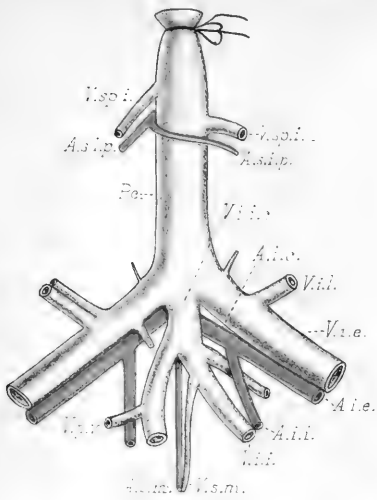


Fig. 1.

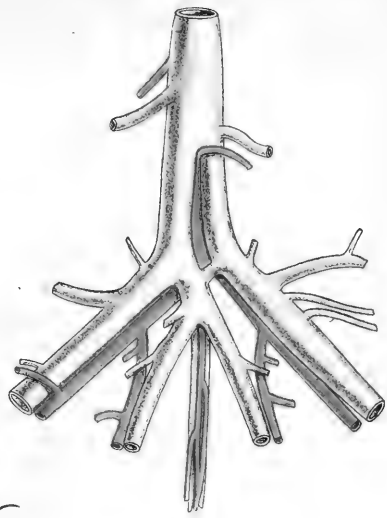


Fig. 2.

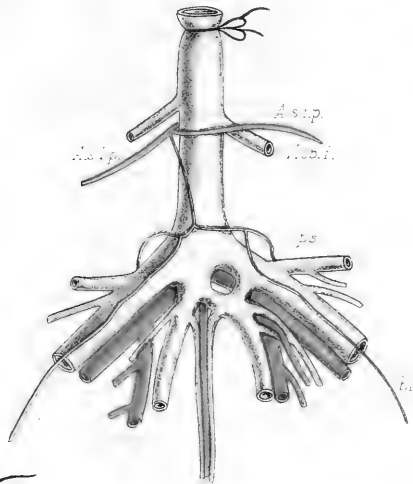


Fig. 3.

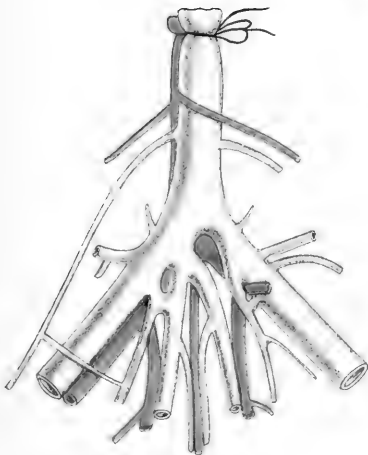


Fig. 4.

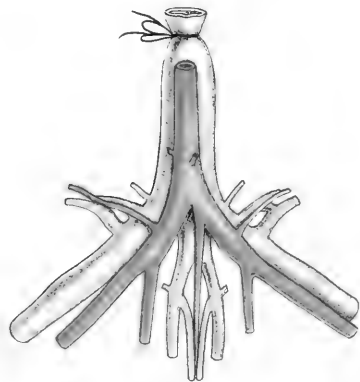


Fig. 5.

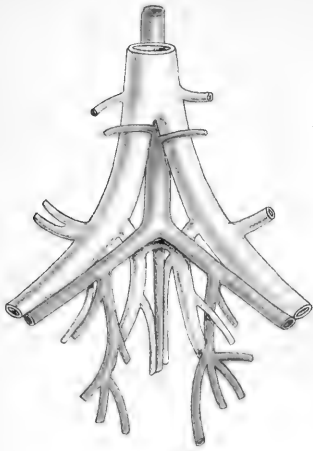


Fig. 6.

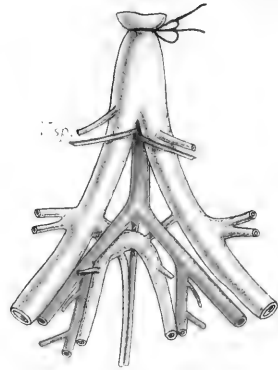


Fig. 7.

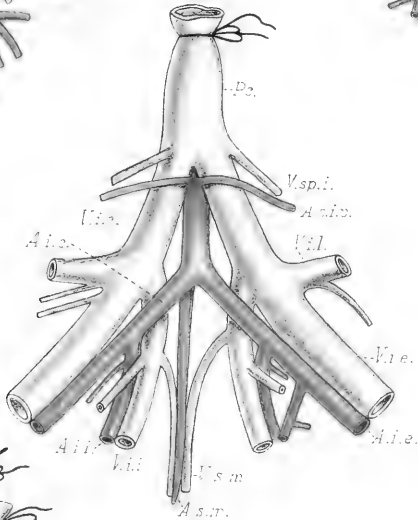


Fig. 8.

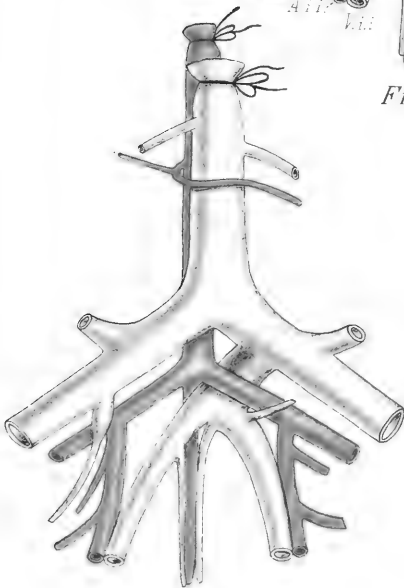


Fig. 9.

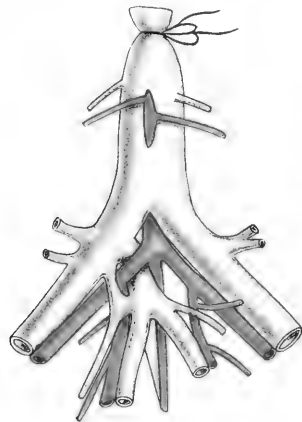


Fig. 10.

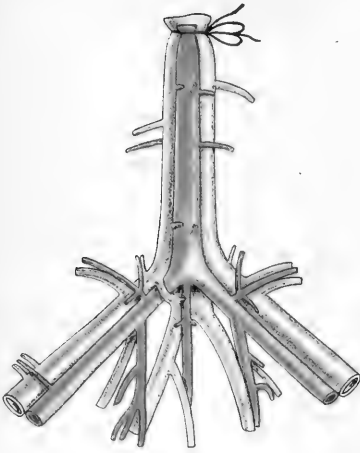


Fig. 11.

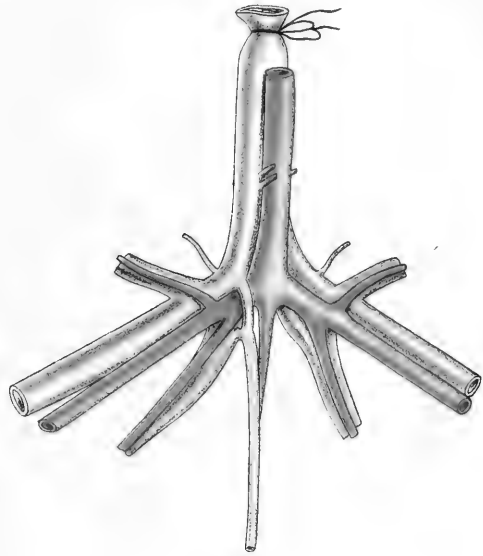


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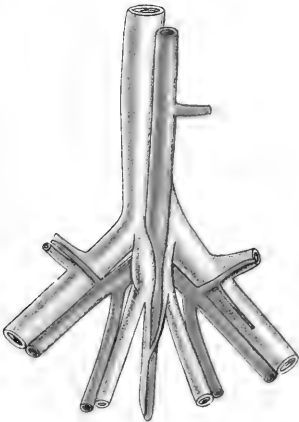


Fig. 13.

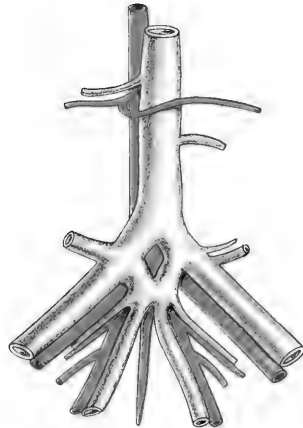


Fig. 14.

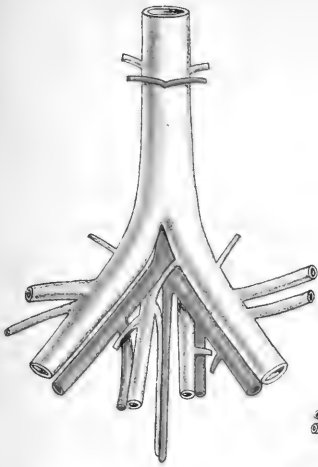


Fig. 15.

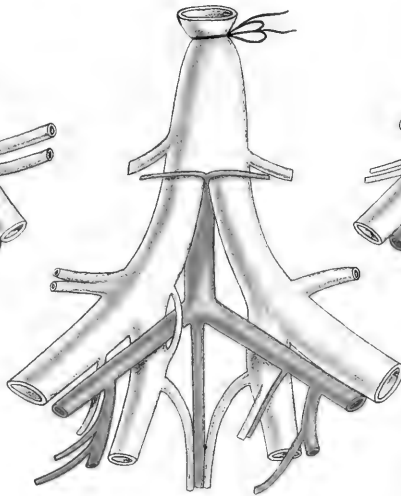


Fig. 17.

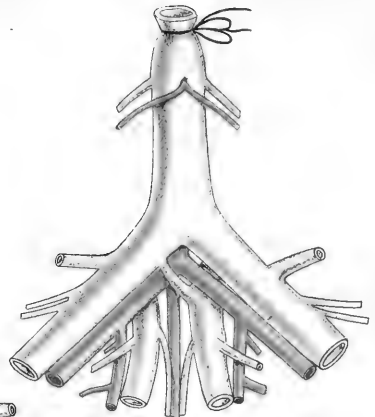


Fig. 16.

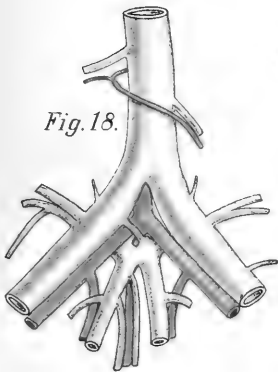


Fig. 18.

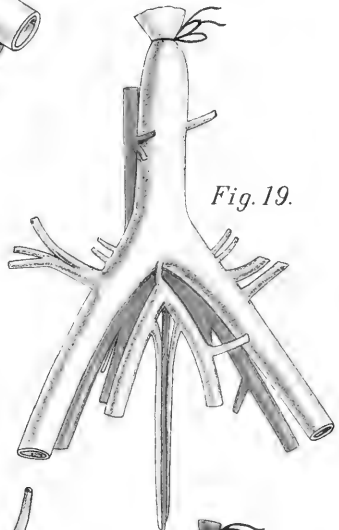


Fig. 19.

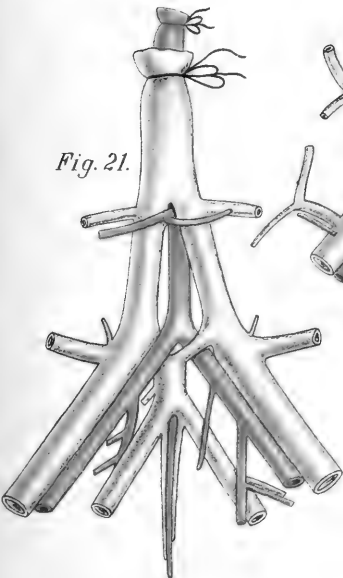


Fig. 21.

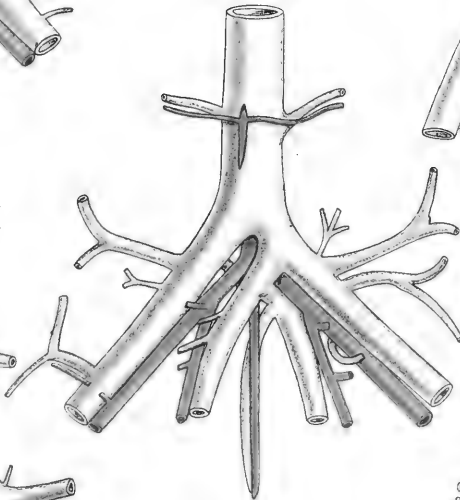


Fig. 20.

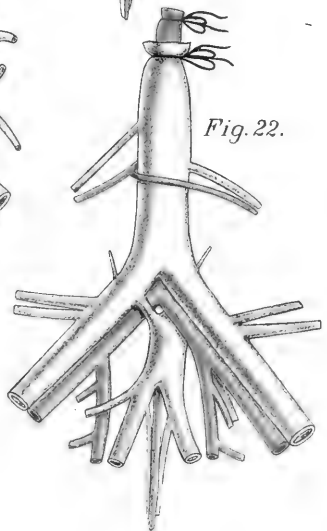


Fig. 22.



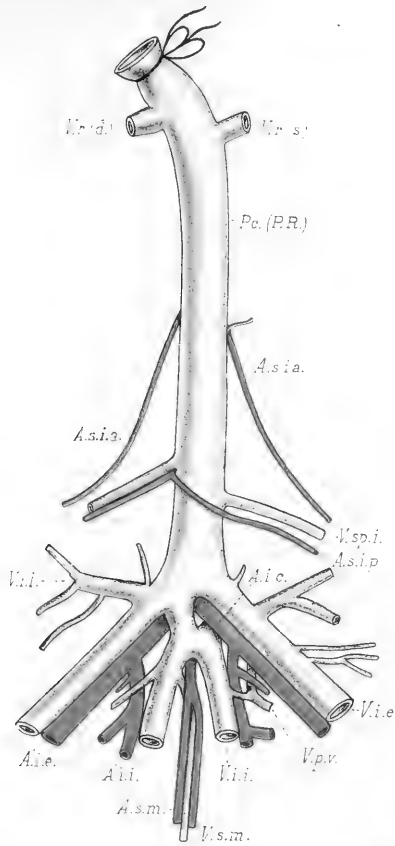


Fig. 23.

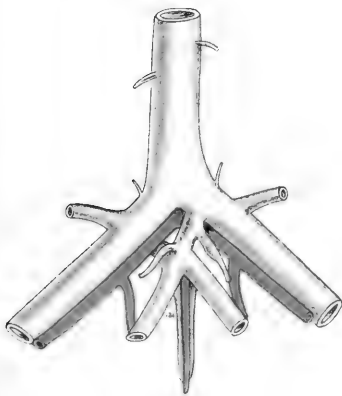


Fig. 24.

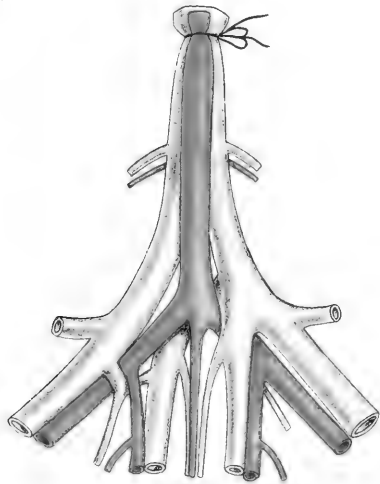


Fig. 25.

WANDERING PIGMENTED CELLS ARISING FROM THE
EPITHELIUM OF THE OPTIC CUP, WITH OBSERVA-
TIONS ON THE ORIGIN OF THE M. SPHINCTER PUPIL-
LAE IN THE CHICK.

BY

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Associate in Anatomy, Johns Hopkins University.

WITH 1 TABLE AND 15 TEXT FIGURES.

INTRODUCTION.

Nussbaum's¹ important discoveries of the origin of the M. sphincter pupillae in birds and mammals from the epithelium at the pupillary margin of the optic cup and of the origin of the retractor lentis muscle in fishes from the epithelium bordering on the choroid fissure are of deep significance. His discoveries have recently been confirmed by Szili,² who has traced carefully the development of the sphincter pupillae muscle in man from the epithelium about the pupillary margin of the optic cup. Herzog³ has also found a similar origin in a series of vertebrates. These authors have also studied the development of the dilator pupillae from the epithelial cells of the outer layer of the optic cup. The origin of the retractor lentis, the muscle of accommodation in fishes (*Salmo salar*), lead Professor Nussbaum to suspect that the ciliary muscle, the muscle of accommodation in higher vertebrates, might also be of epithelial origin. With this in view I attempted at the suggestion of Professor Nussbaum to determine if the ciliary muscle in the chick was of epithelial origin. It is a pleasure to express my thanks to Pro-

¹Nussbaum: Die Entwicklung der Binnenmuskeln des Auges der Wirbelthiere. *Archiv f. mik. Anat. u. Entwickl.* Bd. LVIII, 1901.

——— *Entwicklungsgeschichte des menschlichen Auges.* Graefe-Saemisch. 2. Aufl., 1. T., Bd. II.

²Szili: Zur Anatomie und Entwicklungsgeschichte der hinteren Irisschichten, mit besonderer Berücksichtigung des Musculus Sphincter Pupillae des Menschen. *Anat. Anz.*, Bd. XX, 1901.

——— Beitrag zur Kenntniss der Anatomie und Entwicklungsgeschichte der hinteren Irisschichten, etc. v. Graefe's Archiv für Ophthalmologie, Bd. LIII, 1902.

³Herzog: Ueber die Entwicklung der Binnenmuskulatur des Auges. *Archiv für mikroskopische Anatomie und Entwickl.* Bd. LX, 1902.

fessor Nussbaum for his kindness and the exceptional privileges extended to me at the Anatomical Laboratory of the University of Bonn.

Careful study of the ciliary region by means of complete serial sections of chicks from two and one-half days to the period of striation of the muscle at about twelve days failed to furnish any evidence of an epithelial origin for the ciliary muscle. I studied with great care the outer layer of the optic cup in the iris and ciliary regions and even lateral to the ciliary region and also with especial care the cleft region. Professor Nussbaum drew my attention to a peculiar condensation of the mesenchyme (*CH*, Fig. 1) along the cleft, which I found to appear during the fourth day and to disappear during the eighth day. It had no connection with the origin of the ciliary muscle, but may possibly serve to strengthen the optic cup at what might be considered its weak

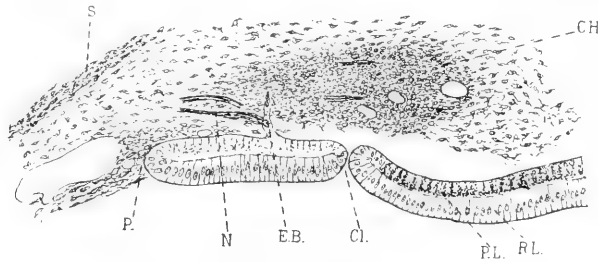


FIG. 1. Tangential section through the optic cup of a chick 6 days, 13 hours old. Magnified 130 diam. *Cl.*, cleft; *CH*, cleft heap; *E. B.*, epithelial bud; *N.*, nerve fibers; *P.*, pupillary margin; *P. L.*, pigment layer; *R. L.*, retinal layer.

place along the cleft. The ciliary muscle appears to develop *in situ* from mesenchyme. Herzog came to the same conclusion. Between the optic cup and the place in which the ciliary muscle develops there is a considerable area of very loose mesenchyme (see Fig. 2), and it would seem easy to detect any migration of epithelial cells across it into the ciliary region if such a migration occurred. While working over this question my attention was attracted by certain peculiar buddings of the outer or pigment layer of the optic cup. More careful study has convinced me that many if not all of the pigmented cells lying amongst the connective tissue cells of the iris and the region lateral to the iris are of epithelial origin, arising from the outer layer of the optic cup.

MATERIAL.

Chicks of various ages (see table, p. 411) were hardened in Flemming's solution and the anterior part of the eye cut into serial sections and stained in safranin. Others were hardened in Zenker's fluid and

stained in haematoxylin and congo red. The sections were cut either five or seven and one-half microns in thickness.

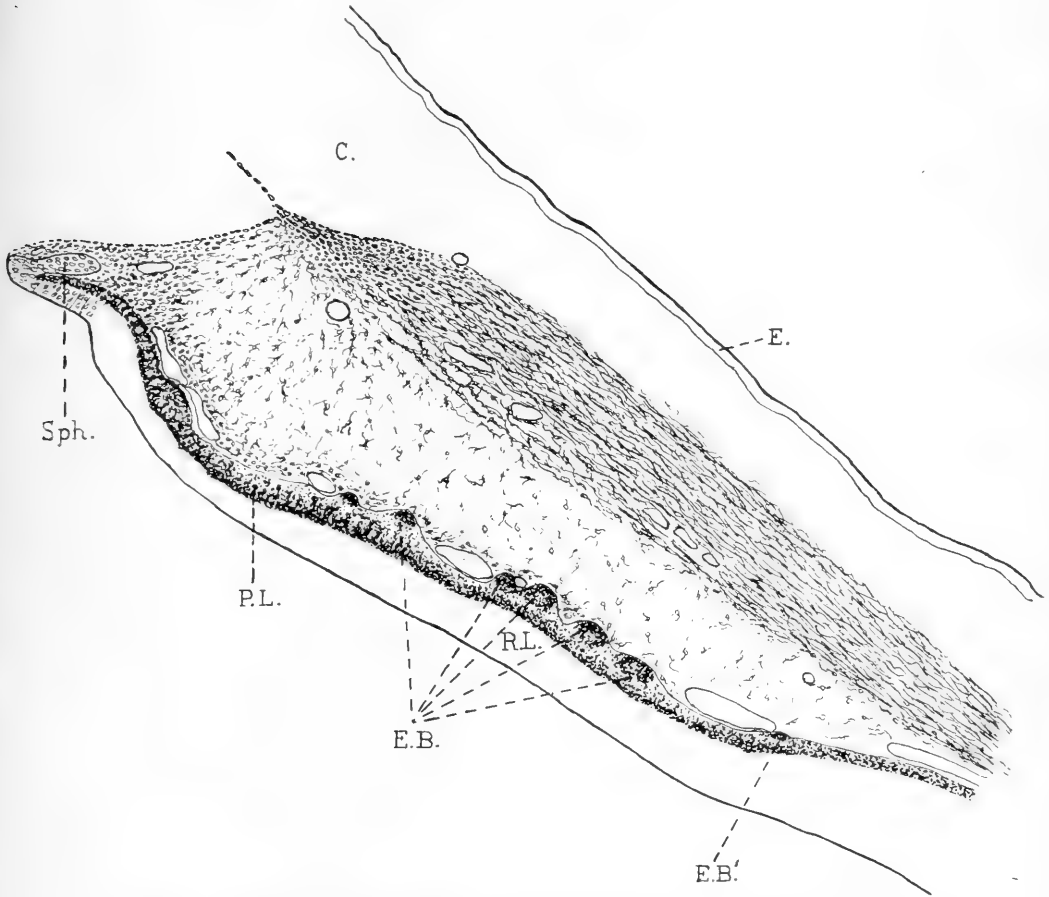


FIG. 2. Radial section through the optic cup of a chick 9 days, 19 hours old. Magnified 180 diam. *C.*, cornea; *E.*, ectoderm; *Sph.*, sphincter bud.

WANDERING PIGMENTED CELLS DERIVED FROM THE EPITHELIAL BUDS
OF THE PIGMENT LAYER OF THE OPTIC CUP.

The time at which the pigment and the wandering cells of the optic cup begin to appear varies considerably in different individuals, as does also the time of origin of the epithelial buds we are to especially consider. In a chick nine days and nineteen hours old (Fig. 2) the beginning of this budding process is clearly seen. Projecting from the outer surface of the pigment layer are numerous elevations, mostly in the region

between the iris and the ora serata. These elevations consist of epithelial cells containing nuclei and pigment granules. The pigment is similar in color, nearly black, to that in the pigment layer, but the granules are very close together and give the buds a darker appearance than the adjoining pigment layer. In this eye there were no buds much farther advanced than those seen in Fig. 2. There were but very few wandering pigment cells, occasionally one here and there, and their pigment was of the same color and character as that in the epithelial cells of the

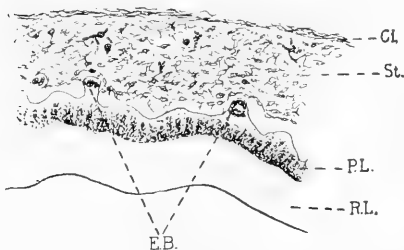


FIG. 3. Tangential section through the optic cup of a chick 10 days old. Mag. 130 dia. *Cl.*, edge of ciliary muscle anlage; *St.*, connective tissue.

optic cup. Fig. 3, from the tangential section of the pars ciliaris retinae of a chick ten days old, shows epithelial buds projecting farther from the pigment layer but still connected to it by a thick pedicle. The pigment in the buds is of the same character as in the pigment layer, the staining of the protoplasm and the character of the nuclei as well as the continuity of the buds with the pigment layer indicate

quite clearly their epithelial origin. There are many other buds in this eye in various stages, some more advanced with small pigmented branches and narrow attaching pedicles, buds which are about ready to separate from the pigment layer and wander farther into the connective tissue stroma where there are numerous wandering pigmented cells. Many and perhaps all of these I believe have come from similar buddings of the pigment layer. The pigment of these wandering cells seems to be identical so far as optical appearances are concerned with that in the pigment layer. The nuclei, the staining and the general appearance of these cells, aside from the pigment, indicate that they are other than the ordinary branched mesenchyme cells. As the buds continue to grow the knob-like ends may send out branches and elongate or may remain spherical for a while, at least after the disappearance of the connecting pedicle between it and the pigment layer.

In Fig. 1, from a chick 6 days and 13 hours old, is a bud with a narrow pedicle and enlarged distal end. The bud is clearly a prolongation of the outer or pigment layer of the optic cup from near the choroid fissure and projects into the cleft heap of condensed mesenchyme. The enlarged distal end is to be found in the neighboring sections and consists of several cells with nuclei. The yellow brown pigment granules of similar character are present in the bud and in the pigment layer. This

was the only bud found in the entire series of this eye and no wandering pigmented cells were found. In Fig. 4 the elongated epithelial bud consists of several cells with nuclei and pigment granules similar to those in the pigment layer. The loose pigment cells (*Pc*), seen in this figure, are evidently derivatives of this bud, their position, size, character of the nuclei, protoplasm and pigment granules all indicate this. The bud in this section is seen to arise from a definite place on the convex angle formed by the bending of the epithelial layers into the ciliary process. In this same eye there are several other buds arising

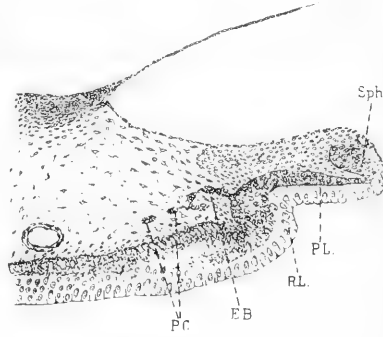


FIG. 4. From a chick 7 days, 22 hours old. Mag. 130 dia. *P. C.*, wandering pigment cells.

from similar locations at the angles where the epithelium bends into other ciliary processes. At some of these places there are detached masses of pigmented epithelium, the pedicles probably having just broken away and left the distal end of the bud in position, not sufficient time having elapsed for migration farther away from the pigment layer into the mesenchyme. There were no buds from more lateral portions of the pigment layer of the eye. From the iris portion of the pigment layer there were numerous buds for the most part free of pigment. They appear to take part in the formation of the lateral portion of the sphincter muscle. These will be more carefully considered later.

Fig. 5 from a chick 8 days and 12 hours old shows a large pigmented epithelial bud arising, in a position similar to that seen in figure 4, from the convex angle where the pigment layer bends into the ciliary process. There are a number of such buds in this eye with knob-like ends containing nuclei and pigment granules similar to those in the pigment layer. There are also detached masses of epithelial cells bearing the same relation to the ciliary processes as the knob-like ends of the attached buds. These loose masses are probably from buds whose pedicles have broken away. The anastomosing pigment cells are very numerous in the surrounding stroma. The pigment of many is a little darker than that in the pigment layer, but there are cells containing grades of colored granules like those in the pigment layer and others with intermediate shares. The general appearance of these cells, their nuclei and the staining of the protoplasm lead me to believe that most if not all of them are derived from the pigment layer. In this eye I

did not find epithelial buds lateral to the ciliary region. The buds we have so far considered have contained several cells and nuclei, occasionally the buds may consist of but a single cell as seen in Fig. 6.

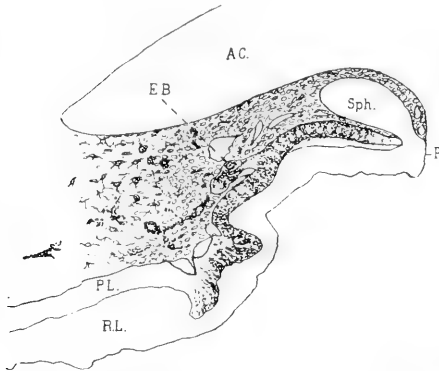


FIG. 5. From a chick 8 days, 12 hours old. Mag. 130 dia. Ac., anterior chamber.

in the pigment layer, but no such specimen was found; or again, we might expect to find numerous transition stages among the connective tissue cells with varying amounts of pigment from a few granules (of a yellowish color) to the heavily laden ones with dark granules. Such transitions practically never occur in the same specimen. On the contrary the wandering cells appear to contain pigment of about the same color and density, which corresponds closely to the condition of the pigment in the pigment layer. Where there is a difference that of the wandering cells is generally a little darker than that in pigment layer as though the progressive changes from brown or yellow to black had gone on faster in the isolated wandering cells than in the pigment layer. Again if the connective tissue cells were sending processes into the epithelial layer we would expect to find such pigmented wandering connective tissue cells in the stroma previous to their attachment to the epithelial layer, but in only one specimen did I find the wandering pigmented cells without the pres-

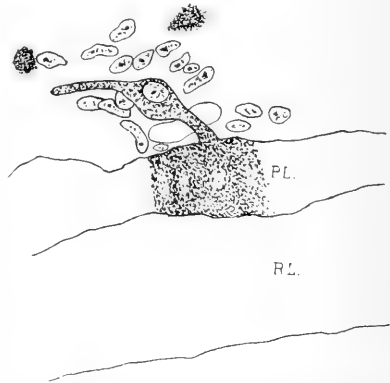


FIG. 6. From a chick 11 days, 3 hours old. Mag. 550 dia. Showing epithelial bud of one cell from pigment layer.

ence of buds from the pigment layer. In this specimen, chick 10 days and 8 hours old, there were very few wandering cells and the pigment

Table giving the ages of the chicks examined, with the absence or presence in the eyes of the following structures: (1) Buds from the pigment layer which form wandering cells, (2) wandering pigmented cells, (3) buds for the sphincter anlage from the iris portion of the pigment layer or from its pupillary margin, (4) pigment in the pigment layer. 0 indicates none present. The number of (+) indicate in a rough way the number or amount present. S indicates eggs incubated during the spring and early summer, the others were incubated in the fall.

Age.		Buds from pigment layer which form wandering cells.		Wandering pigmented cells.	Buds for sphincter anlage.		Pigment in pigment layer.
Days.	Hours.	Lateral buds.	Ciliary buds.		Iris.	Pupil.	
4	.. S.	0	0	0	0	0	0
4	9 S.	0	0	0	0	0	0
4	17 S.	0	0	0	0	0	0
4	20 S.	0	0	0	0	0	0
5	.. S.	0	0	0	0	0	++
5	12 S.	0	0	0	0	0	+
5	13 S.	0	0	0	0	0	++
6	13 S.	+	0	0	0	0	+++
6	21	0	0	0	0	+	+
7	.. S.	0	0	0	0	+	++
7	3 S.	0	0	0	0	+	++
7	22	0	++	+	+	+	++++
8	2	0	0	0	0	+	+++
8	10	0	0	0	0	+	++
8	12 S.	0	++	++	+	+	+++
8	13	0	0	0	0	+	+++
9	.. S.	+	+	++	0	+	+++
9	4	0	0	0	0	+	+++
9	6 S.	+	0	0	0	+	++++
9	19	+++	0	+	0	+	+++++
10	.. S.	+++	+	++	+	+	+++
10	1	+	+	+	+	+	+++
10	8	0	0	+	+	+	++++
10	18 S.	++	+	+++	+	+	++++
10	23	+	+	+	+	+	++++
11	..	+	0	+	+	+	+++
11	3	+	0	+	+	+	++++
12	23	+	0	++	+	+	+++++
14	1	+	+	++	+	+	+++++

in them as well as the general character of the cells indicated their epithelial origin. In this specimen a very few buds may have appeared from time to time to give origin to these cells and at the moment when the chick was killed none happened to be attached by connecting pedicles, these having already broken away. The budding process would

appear to extend over a period of several days from the eighth to the fifteenth day at least and probably for some time after this, but I have not as yet examined specimens older than the fifteenth day. The intensity of the process varies in different individuals, as will be seen from the table. The two specimens where buds occur without wandering cells would seem to indicate that the buds precede the occurrence of wandering pigmented cells. In the remaining specimens we see that where but few buds are present but few wandering cells occur, or where no buds are present no wandering cells occur, and where there are numerous buds there are as a rule numerous wandering cells.

M. SPHINCTER PUPILLAE BUDS FROM THE EPITHELIUM OF THE OPTIC CUP.

Arising from the iris portion of the pigment layer are large epithelial buds which appear to take part in the formation of the M. sphincter pupillae anlage. As will be seen from the table they appear later than those sphincter buds arising from the pupillary margin of the optic cup. Fig. 7 shows an iris bud which might perhaps break up into wandering cells or lose its pigment and take part in the formation of the sphincter muscle. There were a number of such buds in this

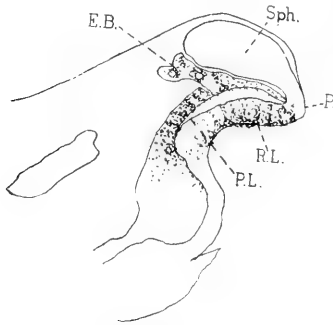


FIG. 7.

FIG. 7. From a chick 8 days, 12 hours old. Mag. 130 dia.

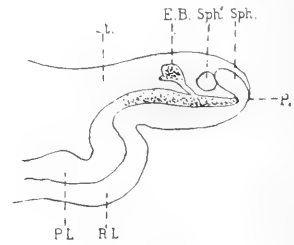


FIG. 8.

FIG. 8. From a chick 7 days, 23 hours old. Mag. 130 dia. *Sph'*, sphincter mass from pigment layer.

eye arising from just about the same position on the pigment layer, namely about half way between the pupillary end of the pigment layer and the ciliary process, and most of these seem to arise opposite the ciliary processes and are thus arranged in a circle about the pupil at equal distances from its margin and at fairly equal distances apart. Fig. 8 shows another such bud attached by a slender pedicle and containing pigment. It does not seem possible to decide whether such a bud would develop into wandering pigment cells or lose its pigment and form

part of the sphincter anlage. Fig. 9 shows an epithelial bud (*Sph''*) which I believe would have soon broken away from the pigment layer to form the lateral portion of the sphincter anlage. The pigment stops abruptly in the pedicle and the enlarged end of the bud is entirely free from pigment and similar in appearance to the sphincter bud (*Sph*) derived from the pupillary margin of the optic cup. In this eye there were many such buds as *Sph''*, and as in the chick 8 days and 12 hours old, arise about the same distance from the pupillary margin, and the greater number of them

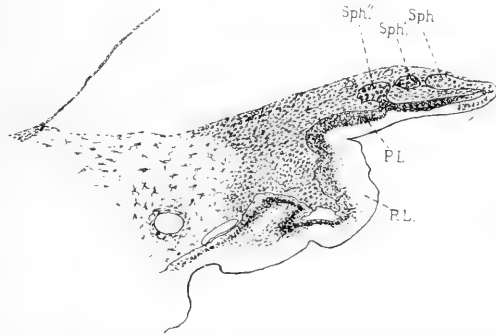


FIG. 9. From a chick 10 days, 9 hours old. Mag. 130 dia. *Sph''*, sphincter bud from pigment layer.

are opposite the ciliary processes. Fig. 10 is a diagram showing the distribution of these buds over one-half of the iris. There were thirty on this half of the iris arising at about the same distance from the pupillary

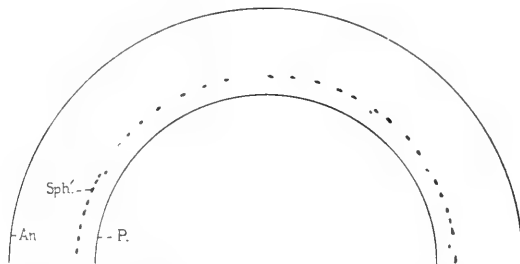


FIG. 10. Diagram of the position of the sphincter buds arising from the pigment layer over one-half the iris in a chick 10 days, 9 hours old. Mag. 30 dia. *An.*, angle of anterior chamber; *P.*, pupillary margin.

margin. Figs. 11, 12 and 13 show similar buds in a chick 13 days old. The buds are arranged in two series, as will be seen in the diagram (Fig. 14). The more lateral series (*Sph''*) are the most numerous. The pedicles of many of the buds have disappeared, leaving the free epithelial masses in the stroma of the iris as *Sph''*, Fig. 12, and *Sph'*, Fig. 13. The detached masses and buds are free from pigment except the basal portion of the pedicle and for an occasional granule or so in enlarged end. In all of these buds and free masses within the staining reaction and the nuclei are

similar to the sphincter pupillary buds. The peripheral portion of the muscle would thus seem to be formed by these iris buds and the inner portion near the pupillary margin by the large buds arising from the pupillary margin.

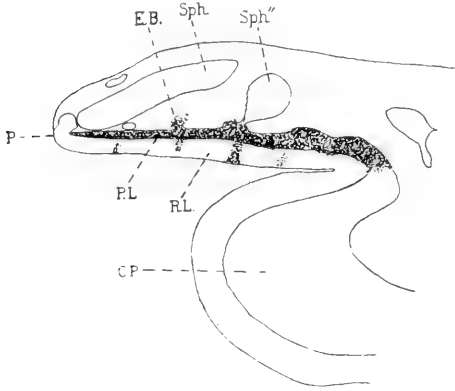


FIG. 11.

FIG. 11. From a chick 13 days old. Mag. 260 dia. C. P., ciliary process.

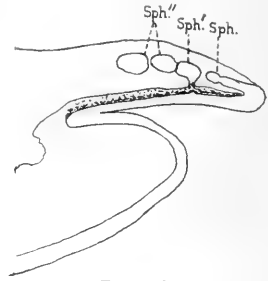


FIG. 12.

FIG. 12. From a chick 13 days old. Mag. 130 dia.

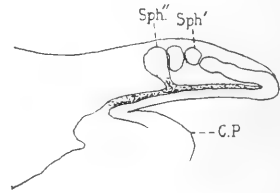


FIG. 13.

FIG. 13. From a chick 13 days old. Mag. 130 dia.

THE FORMATION AT THE PUPILLARY MARGIN OF BUDS FOR THE M. SPHINCTER PUPILLAE.

The first indication of the formation of the sphincter buds at the pupillary margin occurs during the seventh day by a gradual disappearance of the pigment of the outer layer for a short distance from the pupillary margin. Soon a distinct line separates this area from the rest of the pigment layer, and by this time all the pigment is lost and the bud is easily recognized. It becomes thicker than the neighboring portion of the pigment layer and stains exactly as the inner layer with haematoxylin and congo red. The line of demarcation between the bud and the pigment layer becomes sharp and oblique and in places the two appear to separate (see Fig. 15). This process proceeds faster on one side of the eye than the other. At first the processes do not form a continuous bud around the pupil, but a series of them separated at fairly regular intervals by areas where the formation of the buds is going on at a slower rate. By the tenth day, however, these intervals have developed so far as to form a continuous bud band about the pupil. As the bud band continues to enlarge and thicken it overlaps more and more the

pigment layer, which diminishes in thickness and pushes tongue-like into the cleft between the bud and the inner layer until it reaches the angle indicated by *A*, Fig. 15. In many of the specimens this tongue of the pigment layer does not seem to fuse with either the bud or the inner layer; in other specimens it is impossible to determine whether fusion has taken place. It is thus unlikely after the first separation of the bud from the outer layer that it receives any more cells from it. It remains attached to the inner layer, which may contribute to the enlargement of the bud, but it seems more likely that the lengthening of the bud is brought about by extension of the pupillary margin of the optic cup towards the centre of the pupil

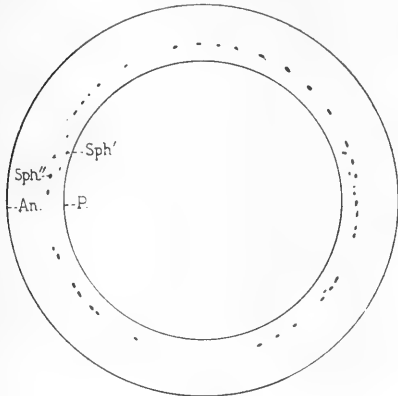


FIG. 14.

FIG. 14. Diagram of the position of the sphincter buds arising from the pigment layer of the iris in a chick 13 days old. Mag. 25 dia. *Sph.*' and *Sph.*'' correspond to same in figures 11 and 12.

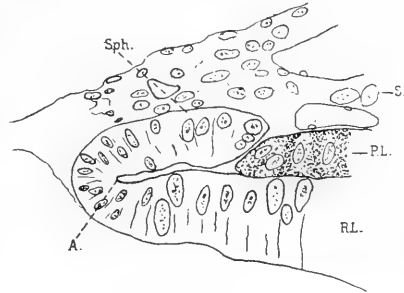


FIG. 15.

FIG. 15. Radial section of margin of optic cup of chick 6 days, 22 hours old. Mag. 550 dia. *A.*, angle between sphincter bud and inner layer.

by multiplication of cells in both the inner layer and the bud. The tendency to narrowing of the pupil is more than counteracted by the general expansion of the optic cup.

CONCLUSIONS.

Most, if not all, of the wandering pigmented cells in the stroma about the anterior portion of the optic cup during the first 14 days, and probably later, arise from buds of the pigment or outer layer of the optic cup and are thus ectodermal in origin.

The *M.* sphincter pupillae anlage is formed not only by buds from the pupillary margin, but its peripheral portion is formed by many distinct buds arising from the pigment layer some distance lateral to the pupillary margin of the optic cup.

There arise from the epithelium of the optic cup under normal conditions such varied tissues as muscle, branched and anastomosing pigmented wandering cells, simple layers of epithelial cells and the nerve cells of the retina. The origin of the first two from the epithelium must modify our idea of a rigid specificity of the outer germ layer. Mauer's⁴ discovery that in the frog smooth muscle develops from the ectoderm of the skin; the possibility, according to Kodis,⁵ that wandering cells may come from the ectodermal cells of the tadpole's tail, and the numerous observations on the origin of lymphocytes from the epithelium of the tonsil shake our faith in the rigid specificity of the outer germ layer.

⁴ Mauer: Die Epidermis und ihre Abkommlinge. Leipzig, 1895.

⁵ Kodis: Epithel und Wanderzelle in der Haut des Froschlössenschwanzes. Archiv f. Anat. u. Phys. Phys. Abt., 1889.

THE ANGIOLOGY, ANGIOGENESIS, AND ORGANOGENESIS OF THE SUBMAXILLARY GLAND.

BY

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WITH 14 FIGURES.

In a preliminary note¹ on the blood-vessels of the submaxillary gland and their development, the writer outlined briefly the angiogenesis of the circulation, together with its arrangement and distribution in the adult organ. At the same time, attention was called to certain researches of Thoma concerning the principles involved in the development of blood-vessels and their application to the evolution of the circulation in highly organized glands. The following extracts from this paper may emphasize these points again briefly.

“The well-known researches of Thoma on the histogenesis of the vascular system offer an explanation of some of the phenomena of vascular development, particularly to the relation between the velocity of the blood current and the size of the vessel that conducts it. The question of the ancestry of arteries and veins was solved by Thoma, who showed in chick embryos that originally they were always simple capillaries. Their subsequent transformation, according to this author, was due to their fortuitous location with reference to the primitive aortae, and the venous ostia of the heart. It has been shown that these facts apply to the vascular development in mammals as well as the chick, and for vascular systems developing in three dimensions, as well as those found in the area vasculosa where the vessels grow in two directions only. In considering the problems of angiogenesis in mammals, it is apparent that Thoma's histo-mechanical principles do not suffice to explain all the facts, nor do they even entirely accord with them. The statement that a new growth of vessels follows a rise of blood pressure in the capillary area must be considered only as an hypothesis and not a demonstrated fact, for this would make the vascular system the stimulus to the development of new cells, while there is considerable probability that it is the new cells

¹ Journal of Medical Research, Vol. VII, No. 4.

which give the stimulus for the growth of new capillaries. It must be obvious that the principal factors that govern organic growth are resident in the cells rather than in the blood-vessels, as is indicated by their behavior in the embryo before the vascular system is laid down. We have still much to learn concerning the factors that arrest the growth of organs when they reach the adult type, but there is little doubt that these phenomena are expressions of cellular rather than vascular activity, since the vascular system maintains far beyond the usual period of growth, its power of progressive development. It is, so to speak, always in a state of unstable equilibrium, in which both progressive and regressive changes are possible. Certain facts in the development of the blood-vessels of organs have already been demonstrated, the most important of which is that the intrinsic blood supply of organs usually marks out the paths along which the units of structure that compose it have developed.² And by following the gradual increase in complexity through a series of injected embryos, the succeeding changes from the simple embryonic to the adult form can be easily demonstrated. It is important to trace these changes not only for the light they shed on the development of the vascular system, but because many obscure features in the structure of organs are elucidated when the mechanics of their development are known.

Excepting certain radical modifications that take place at the time when the embryo ceases to receive its nourishment from the maternal blood sinuses and independently undertakes the aëration of its own blood, it has been shown that the conditions of the systemic circulation in embryos at term approximate very closely that in adult life. At the same time considerably less differentiation occurs in the intrinsic circulation of the individual organs than in the larger vessels of the general circulation. At the time of birth the structure of most organs is well developed, and the changes which take place are usually quantitative rather than qualitative. Accordingly, the material for this research was obtained from the submaxillary gland of injected embryo pigs, and the results were subsequently shown to conform to the conditions found in the glands of dogs and human beings.

METHODS.

The technique for the injection of embryos used in the study of the angiogenesis of the submaxillary has been described in detail in another

² Flint, Welch, *Festschrift*, 1900, and Reports of the Johns Hopkins Hospital, Vol. IX., 1900.

place.³ In working up the blood supply of the submaxillary two of the simpler methods have been found especially serviceable, namely, the use of silver nitrate and a saturated aqueous solution of Prussian blue. The chief value of the silver nitrate method lies in the fact that by far a greater proportion of the silver is precipitated in the arteries, giving by a single injection a natural differentiation between them and the veins. Moreover, the endothelial lining of the blood-vessels is beautifully demonstrated by this method. A $\frac{3}{4}$ to 1 per cent solution gives good results. The only disadvantage lies in a tendency for this solution to extravasate somewhat more than the Prussian blue, but there is compensation in the fact that silver injections are usually incomplete. These give clearer pictures of the blood supply in the developing organ, because the details are not obscured by a general filling of the entire capillary system. Double injections are possible and serviceable in the embryos where it is necessary to differentiate arteries and veins, but in the submaxillary, at least, most of the differences between the arterial and venous systems can be clearly shown in the silver nitrate specimens. (Figures 2 to 8.) For the blood supply of the adult organ Prussian blue and lamp black gelatin or a carmine mass followed by a suspension of lamp black in gelatin gives very sharp pictures. The circulation in the adult organ, however, differs in no marked feature from that of the pig at birth, except quantitatively. For a study of the relationship between blood-vessels and cells, sections made by the routine methods demonstrate clearly these points. And, in following the development of the cellular elements of the ducts and alveoli, Mallory's aniline blue connective tissue stain is of great value. This stain seems to be peculiarly adapted to the use of the submaxillary because it brings out in sharp relief differences between mucous and parietal cells, and stains as well the duct epithelium. Moreover, it differentiates clearly between connective tissue fibers and cell elements.

ANGIOLOGY.

In man, the A. submaxillaris is derived from the A. maxillaris externa, which runs in a small sulcus on the surface of the glandula submaxillaris or directly through its substance as it mounts up over the lower border of the ramus of the mandible. Occasionally the A. submentalis contributes submaxillary branches that enter the organ. The Vv. submaxillares sometimes empty into the V. submentalis, but usually are tributaries of the V. facialis communis. In man the arteries do not

³ Flint, Welch, Festschrift, and Johns Hopkins Hospital Reports, Vol. IX.

enter the hilus of the organ with the duct, but join the latter a short distance after it penetrates the gland and take up immediately the close relations which are observed throughout the developmental and adult periods of life. The veins follow the arteries throughout their course. In the pig, however, the duct is joined by the blood-vessels almost immediately after their passage through the hilus, even before branches of the first order are given off. The relationship between the duct and vascular systems is absolutely constant and dates from the earliest embryonic history of the organ.

Inasmuch as the nomenclature of the blood-vessels is taken from that of the ducts, a short account of the latter may simplify the description of the vascular system. In pigs, the distribution of the ducts is not unlike that in man, although in the former it is somewhat more regular. In man the ductus submaxillaris enters the hilus of the gland and almost immediately breaks up into branches of the first order. These run a very short distance and then terminate in a secondary system, forming interlobular ducts that ramify extensively throughout the gland. From the latter are derived a set of sublobular ducts. These divide once or twice and then terminate in lobular ducts which, entering the hilus of the ultimate lobules, at once exhaust themselves in the extensive ramifications that form the intralobular ducts and radiate from the hilus to the periphery of the lobule. They terminate in a short duct of slightly smaller caliber termed the intercalary portion connecting them directly with the secreting alveoli of the gland. The intercalary ducts are usually considered as having a much smaller caliber than the ducts of the next lower order. This, however, is not the case, as their lumen, as shown by corrosion preparations, is only slightly smaller than those just preceding. This mistaken impression probably arose from the consideration of the ducts when clothed with their epithelium. The total diameter of the intermediate ducts is much smaller, because the intralobular ducts on one side are lined with columnar epithelium and the alveoli have either high mucous or serous cells on the other, while the intercalated portions of the duct between them have only flattened epithelial cells for their walls. Running in the thick processes of fasciculated connective tissue that form the interlobular spaces, are the blood-vessels that always accompany the ducts. In one way, the interlobular spaces of the salivary glands have a certain resemblance to those of the liver except that the former have two veins instead of the single branch of the portal system found in the hepatic interspaces.

In describing the blood-vessels of the adult organ, it is convenient to divide them into three systems:

1. The glandular circulation from the A. submaxillaris to the alveolar plexus and back to the Vv. submaxillaris.
2. The circulation about the ducts.
3. Circulation in the capsule and septa.

THE GLANDULAR CIRCULATION.

The submaxillary artery in pigs at the hilus or point of entrance is separated by a short distance from the ductus submaxillaris. The two rapidly converge, however, and, as a rule, meet just before the point where ducts of the primary order are found. Before joining the duct, the artery may give off one or two short branches that enter adjacent lobules, as well as a few branches to the large mass of connective tissue which enters the organ at the hilus. The ducts of the first order are accompanied by the Aa. principales. These now run in the connective tissue of the larger interspaces at a short distance from the lumen of the duct. There is no marked tortuosity of the main artery or its principal branches, but, at the different angles where the chief ducts are given off, the arteries sometimes wind partly around them or may take a slightly spiral course about the duct. As a rule, however, while there is a slight wavy irregularity in the course of these vessels, a complete spiral arrangement about the ducts is rarely observed. From the principal branches of the main artery the Aa. interlobulares are derived, accompanying ducts of the same order in the interlobular interspaces. From these branches the blood is distributed in radiating directions throughout the gland. They are longer than blood-vessels of any other order. In their course they may divide once or twice and finally exhaust themselves in lateral branching in the sublobular arteries which run with the sublobular ducts in the center of the primitive lobules. Arteries of this order may in thick injected specimens be easily recognized running in the center of the groups of ultimate lobules bounded by the secondary septa. They divide three or four times with the sublobular ducts and then exhaust themselves in the Aa. lobulares, each one of which enters a primitive lobule at its hilus together with the lobular duct. Once within the limiting membrane of the lobule, the ramification is more abrupt and more marked. The intralobular branches of the A. lobularis radiate from the hilus toward the periphery of the lobule, divide with and accompany the intralobular ducts. The terminal divisions of the intralobular arteries run with the intercalary ducts and divide under the clusters of alveoli into the alveolar capillary plexus. The capillaries mount up over the alveoli external to the reticulated basement membrane and anastomose with the capillary plexus

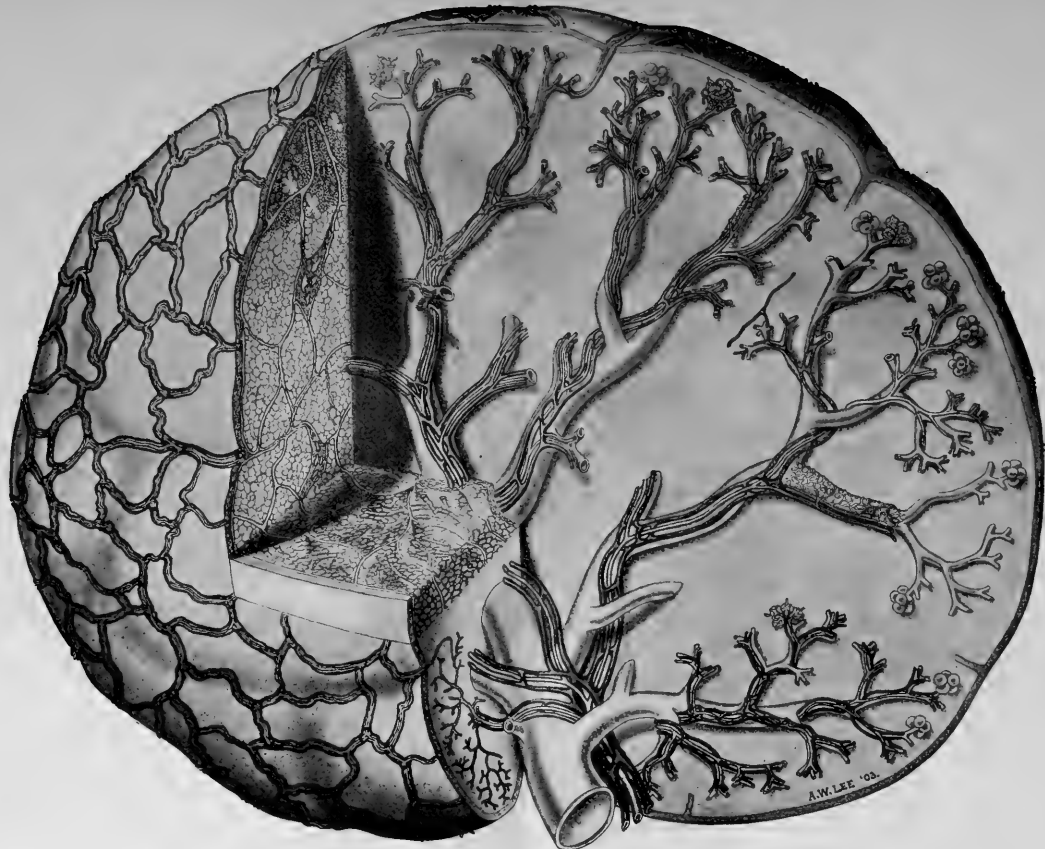


FIG. 1. Diagrammatic reconstruction of the submaxillary gland. Magnified 12 diameters. The reconstruction shows the distribution of the ducts and their termination in the alveoli, together with the arrangement of the accompanying blood-vessels. For the sake of clearness in drawing, there is some discrepancy between the relative size of the blood-vessels and ducts. The blood supply is taken from a pig at birth where the type of circulation is so developed that it differs in no way from that of the adult. The histological portion and the digested section are from the human submaxillary, while the piece digestion is from the submaxillary of the dog. The limiting membranes of these two tissues have simply been forced to meet in order to show their relationship by the different methods. Otherwise no violence has been done to the original specimens. (J. M. Flint, *Angiology of submaxillary gland.*)

of adjacent alveolar groups. The meshes are small and regular, and occupy three dimensions. This plexus has anastomoses extending throughout the lobule, but terminates on all sides at the *membrana limitans*. Each lobule has, therefore, with certain exceptions that will be considered later, an independent circulation.

Beginning in small radicals around the base of the alveoli, venules are formed through the coalescence of capillaries. These rapidly converge to a point near the terminal arterioles about the intercalary duct to form *venae terminales*. The veins are short and there is but a single one accompanying each terminal arteriole. At the point of junction of several intercalary ducts, the accompanying terminal veins through their confluence form the intralobular veins which collect the blood from different portions of the lobule and terminate in the lobular vein. This vessel makes its exit from the lobule at the hilus, side by side with the lobular artery. There is no reduplication of the veins of the intralobular system. As soon as the veins leave the lobules, however, and enter the sublobular interspaces, the venous system is doubled, yielding *venae comites* to each successive division of the *A. submaxillaris*. The sublobular veins parallel the course of the artery, giving off numerous anastomotic branches which run over and under the artery forming oblong meshes. It is not uncommon, however, to have the veins separate and pass around the duct and then join on the opposite side, or else have anastomotic branches pass from the *venae comites*, embrace the duct, and finally join the main veins lower down. The *venae comites* with their blood current flowing in the reverse direction follow in a convergent manner the previous divergence of the arteries. Thus the sublobular veins unite to form those of the interlobular system, while these, in turn, join to make the *venae principales*. The principal veins part with the ducts at the same point where the artery joins them and leave the gland along with the *A. submaxillaris* as the *Venae submaxillares*. These usually empty into the *vena facialis communis*. In the general glandular circulation we find two vascular units, one, a complete terminal system, forming, in Ludwig's sense, the true unit of circulation, that is to say, blood-vessels supplying a group of structures which have definite relations throughout the organ with the general framework. These form, in this way, the ultimate indivisible complete unit of structure of which the organ is built up. Such a unit in the submaxillary gland would be represented by the lobule and the whole organ is simply formed of a series of these units. Another vascular unit could be formed of the terminal arteries. These break up in the alveolar capillary plexus which reunite into small venule radicals and empty

into the terminal vein. Each lobule is composed of a series of such units. Even another larger unit might be constructed from the circulation embraced between the sublobular artery and the sublobular vein, supplying groups of lobules that have definite relations with the secondary septa. The ultimate lobular unit might well be considered the least, while the primitive lobule would be the greatest common structural divisor of the submaxillary gland. The smaller terminal units are comparable to the conditions of the circulation in such glands as the stomach and adrenal where cell complexes having definite relations with larger bands of connective tissue do not exist.

CIRCULATION ABOUT THE DUCTS.

The ductus submaxillaris is embraced by a rich supply of arteries derived from the Aa. principales, branches of which run in a recurrent



FIG. 2. Blood-vessels about the ductus submaxillaris in a pig 26 centimeters long showing the arterial, venous and capillary plexuses: arteries light, veins and capillaries dark.

direction along the walls of the ducts as far as the hilus. These arteries may anastomose with some frequency (Fig. 2), although the plexus formed by them is not a rich one. They are distributed around the surface of the duct and give off terminal branches which sink to the region just around the base of the duct epithelium and terminate in a capillary plexus formed of small, irregular, polygonal meshes. Through the confluence of the capillaries, numerous venules are derived which empty into large veins forming an irregular venous plexus about the duct. The caliber of these veins is larger than the arteries, and the meshes formed by them are irregular and polygonal. The venous plexus lies below the arterial and from a convergence of its elements larger veins are formed

that terminate in the venae principales. In ducts of the interlobular order there is the same arrangement of the blood-vessels around the ducts, except that the elements of the venous plexus are not so large nor is the connection between them so frequent. As one progresses upward from the main ductus submaxillaris to the lobular ducts, there is a gradual simplifying of the duct circulation, until, in the ducts of the sublobular order, we have afferent arteries derived from the Aa. sublobulares running part way around the duct, breaking up into capillaries which reunite in small anastomosing veins, that pass around the walls of the ducts to terminate in the venae comites. Alternations of artery and veins in these instances are not uncommon and arterioles and veins are in all cases above the capillary plexus. Fig. 3, which shows the circulation in a duct of this order, gives the relations beautifully. It should be noted, however, that one of the venae comites has been re-

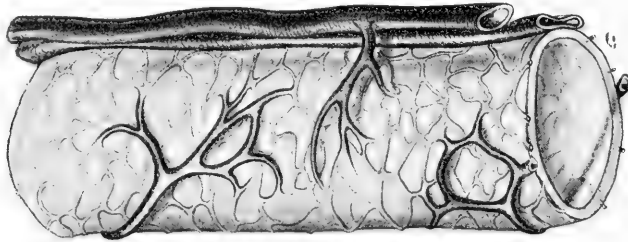


FIG. 3. Blood-vessels about a sublobular duct. The artery is the upper of the two vessels. One of the venae comites has been left out for the sake of clearness.

moved for the sake of clearness. The lobular and intralobular ducts show a still simpler form of duct circulation. Small arterioles almost immediately break up into capillaries when they are derived from the lobular or intralobular arteries. These quickly reunite again into veins that terminate into venules which empty directly into intralobular veins. This gradual simplification of the circulation about the ducts gives a characteristic demonstration of their age, and, in the angiogenesis of the submaxillary circulation, parallels can be drawn between the circulation about the ducts at different periods of embryonic life and the conditions found in the vascular supply of ducts of the different orders. In the very earliest stages the circulation of the main ductus submaxillaris is much like that about the adult lobular duct. At a somewhat later stage it approximates that of the duct of the sublobular order, while still later there is a similarity to that of the interlobular system, and finally the highest development is attained with the complete formation of the arterial and venous plexuses which embrace the main ductus

submaxillaris in the adult. It is very easy, moreover, to follow in a single, well-injected gland the evolution of the duct circulation from that of the lobular type to that which embraces the main duct. The small arterioles break up into capillaries and reunite into small venules that finally terminate in the accompanying veins. These vascular elements enlarge so that the arteries branch and come to lie upon the capillary plexus and the isolated veins

receive a few anastomoses from each other. With the growth of the duct and the lengthening of the artery and its ramifications, the venules which are last formed from capillaries come to lie under the arterial but over the capillary system,



FIG. 4. Circulation about an intralobular duct. The artery is the upper vessel of the two.

and thus we have the three superimposed series of vessels noted about the ducts of the larger order. Throughout the course of the successive divisions of the submaxillary arteries, branches are given off which supply the framework of the interspace. These vessels are extremely irregular and after breaking up into a capillary system that ramifies around the fascicles of connective tissue, venules are formed emptying into the venae comites at irregular intervals. The circulation to the sympathetic ganglia buried in the interspaces also has a similar derivation.

CIRCULATION OF THE CAPSULE AND SEPTA.

Blood-vessels that run to the primary and secondary septa are derived from the Aa. intralobulares. Branches from vessels of the latter type perforate the limiting membrane and almost immediately break up into a loose irregular plexus, the venules from which unite into a single vein that accompanies the septal artery and flows back into the lobular circulation. The blood-vessels in the capsule are derived from two sources, in part from the arteries and veins in the periglandular connective tissue which run on the surface of the connective tissue envelope of the organ in the form of a very irregular plexus of polygonal spaces. These vessels are very small. Frequently capsular branches from the lobular arteries perforate the capsule and join the capsular plexus. These capsular arteries are accompanied by capsular veins. When septal arteries arise from lobules at a point near the capsule, they may pass from the septa and finally unite with the capsular plexus. With these two exceptions, the circulation in each lobule seems to be complete and independent, save in those cases where a lobule of the first order is not completely

subdivided into ultimate lobules, so that at their bases anastomoses may occur between the alveolar capillaries of the peripheral portions of adjacent ultimate lobules.

ANGIOGENESIS.

Chievitz⁴ has shown that the submaxillary gland develops as a bud from the buccal epithelium. This grows backward toward the angle of the mandible and there begins a dendronal branching that marks the anlage of the submaxillary gland. Owing to the difficulty in injecting very early embryos, a study of the relationship between vessels and cells can best be made in stained sections. The submaxillary gland is shown in a simple form in pigs represented by about $3\frac{1}{2}$ centimeters, nape-breech measurement. At this time the branching column of cells is accompanied by an artery that enters with the duct at the simple hilus and lies close to the developing basement membranes. Capillaries forming an irregular plexus can be seen here and there about the ramifications of the simple tube forming the ductus submaxillaris. The arterioles, venules and capillaries at this stage are usually separated from the reticulated basement membranes by a short intervening mass of syncytium, but as the ducts increase in size this distance is diminished. These relations can be found in stained sections from the glands of pigs $4\frac{1}{2}$ to 6 centimeters in length. When, however, the pig reaches an age represented by $8\frac{1}{2}$ centimeters, the injection of the gland becomes a simple matter and the description can be taken up from injected organs that are cut in half and studied under the stereoscopic microscope. This gives not only the relations of the vessels throughout their course, but also enables the observer to follow them in three dimensions. At this time the gland is reniform, and the vascular supply is comparatively rich. Since the relationship between arteries, veins and ducts established in pigs of earlier age always persists, the course of the ducts accordingly may be determined by the course of the blood-vessels. Indeed, in a pig of this age the duct and its branches are represented negatively, making it possible to follow them nearly as well as though they were either stained or injected. At this period the artery enters the primitive organ at the hilus and branches with the duct. This is the simple stage of the arteria submaxillaris. In its course the artery gives off small branches which almost immediately break up into capillaries. These run around the column of cells and empty at once into the vein accompanying the afferent vessel. The meshwork formed by this capillary plexus is small

⁴ Chievitz, Arch. f. Anat. u. Phys. Anat. Abth., 1885.

and irregular and the vessels composing it are often unequal in caliber. Following the branching ducts, the *A. submaxillaris* divides with each successive ramification, giving off still the collateral arterioles that embrace the walls of the ducts. The ramification at this time extends to about four orders and the arterioles terminate in a capillary plexus embracing the terminal buds or swellings that form the apices of the growing ducts. These vary in number from four to seven and are distinctly seen as clear spaces sharply demarcated by the embracing capillary plexus. At this age the terminal capillary system surrounding each group of primitive alveoli are entirely independent and have as yet no anastomoses with each other. The

blood, derived from the terminal arterioles, passes through the capillary plexus and is gathered again into venules which accompany the terminal artery along the walls of the duct from which the buds have grown, but the alveolar plexus is finer than that around the ducts. Already at this stage, it is possible to see that the blood supply of the entire gland now looks like the vascular distribution in a single lobule of the adult organ. Attention has already been called to the analogy between the two, so the four ramifications of the *A. submaxillaris*; *Aa. principales*, *Aa. interlobulares*, *Aa. sublobulares*, *Aa. lobulares* are like the divisions of the intralobular arteries in the adult. Fig. 5 represents half of an injected gland at this stage, photographed so as to obtain a stereoscopic effect. The branching of the ducts is shown by the course of the blood-vessels and the irregular plexus formed by the latter upon the former is clearly visible. The alveolar plexus, however, does not stand out clearly in this specimen.

In a pig 12 centimeters in length the ramification has proceeded to higher orders, the ducts as shown by the embracing meshwork have increased in size and the plexus embracing them is more highly differentiated. Small lateral arterioles are now given off from the main arteries which divide into capillaries. These reunite into little venules emptying into the main *venae comites*. In a pig 8 centimeters in length, the veins are duplicated as high as the third order, but have not yet taken up their course in such close relation to the artery. In the next stage, however, the veins follow more closely the course of the artery and the

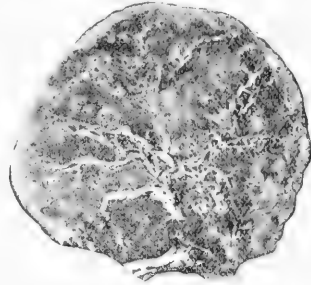


FIG. 5. Submaxillary gland of pig's embryo 8 centimeters long, injected with silver nitrate and cut in half. X 10 diameters. The simple arterioles and capillary plexus around the growing column of cells is distinctly shown. In points a few capillaries about the terminal buds may be made out.

capillary plexus extends around the duct from the point where they are situated. Each successive ramification remains practically a terminal system, although occasional anastomoses are found running from the vessels accompanying one branch of the duct to those about another. These communications, however, are usually venous and not arterial, although connections between vessels of the latter type are occasionally found. The capillary plexus embracing the terminal buds is now much finer and more definitely organized than in the earlier stages. Arterioles run along with the terminal ducts and suddenly break up into an irregular, fine plexus composed of small polygonal meshes which mount up

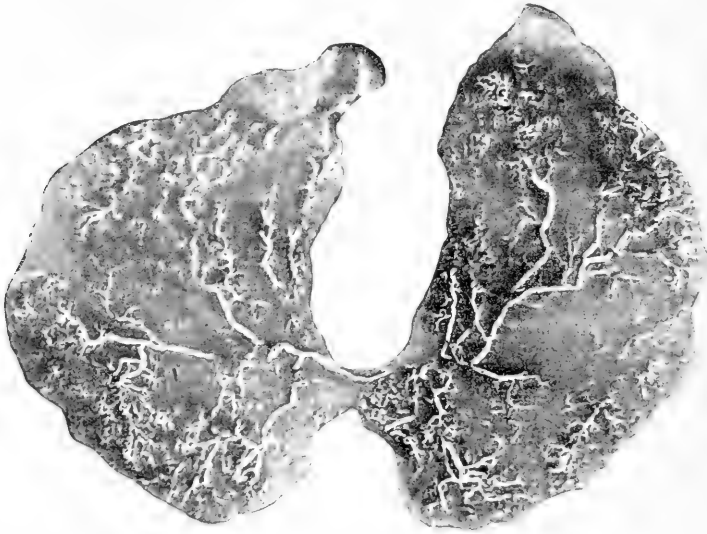


FIG. 6. Submaxillary gland of pig's embryo 12 centimeters long. Same method of preparation as Fig. 5. $\times 10$ diameters. In this specimen only the arteries accompanying the ducts and the terminal alveolar plexus are visible.

over the summit of the alveoli and are collected into venules which return to the point of junction of the ducts and alveoli, and there unite into little terminal veins that accompany the ultimate arterioles. At this period an occasional branch from one of the terminal arteries passes out from between the buds and joins the small plexus that is being formed on the capsule of the gland. As yet septal arteries are not found. Fig. 6 shows an injected silver preparation of a pig at this stage. Except in certain points the mass has not passed over into the veins, for the most part leaving the arteries and capillary plexus around the alveoli the single visible portion of the vascular system. The greater regularity of the alveolar plexus is now clearly shown.

In a pig 18 centimeters long the main submaxillary vessels and submaxillary duct are now somewhat separated. Arteries and veins are distinctly seen in the plexus embracing the ductus submaxillaris. These are derived from its vasa comites. The ramification has not increased so much in number of orders as in the number of branches. The arteries still preserve their individuality but a duplication of veins is observed as ducts increase in size. Here and there one finds not infrequently a vein looping around the arteries and even embracing the ducts. At this period vessels of the lobular type have just been formed



FIG. 7. Submaxillary gland of pig's embryo 18 centimeters long. Same method of preparation and magnification as Fig. 5. The arteries and venae comites are distinctly seen. These may follow as far as the terminal arterioles which are now forming those of the lobular type. Little capillary clusters with their arterioles and venules represent the secondary or ultimate lobules. The plexus about the ducts is not injected.

and the capillary plexus around the alveoli is very sharp and distinct. Anastomoses have been established between the capillary systems of adjacent alveolar groups. This forms for the first time in the history of the organ the final arrangement of the circulation in the lobule, although representing it in a very simple form. Here and there the connections between the alveolar circulation and the circulation of the capsule are seen, while, for the first time, perforating vessels leave the lobules and ramify in septa of the first and second orders. These appear best in Prussian blue specimens where the injection is complete. Compared with other organs, the amount of syncytium from which the fibrillar and cellular parts of the submaxillary framework are derived is proportionately excessive to the quantity of cells forming the primitive ducts which are destined to yield all of the epithelial elements of the gland. In all of the early stages, the blood-vessels are confined to the immediate neighborhood of the ducts, while the syncytium has none. As this syncytium is transformed into strands and septa, they receive a vascular supply of their own, which is not well shown until the pig reaches an age indicated by a nape-breech measurement of 18 centimeters. The interspaces have now attained a definite size and blood-vessels derived from the vasa comites of the main ducts leave the plexus and ramify in the substance of the connective tissue, here and there giving off arteries to supply the

sympathetic ganglia that are embedded in the fibrous tissue forming the main interspaces. Even at this period there is no connection between the circulation in one lobule and that of its neighbor, save occasionally at the lobular hilus where lobules of the first order have been incompletely separated by membranæ limitantes into ultimate lobules. Fig. 7 shows an incomplete silver injection of the circulation at this stage. The arteries are seen as definite round tubes while the veins in the photograph appear collapsed. Owing to the lack of depth, many of the finer relationships of the blood-vessels are lost. The alveolar plexuses are clearly shown, together with the beginning of the demarcation of the ultimate lobules by the branches of the lobular arteries.

In a pig 22 centimeters long the arrangement of the blood-vessels has not been altered in any marked degree. Each of the six divisions of the branches of the arteria submaxillaris has been formed. The growth subsequent to this stage, therefore, lies more in the differentiation and complexity of the lobule rather than in the general plan of the organ, a fact which is confirmed by the study of stained specimens. The plexus about the main submaxillary duct as it enters the gland becomes more complex. Branches derived from the main artery anastomose and ramify a short distance, and then break up into a dense capillary plexus formed by irregular polygonal spaces which entirely embrace the duct, lying just external to the basement membrane. Venous radicals formed in this plexus unite and flow into larger units which form an irregular venous plexus lying on top of the capillary plexus. Emissary veins from this plexus empty into the venæ comites. The double plexus can now be followed as far as the interlobular ducts, where the two layers of vessels are replaced by one. In the development of the circulation the growth of the vessels like the growth of the ducts has been entirely centrifugal.⁵ If one takes a thick tangential section of the gland and views it with the stereoscopic microscope from above, the outlines of the lobules are clearly shown and the branching and radiating vessels are always found in the center looking much like the branches of a small tree viewed from above. At birth the relations of the last stage remain

⁵ In another communication, *Archiv für Anat. u. Phys. Anat. Abth.*, 1903, the writer has called attention to the centrifugal growth of the ducts of the submaxillary with reference to the formation of the lobes and lobules of the first and second orders. These structures always occupy the center of the lobes and the center of the lobules, from which point they radiate out towards the capsule or the limiting membranes. The entire arrangement of the frame-work of the submaxillary depends, in fact, upon physical factors involved in successive action of this principle of centrifugal growth upon the fibrils that compose the supporting tissue of the organ.

practically unchanged, save in the enlargement and differentiation of the lobules brought about by an increase in the ramifications of the intralobular ducts and consequent increase in the number of alveoli. *Pari passu* with these changes the Aa. intralobulares have undergone a numerical increase corresponding to the division of the intralobular ducts. The capsular plexus is now very well marked. Arteries in the connective tissue surrounding the gland, run to the capsule, forming there an irregular polygonal plexus which breaks up into capillaries that pass irregularly in the outer layer of fibrous tissue that composes it. These capillaries reunite into venules which flow into venæ comites that accompany the arteries forming a capillary plexus. As in the earlier stages, perforating branches from the lobules and septal arteries run up and join this plexus.



FIG. 8. Submaxillary gland of pig's embryo 24 centimeters long. X 10 diameters. Aa. principales, interlobulares, sublobulares, lobulares, and intralobulares are now distinctly seen. The lobules have increased somewhat in size and the lobular veins and the venæ sublobulares, interlobulares, principales are well formed. The plexus about the duct is not injected, arteries appear tubular and glistening while the veins are brownish and collapsed. The photographs from Figs. 5 to 8 are given their stereoscopic effect by painting the back of the slides with india ink and focusing a strong light on the cut surface of the glands. They were then photographed with a Zeiss apparatus with the above result.

LITERATURE.

The only investigations on the blood supply of the submaxillary are those of Kowalewsky,⁶ who described the blood supply and drew from the arrangement of the vessels certain conclusions concerning the secretion of the gland, depending upon the anatomical relations of the vascular system to the cells and the lymphatics. Kowalewsky worked upon the parotid and submaxillary of the cat and dog. He believed many instructive ideas could be gained from the different resistances of the vascular stream in different parts of the blood system as shown by complete and partial injections. His description is taken from the submaxillary gland of the cat. Both the arteria carotis communis and the vena jugularis externa were used for injection. An incomplete injection from the arterial side filled the capillary plexus in the walls of the ducts, while

⁶ Kowalewsky, Arch. f. Anat. u. Phys. Anat. Abth., 1885.

the interalveolar capillary plexus remained completely empty as the mass reached only the arterioles running in between them. He concludes that these facts indicate "the presence in the salivary glands of two vascular systems with unequal resistances; a system of diminished resistance with capillaries in the walls of the ducts, and the system of greater resistance with capillaries in the lymph spaces between the alveoli." The arteries of the salivary glands, according to Kowalewsky, as well as the ducts and veins, run in the connective tissue between the lobules. They give, in their course, small twigs that divide twice or three times and run mostly in recurrent direction in the connective tissue wall that surrounds the ducts. Here the arteries pass over into capillaries which sink quickly to reach the neighborhood of the epithelium under which they form a comparatively thick plexus. The veins from these capillaries appear in a more superficial position, change their direction so that it is parallel to the surface of the ducts and unite to form larger trunks which, at a certain distance from the afferent arteries, terminate in the accompanying veins. Small branches are also given off from the interlobular arteries which supply the sympathetic ganglia situated in the interspaces. As the ramification proceeds there is a thinning of the connective tissue wall of the salivary ducts and the capillary plexus at these points is not so well developed. The arteries and veins accompany the interlobular connective tissue until they finally penetrate into the interior of the lobules. The intralobular ducts, like those of the extralobular system, have a capillary plexus derived from the intralobular arteries. This empties into the vein that accompanies the duct. The intralobular system divides with the ducts until they reach the surface of the lobules. Arriving at this point, the terminal arteries are somewhat thicker than capillaries, but in the absence of muscle elements they can scarcely be distinguished from them. As soon as the lobular surface is reached, the arteries customarily divide into several divergent branches which form recurrent arched loops and immediately break up into capillaries around the alveoli. These vessels or vascular arcades, according to Kowalewsky, are already in the lymph spaces and send from their concave portion capillary twigs into the interalveolar lymph spaces which surround the single alveoli. From these capillary plexuses between the alveoli appear numerous short venous radicals which run in the neighborhood of the salivary tubes and soon terminate in large veins which accompany the ducts in their subsequent course. In this short description Kowalewsky does not trace the exact transition from the arterial to the venous system in various parts of the gland, nor does he discuss the important relations of the vascular and anatomical units. Moreover,

this author does not describe the vascular units in the different circulatory systems as such, nor does he consider the capsular and septal circulation and their relations to that within the lobules.

The alveolar capillaries are not situated in the lymph spaces, as Kowalewsky believes, but in the interalveolar spaces between the basement membranes of adjacent acini. Here they are limited by the reticulum fibrils that bind together the alveoli which they supply.

DEVELOPMENT OF THE ALVEOLAR EPITHELIUM AND THE DEMILUNES OF GIANUZZI.

In a pig 3 centimeters long (Fig. 9) the terminal buds of the branching column of cells forming the ductus submaxillaris indicate the primitive

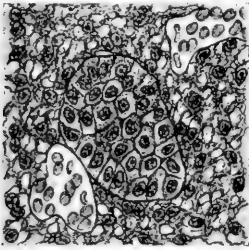


FIG. 9. Section of primitive alveolus from submaxillary of pig's embryo 3 centimeters long. Hardened in Zenker's fluid, stained by Mallory's method. $\times 650$ diameters. This drawing shows the irregular columns of the cells forming terminal bud or apex of the growing column of cells in the developing submaxillary.

alveolus in its simplest form. It is composed of a group of irregular polygonal cells embraced and enclosed in a reticulated basement membrane.

Outside of a slightly definite arrangement of the outer layer of cells, the remainder are packed irregularly within the alveolus.

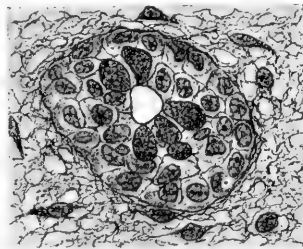


FIG. 10. Alveolus from glandula submaxillaris of pig's embryo 8 centimeters long. Hardened in Zenker's and stained by Mallory's method. $\times 650$ diameters. The arrangement of the cells in two or three layers about the lumen is now apparent, together with the beginning of the formation of the mucous globules within the cells of the inner layer.

The cells are polygonal in shape, have a definite outline and granular cytoplasm, staining a golden brown by Mallory's method. The nuclei are vesicular or ovoid, have a distinct nucleolus and considerable chromatin deposited on the linen threads. Exclusive of the regularity of the arrangement, there is, however, no morphological difference at this stage between the cells of the central and peripheral portions of the acinus. In a pig 8 centimeters long (Fig. 10) a lumen has appeared in the center of the developing alveolus and the cells are arranging themselves in two or three fairly definite layers. No marked changes are observed in the character of the parietal group of cells, but in those of the inner layer of the lumen of the

alveolus, one notes the formation of mucous globules within the cells

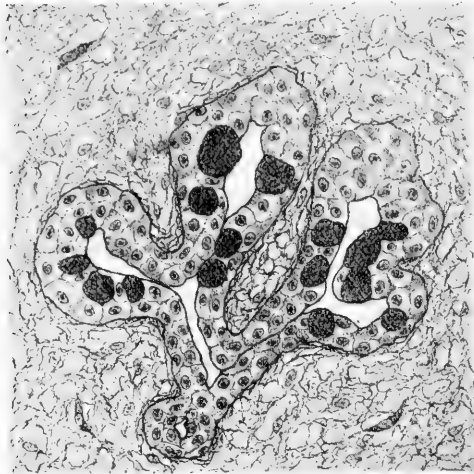


FIG. 11. Terminal cluster of alveoli from the submaxillary gland of pig's embryo 12 centimeters long. Hardened in Zenker's fluid and stained by Mallory's method. $\times 650$ diameters. The definite arrangement of the cells of the ducts and alveoli is now apparent. Mucous cells formed from the central layer are apparent. Alveolar ampullae are also well shown.

which stain a deep blue with one of the elements of the Mallory stain. The mucous globules appear to be formed in the part of the cell next to the lumen, as the nucleus is pushed off to the edge nearest the basement membrane where it begins to show some signs of intracellular pressure, evidenced by its semilunar form. At the same time the nucleus takes a red stain, while the nuclei of the parietal cells remain brown in color.

At this time the mucous cells are not much larger than those of the parietal group and their cytoplasm looks like a reticulum of

even blue lines or else as a mass of minute globules closely pressed together within the limits of the cell. At a somewhat later stage (Fig. 11) the arrangement of the cells is more definite and they are placed in two distinct layers. Mucous cells have increased in size but otherwise show the same characteristics of the cells at an earlier period. In an alveolus of a pig 18 centimeters long (Fig. 12) the mucous cells have begun to approximate laterally and, in some instances, have reached and impinged upon the reticulated membrana propria of the alveolus. The parietal cells now show evidences of pressure and are grouped off towards the reticulated membrane between adjacent mucous cells. In these instances, however, the parietal cells are not as a rule single, but occur in clumps of three or four. In many places the mucous cells are still separated from the basement membrane by an entire layer of parietal cells.

The alveoli in a pig two days old (Fig. 13) show, in general, a considerable advance in the arrangement of the mucous cells. They become larger and, as a rule, either rest upon the basement membrane or are separated from it by a very slight distance. The distended mucous

cells have increased in size, but otherwise their character is not altered. The parietal cells, however, are wedge-shaped and already begin to have some of the typical appearances of the demilune. Throughout the series of embryos there is a considerable variation in the alveoli of the same gland, but the series of illustrations represents, however, the average condition found in the alveoli at the ages mentioned. In the adult submaxillary of a pig (Fig. 14) stained by Mallory's method, there is a marked difference in the microchemical reactions of the two classes of alveolar cells. The mucous cells have increased greatly in size, the

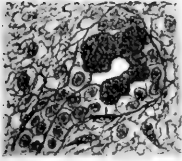


FIG. 12.



FIG. 13.



FIG. 14.

FIG. 12. Terminal alveolus from the submaxillary gland of pig's embryo 18 centimeters long. Hardened in Zenker's fluid and stained by Mallory's method. $\times 650$ diameters. Mucous cells have now in places reached the basement membrane. Parietal cells are pushed off into the spaces left between the cells of the former group.

FIG. 13. Terminal alveolus from submaxillary gland of pig two days old. Hardened in Zenker's fluid and stained by Mallory's method. $\times 650$ diameters. The mucous cells have in most cases reached the basement membrane. Parietal cells are now found here and there between them, already giving the final and definite relations of the demilunes of Gianuzzi.

FIG. 14. Terminal alveolus of submaxillary gland of adult pig, showing the final form and arrangement of the demilunes. Hardened in Zenker's fluid and stained by Mallory's method. $\times 650$ diameters. The differences in the staining reactions between the cells of the central and parietal groups are indicated.

mucous globules are slightly larger, and give the body of the cell a clearer, more glairy appearance, while the nucleus still retains its crescentic shape and is pushed off to the pole of the cell nearest the membrana propria. Much more marked changes have occurred in the parietal cells; the cytoplasm has taken on a distinct bluish tinge and is now very granular, while the nuclei are less vesicular but are still brightly stained with the orange element of the dye.

Ever since the demilunes were first described by Gianuzzi they and their functions and relations have been the subject of an extensive discussion in the literature. Stöhr, who believed that the demilunes are

mucous cells in various stages of activity, speaks of the false or pseudolunulae, classifying among the latter Pflüger's demilunes, which are the peripheral protoplasmic portions of unfilled mucous cells and membrana propria demilunes consisting of sections of thickened basement membranes. Another point which has given rise to considerable discussion is the stratification of the alveolar epithelium, many authors holding that the cells are arranged in two layers while others maintain that only a single layer exists. The conditions probably differ in different animals. In man, apparently, both groups of cells, central and parietal, touch the basement membrane, while in pigs it is not uncommon to find even in the adult many mucous cells separated from the basement membranes by demilunes. The chief point of interest in this connection, however, is the fact that the two groups develop from a double layer of epithelium.

The significance of the demilunes has been the point of several theories that have given rise to more or less discussion. Among the prominent ones are the "Ersatztheorie" of Haidenhain, "Phasentheorie" of Stöhr and the doctrine of the specificity of the demilunes suggested by von Ebner.

The "Ersatz" theory is based on the idea that there are two groups of cells, a central group with the characteristic arrangement which consists for the most part of mucous cells and a peripheral group corresponding to the demilunes which through mitosis increase and undergo a mucous metamorphosis to replace the destroyed cells of the central group. Against this theory, however, the following objections are made by Oettel:

1. That the mucous cells are not destroyed or disintegrated during the secretion.
2. Pure mucous glands without demilunes are known to exist.
3. The demilunes never show mitotic figures.

The "Phasentheorie" is based on the assumption that the mucous and parietal cells are merely different functional stages of the same elements. Stöhr and others believe that the mucous cells are not destroyed during the secretion of the gland but persist like the cells of the stomach epithelium and that the parietal cells represent the peripheral protoplasmic part of the mucous cells which are not transformed into mucous globules. Supporting this fact are the pictures obtained during the various stages of activity of the gland, which seem to suggest, according to these authors, that the cells at first have a round nucleus with only the central portion of the cell next to the lumen transformed into mucous. As the production of this substance increases, the nucleus is

pushed more and more toward the periphery of the cell, where, with the remainder of the untransformed protoplasm, it rests against the basement membrane. These with similar neighboring cells form the parietal group. In extreme cases the nuclei may be pressed flat against the base of the cell. Müller raises the following objections to Stöhr's theory:

1. The demilunes are not empty of secretion but contain secretion granules.

2. Intermediate stages between filled mucous cells and demilunes do not exist.

3. The secretion capillaries described by Stöhr with the Golgi method are simply intercellular spaces, while true demilunes have distinct intracellular secretion canaliculi.

The doctrine of the specificity of the demilunes suggested by v. Ebner is based upon the following conclusions:

1. The cells of this group contain secretion granules.

2. They contain secretion canaliculi which may be demonstrated by the Golgi method.

3. Certain substances injected into the circulation of living animals are demonstrable in the demilunes or their secretion canaliculi.

4. They react distinctly to certain microchemical tests.

From the study of the development of the demilunes in the submaxillary gland in a series of embryo pigs, it becomes patent that the doctrine of the specificity of the demilunes is the only one which is at all tenable. Aside from the various conclusions given by Müller supporting this fact, the indisputable evidence of their ancestry shows that, throughout the period of embryonic life, they are cells of an individual specific group, derived from the peripheral layer of epithelium in the embryonic alveolus. They maintain their identity throughout life and represent neither young cells which undergo, at a later period, transformation into the mucous cells of the alveolus, nor one of the functional stages of the mucous group. Embryologically and anatomically they are definite units and must be considered as cellular complexes which form definite structural elements of the alveoli of certain of the salivary glands.

CHANGES IN THE DUCT EPITHELIUM.

In a pig $4\frac{1}{2}$ centimeters long the main ductus submaxillaris is already composed of two layers of cells which are cubical in shape and not distinctly columnar. These can be followed in the main divisions of the ducts and terminate in the solid buds that form the apices of the grow-

ing ducts, which we have termed the embryonic alveoli. The cells are polygonal in shape and have deeply staining nuclei, while the cytoplasm is granular.

In a pig $8\frac{1}{2}$ centimeters long the epithelial lining of the ducts of all orders from the ductus submaxillaris to the alveolus is in the form of a double row. The character of the epithelium is not changed from the simple form shown in the earliest embryos, where a similar condition also exists, but only in the larger ducts.

In a pig $12\frac{1}{2}$ centimeters long, the rami principales, interlobulares and sublobulares are already formed. At this time the epithelium of the inner layer of the ducts of the lower orders shows a tendency to become columnar, the nuclei ovoid, with their long axes parallel to the long axis of the cell. The epithelium of the outer layer is more irregular and conical in shape, while the nuclei are rounded and vesicular. The portion corresponding to the intercalary ducts in the adult now joins the alveolus directly to the sublobular duct. This indicates accordingly that ducts of the lobular order have not yet been formed, but in these intercalated portions, the cells appear quite like the parietal cells of the alveoli, and are arranged in two definite strata.

At 19 centimeters there is no change in the ducts of the higher order, but, with the definite appearance of the secondary lobules, we note the formation of the lobular and intralobular ducts for the first time. The epithelium of both orders is in two layers, an inner cubical and an outer more irregular layer. The ducts connecting them with the acini show a considerable flattening with a tendency for the inner stratum to take the stain more intensely than those of the outer layer.

At 22 centimeters the ducts of the higher order show an increase in the columnar arrangement of the inner layer of cells; the central portions now stain a deep blue with a clearer peripheral portion on the side of the nucleus near the basement membrane. The ducts of the sublobular, lobular and intralobular order remain unchanged. Definite intercalary ducts have now been formed and appear to have but a single layer of epithelium with the long axis of the nuclei parallel to the axis of the duct.

In a pig $26\frac{1}{2}$ centimeters long the main ducts have now a distinct columnar epithelium adjacent to the lumen. This has a bluish staining pole and a clearer peripheral pole. As the ramification proceeds, particularly in ducts of the sublobular order, there is a tendency for the epithelium to become more columnar. There is no striation in the cytoplasm of the cells of the intralobular ducts. These now appear in many

places as though composed of a single layer of epithelium. Other intralobular ducts have a distinct double layer even at this stage of development.

In a pig two days old there has been scarcely any change in the character of the epithelium and the larger ducts, except that goblet cells filled with plugs of mucous stained with aniline blue are now occasionally found between the elements of the inner columnar layer. These can be observed in ducts as high as the sublobular order. Ducts of the lobular and intralobular type have in many places a double layer of epithelium but show as yet no evidences of the fibrillation observed in the intralobular ducts of the adult. Intercalary ducts in some places appear to be lined by a single layer of flattened epithelium, while in others indications of a double layer are found, but sections that pass directly through the lumen of the intercalary ducts ordinarily have only one row of epithelial cells lining them. In the adult, the height of the columnar epithelial cells forming the inner stratum of the larger ducts is considerably increased as well as the number of goblet cells found between them. In a two-day pig the goblet cells are rounded, while in the adult, unless greatly distended, they are elliptical in form. The intralobular ducts in the adult have but a single layer of epithelium, and the cell pole away from the lumen of the duct is distinctly striated. Intercalary ducts which are extremely difficult to find owing to the increase in size and the thickness of the alveolar groups, now show usually but a single layer of flattened epithelium. In each of the lobules there are a few groups of serous alveoli embedded among those of the mucous type. These are provided with intercalary ducts not dissimilar from those that enter the mucous alveoli. The serous alveoli are extremely few in number and are difficult to find in sections of the pig's submaxillary at the time of birth. But they may occasionally be noted in pigs $26\frac{1}{2}$ centimeters long coming off from intercalary ducts adjacent to a group of the regular mucous alveoli. Whether they represent a special differentiated form of alveolus concerned with the production of special elements of the submaxillary secretion is not certain, but the method of their development is obvious. They represent simply an alveolus in which the cells of the inner layer have not been differentiated into the cells of the mucous type. It does not follow, of course, that they would then be analogous to the parietal cells of the mucous alveoli, although this hypothesis must be considered. It is interesting to note, however, that in pigs of this age one finds these alveoli with a double layer of cells. It should be remembered, moreover, that in pigs

22 centimeters long it is not uncommon to meet with alveoli without mucous cells. These may be, in part, alveoli of the serous type which we find in the adult, but probably also represent a group in which mucous cells have not yet developed.

RÉSUMÉ.

1. The blood-vessels of the submaxillary gland form practically three circulatory systems:

(a) The glandular system in which the main artery enters the gland at the hilus rapidly approaches the ducts and runs with them in the interlobular spaces until the lobules are penetrated where the arteries terminate in a capillary plexus around the alveoli. From these capillaries venules are formed which follow the course of the arteries, leave the lobule at the hilus where they become duplicated into the *venae comites* of the main arteries. They now run with the arteries, giving off frequent anastomoses which pass over and under them, and finally leave the gland at the hilus to empty into the *V. facialis communis*.

(b) A system around the ducts, the arteries of which are derived from the ramifications of the main arteries of the submaxillary gland, the branches of which course in the connective tissue about the ducts forming around those of the higher orders a simple indefinite arterial plexus. The ultimate terminals pass downward and divide into a capillary network just beneath the epithelium lining the ducts. Small veins originating from the union of capillaries pass upward and unite into larger venous elements to form an irregular plexus of veins just beneath the arteries. Larger emissary veins leave this plexus and flow as tributaries into the *venae comites* accompanying the main arteries. In the interlobular system both the arterial and venous plexuses become less definite, but the scheme of the duct circulation is the same. In ducts of the sublobular order there is no definite arterial or venous plexus, the capillary plexus still persists and the arteries and veins lie above it. The same thing is true of the lobular and intralobular ducts except that the circulation about them is much simpler.

(c) The circulation in the framework. A well-marked capsular plexus is derived from vessels in the periglandular connective tissue. These run on the surface of the submaxillary gland and break up into an irregular arterial plexus formed of polygonal spaces. *Venae comites* accompany the arteries. Derivatives of this plexus give off the capillaries to supply the capsule which unite into venous radicals and flow into the accompanying veins. Occasional branches from the intralobular arteries

penetrate the membranæ limitantes and then join the plexus in the capsule. These arteries are accompanied by a single vein. Similarly, arteries are derived from the intralobular system which perforate the limiting membrane of the lobule and break up in the septum. Occasionally septal arteries will pass out through the primary or secondary septa and communicate with the capsular plexus. With the single exception of this connection between the vessels of the framework and the glandular system, the circulation within the lobules is absolutely independent. The capillaries of adjacent lobules do not anastomose. Limiting membranes are not bridged by blood-vessels.

2. The rôle played by the circulation about the ducts in the secretion of the submaxillary is uncertain. Obviously they nourish the duct epithelium and therefore any part that the latter takes in the production of saliva must be traceable to this portion of the vascular system.

3. The vascular system of the submaxillary develops *pari passu* with the ducts. The latter form the stimulus for the production of new blood-vessels. In the earliest stages the simple branching column of cells forming the submaxillary receives an arteriole which breaks up into a capillary plexus about the columns and finally empties into the vein accompanying it. The terminal buds of the cell columns are embraced by an irregular capillary plexus, the prototype of the future alveolar plexus. The circulation around each separate division of the main duct is independent, anastomoses between them occurring with great rarity. As the ramification of the ducts proceeds, they are followed by an extension of this simple vascular system. Venae comites are formed that accompany the main arteries from the sublobular interspaces to the hilus, and the simple capillary plexus about the main ducts develops into an irregular arterial, capillary and venous plexus. Finally, in a pig 18 or 19 centimeters long, the division of the ducts has increased to those of the lobular order and, as a result, a lobular circulation of simple type is finally produced. From this point the further development of the circulation is simply one of degree as the general plan is now completely established. A little later branches of the intralobular arteries perforate the limiting membrane and join the circulation developing in the capsule and the septa.

4. Like the blood-vessels of the adrenal, those of the submaxillary gland mark out the paths of development taken by the cell groups of the organ, forming, in a measure, a record of the ontogeny of its parts. This is known to be generally true of the systemic circulation and now holds for the submaxillary as well as the adrenal gland. It may then be

assumed with safety that "the angiology of an organ is in a measure the recapitulation of its ontogeny."

5. The epithelium of the ducts in early embryos consists of a solid column of cells. At an early period the lumen is formed and the cells arrange themselves in two fairly definite layers. As the ramification of the cell columns proceed, the penetration of the lumen extends upward until all the ducts as far as the small terminal buds have a double layer of cells. In a pig 8 centimeters long the lumen appears within the alveoli, the first formation of the ampullae. The size and definition of the duct epithelium increase up to the time of the adult, the cells increasing chiefly in size. At the period just before birth mucous goblet cells appear in among the columnar epithelium and the inner layer of the larger ducts. The fibrillation in the external portion of the cells lining the intralobular ducts is not manifest in sections stained by Mallory's method until after birth. Usually the ducts of the intralobular system appear to have but a single layer of cells in the adult, although in some cases, particularly in the intercalary ducts, one finds an occasional double row.

6. The alveolar epithelium consists in the pig 4 centimeters long of a solid group of polygonal cells. At a little later period these cells arrange themselves in two or three indefinite layers about the lumen or ampulla of the alveolus. In the cells of the inner layer mucous globules begin to appear. These increase in size until they finally reach the basement membrane, leaving the cells of the outer layer in the interstices between the bases of the mucous cells. In this way the mucous elements of the alveoli are formed from the cells of the inner layer, while the demilunes of Gianuzzi are derived from the parietal cells. In following so definitely the ancestry of the demilunes, it become obvious that they are definite elements in the alveolus and are neither mucous cells in one or another stage of activity, nor do they represent young mucous cells.

In conclusion I wish to express by thanks to Dr. A. W. Lee, of this department, for the painstaking care he has taken in the production of these drawings.

THE DEVELOPMENT OF THE ISLANDS OF LANGERHANS IN THE HUMAN EMBRYO.

BY

RICHARD MILLS PEARCE, M. D.

*From the Pathological Institute, University of Leipzig, Prof. Marchand, Director,
and
The Pathological Laboratory of the University of Pennsylvania.*

WITH 3 TEXT FIGURES.

The investigations upon the pathology of the pancreas carried out during the past several years have had, with few exceptions, for their definite object the determination of the existence of an internal secretion with which the islands of Langerhans and carbohydrate metabolism might be brought into harmony. The great importance to pathology of the studies carried out upon these subjects was to be found in the establishment of an anatomical and physiological basis for diabetes mellitus. That this undertaking has been followed by a good measure of success is shown by the important contributions to the pathology of the pancreas in diabetes by Opie, Ssobolew, Weichselbaum and Stangl, Wright and Joslin, and Herzog, as well as the experimental studies of Ssobolew and Schulze. Now that the relationship of a highly important physiological function to the islands of Langerhans seems to be established, it is desirable that the question of the histogenesis of the islands be put on a firm and definite basis. If the islands are wholly independent structures, as conceived by v. Hanseemann, evidence of this fact should be forthcoming from a study of their development; if, at their origin, they are indistinguishable from the proper glandular structure, evidence of this fact should be found in the same study. If the latter conception is the true one, as indicated, but not established, by the studies of Laguesse, Renault, and Diamare, then the period and the manner of the differentiation should be open to demonstration. The study of the development of the islands in the human pancreas has been very imperfectly pursued, Renault, as far as I can discover, alone having examined an early specimen.

I have been fortunate in securing during the past year a series of specimens of the human pancreas which were suitable for a systematic study of the development of the islands of Langerhans. This study

has, I think, supplied convincing proof upon points which have hitherto been in much doubt, and it affords, in my opinion, a consistent and satisfactory explanation of the development of the islands. I have been able, in addition, to confirm the results of the study of their development in normal organs, with a study of the appearances which they present under the peculiar pathological changes which affect the pancreas in congenital syphilis.

The work falls into two categories: (1) the study of the embryonic normal pancreas, and (2) the study of the pancreas in congenital syphilis. Of the second portion of the study, only those parts which confirm or aid in explaining the normal development will be presented at this time.

For the materials for this study, I am indebted to Professor Marchand, of Leipzig, to Professor Mall, of Baltimore, and Dr. Longcope, of Philadelphia, to whom I wish to express my sincere thanks.

Review of the Literature.—A comprehensive description of the development of the islands in the human embryo, I have not been able to find. Laguesse (1) in his description of the embryology of the pancreas of the sheep gives a very complete picture of the early development of the islands. At an early period, the end of the second month (embryo of 18.5 to 50 mm.), the primitive gland structure of the pancreas, composed of solid cell masses, present here and there, generally along the outer border, cells which stain more darkly than the general mass. These cells proliferate, lose their granular appearance, and form protruding loops or swellings, spheroid or ovoid in shape. They remain in connection with the tubules for some time and constitute the "primary islands" (*îlots endocrines*). Later, in embryos of about 90 mm., these structures atrophy and are replaced by similar structures formed by proliferation of the fully formed secreting tubules of the acinus. These "secondary islands" eventually become tunnelled and vascularized. Laguesse at this time, 1897, believed that they were formed not only during embryonic life but throughout adult life and represented a portion of the gland temporarily modified for a special function, an internal secretion apparently essential to foetal life. He believed, also, that it was possible for these modified structures to revert to the glandular type. Later (2), however, he modified this conception in that although he considered this transformation possible, yet he believed that some of the islands persisted as such throughout life. This change of view was due to the work of Diamare (3) who, supported by Massari (4), insisted that the islands were definite, constant, and unchanging formations, formed early in embryonic life and persisting until death. Both of these writers

attributed to the island an internal secretion. Their observations were made on the pancreas of fish.

Renaut (5) studied the development of the islands in a single pancreas of a human embryo of the third month (11 to 12 cm. long), and found it practically to be identical with that observed by Laguesse in the sheep. He also believed that the islands furnish an internal secretion, of unknown nature, of more importance in embryonic than in adult life; for in the embryo the islands reach their full development, while in the adult he considers them to be rudimentary. This is a radical change from an earlier view expressed by him (6) that the islands were lymphoglandular (*points folliculaires*) structures.

Entirely opposed to the above theory of development is that of v. Hansemann (7), who states that the islands originate late in embryonic life by a proliferation of the connective tissue cells of the stroma. The capillaries of the stroma widen and the adjacent cells become richer in protoplasm; the vessels assume a glomerular form and the cells an investing arrangement similar to that of the perithelium of blood-vessels. He finds no relation between the islands and acini, but from the intimate association between the island and blood-vessels and lymphatics, he thinks the islands are concerned in some exchange of substance between the blood and lymph.

Further detailed studies of the development of the islands of Langerhans of the human pancreas I have been unable to find. Different writers mention their presence at various periods of embryonic life, thus Gartier (8), at three months, Ssobolew (9), at six months, and Stangl (10), at about seven months, while Kasahara (11) merely states that they are numerous in the foetus.

Embryology of the Islands.—My study of the development of the islands has been carried out on the pancreases of twenty-one human embryos. Some of the material was poorly preserved and unsatisfactory for detailed study, but fortunately the better preserved material supplied the most important phases of the differentiation of the islands. The process of development which I have observed would seem to be so satisfactory that I have not deemed it necessary to wait for more material before the publication of my results. The study was carried out on serial sections, the greater part of the material having been imbedded in paraffin, but some were imbedded in celloidin. The sections were stained either with haematoxylin and eosin or with safranin and picric acid. The following list indicates the source of the material, and the length and probable age of the embryo. The length given is that from breech to vertex. The method of computing age is that recommended

by Mall (12). Series from a catalogued collection are indicated by a number in Roman characters placed after the name of the possessor.

1. Prof. Mall (No. XXII), Baltimore,	length 20 mm., probable age	47 days.
2. " " (No. XLV), "	" 28 " " "	53 "
3. Dr. Longcope, Philadelphia,	" 54 " " "	73 "
4. " " " "	" 60 " " "	78 "
5. Prof. Mall (No. XLIV), Baltimore,	" 70 " " "	84 "
6. " " (No. XXIII), Baltimore,	" 70 " " "	84 "
7. " " (No. XXXIV), "	" 80 " " "	89 "
8. " Marchand, Leipzig,	" 90 " " "	94 "
9. " Mall, Baltimore,	" 94 " " "	97 "
10. " Marchand, Leipzig,	no measurement, supposed	" 3 months.
11. Dr. Longcope, Philadelphia,	length 115 mm., probable	" 115 days.
12. Prof. Mall, Baltimore,	" 116 " " "	" 116 "
13. Dr. Longcope, Philadelphia,	" 127 " " "	" 127 "
14. Prof. Mall (No. XLVIII), Baltimore,	" 130 " " "	" 130 "
15. Dr. Longcope, Philadelphia,	" 145 " " "	" 145 "
16. " " " "	" 160 " " "	" 160 "
17. " " " "	" 160 " " "	" 160 "
18. Prof. Mall, Baltimore,	" 170 " " "	" 170 "
19. Dr. Longcope, Philadelphia,	" 200 " " "	" 200 "
20. Prof. Mall, Baltimore,	" 205 " " "	" 205 "
21. " Marchand, Leipzig,	" 210 " " "	" 210 "

The earliest stage studied (Nos. 1 and 2) was that in which the glands are represented by branching processes widely separated by a rich framework of connective tissue. The connective tissue is about equal in amount to the glandular portion of the organ, and is the most striking feature throughout the early stages of development. It disappears slowly but even in the fifth and sixth months of foetal life still arrests the attention. Its presence is of great assistance, for it marks off the anatomical units of the pancreas in a way that greatly facilitates their study. Each group of cells is thus distinctly separated from neighboring groups, rendering the study of such a group in serial sections possible and easy. This anatomical condition made it very easy, as will be shown, to trace the relation of an island to its acinus. In this early stage it was not possible to find any arrangement of cells suggestive of the formative stages of the islands, nor was it possible to find the peculiar cells with rich eosinophilic protoplasm which Laguesse and Renaut compare to the parietal or oxyntic cells of the gastric tubules, and which they consider to be the earliest differentiation of cells destined to form islands.

In the next preparation (No. 3), from an embryo 54 mm. in length, the early development of the islands can be easily seen. The freshness

and excellent preservation of this specimen adapted it for a most careful and accurate study of the relations and differentiation of the cells. The glands are still represented by branching processes of cells, lying in an abundant stroma, but here and there a few processes which have become tubular are seen. The cells are closely crowded together, especially at the periphery or growing portion of the process. They have rather deeply staining, round or oval vesicular nuclei, and a very small amount of slightly granular protoplasm. The protoplasm is readily demonstrable in those cells forming tubular processes; the nuclei are seen at the periphery, while the clear protoplasm at the attachment of the cells to the basement membranes forms a ring about the lumen. Here and there, and generally at the periphery, in either the solid or tubular processes, is occasionally seen a much larger cell with deeply staining chromatin and either with clear or eosinophilic protoplasm. These cells correspond to those described by Langerhans and Renault, but I have not been able to convince myself

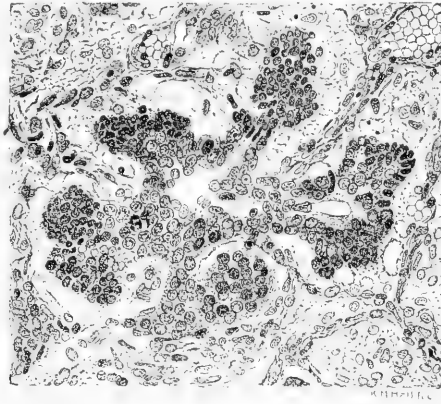


FIG. 1. Pancreas of an embryo 54 mm. in length. Early stage of the differentiation of an island of Langerhans. A round mass composed of cells rich in protoplasm is seen continuous with the periphery of the gland.

that they represent the primary differentiation leading to the formation of the islands. They always occur singly and the arrangement of the chromatin is suggestive of karyokinesis. Entirely distinct from them are the small groups of cells lying at the side of a glandular process, but in direct continuity with it (Fig. 1). Each group is composed of ten to fifteen cells which have a round, lightly staining nucleus, and a comparatively large amount of finely granular protoplasm staining deeply with eosin. The cells are closely applied one to the other and form round or oval masses which can readily be distinguished from the acinar process from which they arise. Sometimes they lie in a semilunar projection of the gland without distinct connections; but in following the group through a series of sections, the continuity with the gland can generally be demonstrated. The masses are generally distinctly separated from the surrounding connective tissue by a narrow space, which gives the effect of a capsule. This differentiation of cells represents, I believe, the earliest stage of the development of the islands, and is identi-

cal with that described by Laguesse in the sheep, and later by Renaut in the human embryo.

In another preparation (No. 4) of about the same age, although the preservation is also perfect, this differentiation is not so distinct. The study of this preparation added little to the above description.

Very little information was obtained from a study of preparations 5, 6 and 7. The sections had evidently been prepared for other purposes than the study of such minute details as this investigation required. The general conformation of the acinar processes can be readily made out, and in places groups of cells suggesting those described above are seen; but a study of their finer characteristics is impossible.

In preparation No. 8 (embryo of 90 mm.) the tubular character of the acini is more prominent, and the solid masses of cells representing the primitive islands stand out distinctly by contrast. The islands are much larger than in No. 3, being made up of from twenty to forty or more cells, and are still in close relation to the acinar processes from which they originate. The tendency of their protoplasm to stain intensely with eosin is more pronounced than in the earlier periods. In this specimen the islands exhibit the first stage of vascularization which is shown by the presence of two, three, or four red blood corpuscles lying here and there between the cells. Occasionally in large islands a small capillary vessel filled with red blood corpuscles protrudes, generally from the acinar side, towards the center of the island. The cells of these larger islands show a tendency to form the intercapillary columns or groups characteristic of the later stages of development. About the islands the reticulum is somewhat differentiated so as to form a distinct capsule composed of one or two layers of cells. Besides this more advanced stage of development, the early stages described in No. 3 are still met with. In this early period no islands were found in the head of the pancreas, which is of interest in view of the observation of Opie (15) that in the adult, the islands are most abundant in the tail and body of the organ.

Preparation No. 9 shows greater vascularization but does not differ otherwise from that just described.

Preparation No. 10 is a perfectly preserved pancreas from a foetus believed to be of the third month; it presents many points of interest. Numerous primitive islands are scattered through the tail and body, while for the first time, a few are seen in the head. These last, however, represent the very early stages of development. Although most of the islands are in intimate connection with the acinus, an arrangement is frequently seen which indicates the manner in which the island eventually becomes separated from the acinus. As illustrated

in Fig. 2, an island may be almost entirely separated from the acinus; the only evidence of continuity being a solid stalk-like process of cells. In the acinar portion of this process, a gradual transition of the cells from the type of the gland to that of the island may be traced. Most of the cells in the process are identical almost with those in the island. Followed through a series of sections, such an island has no connection with the acinus other than this solid process. The connecting process is in some instances short and broad, in others long and narrow; occasionally it may be constricted by the surrounding tissue as though about to be completely separated. Indeed, in this series completely separated islands are seen in the splenic portion for the first time.

A careful study of this stage of the development has convinced me that the separation of the island is brought about by an encroachment of the connective tissue, causing an attenuation of the connecting cells and their final disappearance between the island and acinus. The island then lies free to one side of the primitive acinus in a mass of connective tissue; a condition just the reverse of that in the adult pancreas. Later, in the fifth and sixth month, when the rapid development of the acinus occurs, the glandular elements surround and enclose the island, and it then occupies the center of the lobule. The isolated appearance of the islands at this period of separation recalls and seems to support v. Hanse-
mann's view that the islands develop from the cells of the connective tissue. Without the knowledge of the earlier stages of proliferation and temporary connection with the acinus which I have described, their isolated position would indeed be inexplicable. From v. Hanse-
mann's description, I cannot discover that he studied embryos of a period corresponding to that represented by No. 3 of my series.

The advanced vascularization at this stage affords evidence of the manner in which the vessels enter the island. Unlike the glomerulus of the kidney, to which the island is somewhat analogous owing to its very rich capillary network, we have not one, but several afferent as well as

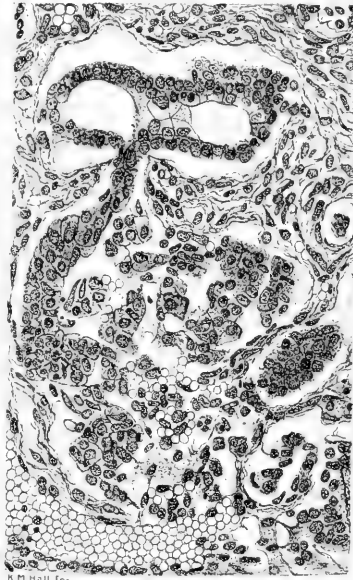


FIG. 2. Pancreas of an embryo of about the third month. A fairly well developed island of Langerhans is seen connected with the gland acinus by a solid process of cells.

efferent vessels. In those islands still connected with the acinus, a vessel does not accompany the connecting process of cells. By following an island through a series of sections, from four to seven branches, without definite arrangement however, may be seen entering from the periphery. The vessels at the periphery anastomose freely and form a network much richer than that about a glandular structure of equal size. At this period the cells between the capillary network of the island assume a definite arrangement in columns or rows.

If the development here described is compared with that observed by Laguesse and by Renaud, an agreement is found only in regard to the method of primary differentiation. These early investigators failed to observe the stage of the process in which the solid column of cells connects the island with its acinus and therefore failed to note the gradual separation leading to final isolation of the island.

The changes just described represent the last important phases in the differentiation of the islands. In the period represented by preparations 11, 12, 13, and 14, the increase in size, the progressive vascularization, and the appearance of a fine reticulum along the vessels may be studied. Occasionally an island may be seen in continuity with its acinus, but this appearance is now unusual. In preparations 13, 14, 15, 16, 17, and 18, the glandular elements may be seen gradually surrounding the islands, while in preparations 19, 20, and 21 this process is completed and the island is seen in the center of its acinus, the position it occupies in the pancreas of the adult.

A number of specimens of the pancreas of children born dead during the last month of pregnancy and at term, as well as of infants surviving a few hours or days, have been examined. Except for slight differences in the amount of granulation of their cells, the islands appear identical with those of the adult. Specimens of this period, the blood-vessels of which are injected with carmine, show the extraordinary vascularity first described by Kühne and Lea (17), but which is not more prominent than may be seen in the adult pancreas.

Syphilitic Pancreatitis of the New-born.—Confirmatory evidence of the development above described has been furnished by a study of the changes occurring in that pancreas in congenital syphilis. This condition, first accurately described by Birch-Hirschfeld, consists of extensive sclerosis of the pancreas with simple atrophy of the glandular structures. The atrophy in the advanced stages is so extreme that the larger ducts, the islands, and a few fragments only of glandular tissue remain.

The persistence of the islands in contrast to the extensive atrophy of the glandular structure is a striking feature of this lesion. In Birch-

Hirschfeld's description the islands are not mentioned. Schlesinger, (14), Ssobolew, (9), and Opie, (15), however, call attention to their persistence in even the most advanced examples of sclerosis.

I have studied the pancreas of congenital syphilis for the purpose of obtaining evidence of arrested development of the islands. The increase of connective tissue isolates these structures so distinctly from the remnants of glandular tissue that their relations may be readily studied. In six cases examined, I found frequently a persistence of the solid mass of cells connecting the island with the acinus.¹ I believe that this appearance represents the arrested development of the island at the period corresponding to preparation No. 10. At this period (third month) the amount of connective tissue in the normal pancreas is very great, and the rapid proliferation of the glandular portion of the pancreas characteristic of the fifth and sixth months has not commenced.

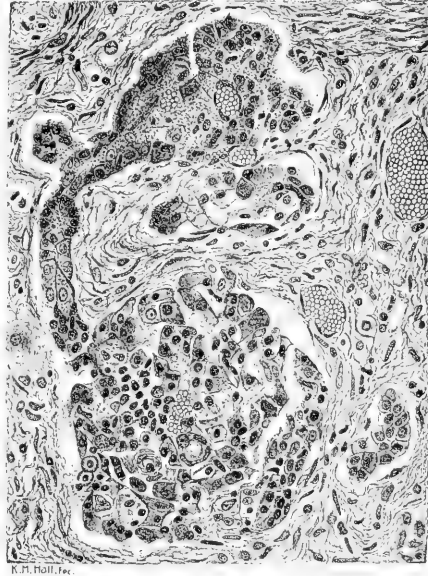


FIG. 3. Syphilitic pancreatitis in a foetus of the seventh month. Arrested development of the island; the persisting solid process of cells still connects the island with the glandular acinus.

Syphilis of the pancreas has been observed as early as the fifth month (Müller, 16), but there are no observations to prove that it does not occur earlier. The increase of connective tissue, which is the characteristic lesion in the pancreas, causes not only an atrophy of existing glandular structures, but what is more important, prevents the further development of the gland. The glandular tissue is represented by small, irregularly scattered gland groups; the ducts are prominent; the islands are arrested at the stage in which they are still connected with the acini. The microscopic picture of the normal pancreas at the end of the third month is very similar to the syphilitic pancreas

¹Opie, in his account of two cases of congenital syphilis, describes and pictures this condition.

at the sixth or seventh month, except that the latter has a larger proportion of connective tissue. In other words, at the latter period, we have the development of the third month plus the connective tissue produced by the syphilitic process. This arrest of development is shown in Fig. 3, which is taken from a specimen of syphilitic pancreatitis in a foetus 21 cm. long.

Summary.—The islands of Langerhans (embryo of 54 mm.) originate through a proliferation and differentiation of the cells of the primitive secreting tubules. The differentiated cells characterized by a rich, finely granular, eosinophilic protoplasm lie as small round or oval masses in direct continuity with the cells of the tubule. Later (embryo of about the third month), the attached portion becomes constricted, and lengthening, forms a stalk-like, solid process of cells connecting the island with the acinus. At this period, a few entirely isolated islands are present. A separation takes place and apparently is brought about by the pressure of the investing connecting tissue. Vascularization has now occurred. In still later stages a progressive vascularization, increase of cells, arrangement of the cells in columns, and appearance of a fine reticulum are observed. The rapidly forming glandular structures finally surround the islands which then occupy the centers of the lobules.

In syphilitic pancreatitis of the new born, a condition in which the normal development of the pancreas is arrested by a rapid proliferation of connective tissue, confirmatory evidence of this mode of development is supplied by the presence of solid processes of cells connecting the islands and acini.

The demonstration of the differentiation and final independence of the islands of Langerhans as here given offers an anatomical basis for the theory, so strongly supported by pathological and experimental observations, that the islands have a physiology independent of the glandular portion of the pancreas.

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A CONTRIBUTION TO THE STUDY OF THE MECHANICS OF THE SPINE.¹

BY

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Our present knowledge of spinal mechanics and of the motions of the spine is of an inexact and unsatisfactory character. The books on anatomy contain for the most part loose descriptions of spinal movements and few careful investigations have been made. An exception is the work of Hughes (3) on the rotation movements of the spine.

The chief study of spinal mechanics has been made in connection with lateral curvature by orthopedic surgeons rather than by anatomists. They have done this in the attempt to explain the phenomenon of "rotation" which occurs in lateral curvature. Any patient who develops a marked degree of side bending of the spine shows also a twisting of the laterally curved portion of the spine upon a vertical axis. To the latter phenomenon the name "rotation" has been applied. This association of twisting with lateral curvature has always been regarded as a most obscure phenomenon and Lorenz (1) in his book on scoliosis agrees with a quotation from Bouvier (2) "Man müsste ein Euklides sein, um dieses Räthsel zu lösen."

In the attempt to solve this problem a very large amount of literature has accumulated without obvious practical result (4). But essentially, all of this work has been done from one point of view and the human spine has alone been investigated with the exception of occasional reports of cases in animals (5) and some experiments on dogs by Wullstein (6). The question has either been taken up from the point of view of the pathological changes found in scoliosis and theories constructed to account for these, or suppositions of a purely theoretical character have been formulated embodying general mechanical principles. The shape of the individual vertebrae, normal and distorted, has been studied, the physiological curves have been investigated, the shape of the articular processes has been formulated and the most complicated and confusing results have

¹ Read before the Boston Society of Medical Sciences, May 19, 1903.

been reached. In this literature one reads of hypomochlions, tangents, horizontal and lateral axes, centres of motion, etc., and mental confusion must result from a careful study of these theories.

One way of approaching the question has been left practically untouched except for a single experiment of Bradford's (7). This line of investigation would be to see what the normal spine would do in a scoliosis artificially produced and again to inquire if there is anything in the normal movements of the spine to account for this phenomenon of rotation in connection with lateral curvature. Perhaps the most popular theory to-day is that of Meyer (8), proposed in 1865 and then falling into discredit until taken up by Albert (9) in 1899. This theory maintained that rotation occurred because the human spine consisted of two columns, the column of bodies and the column of arches, and that these two columns possessed a different degree of elasticity. In lateral curvature, therefore, rotation occurred because these two elements of the human spine reacted in different degrees to side bending and one lagged behind the other in side yielding. In some experimental work upon the cadaver undertaken by the writer at the Harvard Medical School (10) certain phenomena were observed which seemed to have a bearing on the occurrence of rotation in lateral curvature, and Prof. Thos. Dwight suggested that it might be worth while to investigate the question whether the spine did not follow certain general laws of mechanics and did not behave as would a flexible rod under similar conditions. The writer is indebted to Prof. Dwight not only for his anatomical material but for his continued advice and criticism throughout the work.

With the aid of Prof. I. N. Hollis, of Harvard University, two general laws governing flexible rods were formulated as follows:

(A) Although a straight flexible rod (e. g., a quadrilateral rod of rubber or lead) may be bent in one plane without twisting, if such a rod is already bent in one plane it cannot be bent in another plane without twisting.

(B) Although a straight flexible rod may be twisted without acquiring a side bend, a flexible rod already bent in one plane cannot be twisted without acquiring a side bend.

The following experiments were then undertaken:

1. A quadrilateral rod of rubber was fixed at its lower end and then bent forward away from the observer. The top of the rod was then bent to the left and the front of the rod was observed to twist to the right.

2. A similar rod of lead followed the same rule under the same conditions.

3. The backbone of a fish followed the same rule under the same conditions.

4. The backbone of a cat followed the same rule under the same conditions.

5. The spinal column of a human cadaver with ribs attached but with the sternum removed when bent forward to the left, twisted in the same way as the flexible rods described above and could not be made to twist in any other way when bent forward to the left.

6. The spine of the living model, bent in this way, twisted in the same way and when bent forward to the left could be made to twist in no other way.

The following experiments in twisting were then made:

(1). A quadrilateral strip of rubber was fixed at its lower end and bent forward away from the observer and then twisted at its upper end with its front surface to the left. In its upper two thirds appeared a lateral curve to the right as seen by the observer from the median plane behind.

(2). A similar strip of lead behaved in the same way under the same conditions and it was noticeable that the lower third or quarter of the strip did not share appreciably in either the twisting or the side bend when the force was applied to its upper free end.

(3). The backbone of the human cadaver, fastened in a vise at its lower end, and twisted by its upper end, showed a similar lateral bend, beginning when fairly erect in the dorso lumbar region.

(4). The spine of the living model in active and passive twisting showed a similar curve to the same side under the same conditions.

Here then were certain tangible facts to be looked into. The suggestion from the above mentioned experiments is that in its association of side bending and twisting, the human spine follows certain more general laws than are to be formulated by a study of its especial structure, in short that its general behavior is governed by the laws which would control any flexible rod of similar shape, size, and elasticity.

The history of the spine in its evolution is of interest. In the Cyclostomata the vertebral column consists of a non segmented homogeneous cartilaginous rod. Articular processes first appear in the Rays and Teleostei. The backbone of the lower fishes consists of a series of bony discs bound together by elastic intervertebral discs. It would seem from the history of the spine as if articular processes developed concomitantly with the elaboration of structure, as if they were incidental to its use rather than factors determining of themselves its types of motion. In the human spine, from this point of view, they would be regarded rather as helping it to carry out its functions as a flexible rod than as causes of its particular movements.

An experiment was then undertaken to determine whether the articular

processes were a factor in causing rotation in side bending and also whether Meyer's theory of rotation was true.

In the spine of an adult cadaver from the dissecting room the column of vertebral bodies was separated from the laminae and arches by cutting through the pedicles and the column of bodies was observed by itself.

1. When fixed at the lower end and bent forward and to the left, the column of bodies turned with its front to the right, twisting to the right as did the intact spine and apparently to the same extent. In all other motions it behaved in the same way as did the intact spine.

2. When fixed at the lower end and twisted with its front to the left, a lateral curve to the right of the same character and extent as in the intact spine occurred. In all other manipulations, also, it behaved as did the intact spine. Even the absence of torsion movement in the lumbar region in the intact spine, supposed to be due to the close interlocking of the articular processes, was present to the same extent in the column of vertebral bodies alone. The column of arches on the other hand did not behave as did the intact spine in its relation of twisting and side bending as demonstrated in a former paper. The whole experiment was repeated with similar results on a second cadaver. It would therefore seem reasonable to conclude:

- (1) That the articular processes do not cause the torsion of the spine in side bending.
- (2) That torsion of the spine in lateral bending is not caused by the fact that the spinal column is made up of two components, the column of bodies and the column of arches.
- (3) That the column of vertebral bodies is the determining factor in this association of movements.
- (4) That the column of vertebral bodies alone and the intact spine behave alike and behave as would any flexible rod of the same shape, size, and elasticity.

The bearing of this is obvious in its practical aspect. There is no such thing, as is generally taught in anatomies, as a pure side bending of the spine. Every side bending of the whole spine and every side yielding of any part of the spine is also a torsion, and carries with it from the first an element of torsion. Every twisting of the spine carries with it a side bending of the spine and there exists no such movement as a pure twist or torsion of the spine.

There are, therefore, apparently only three types of spinal movement:

1. Forward bending (flexion).
2. Backward bending (extension).
3. { Side bending } a compound movement of the two elements which
 { Torsion } can not be disassociated.

This is the case because from a mechanical point of view the spine is a flexible rod permanently curved by the physiological curves in the antero-posterior plane. Side bending necessitates movement in another plane and consequently a twist, and twisting for a similar reason causes side bending.

In lateral curvature the problem is simplified by a recognition of these facts. Any lateral yielding of the spine at any part must be accompanied by a twist of the spine and the transverse axis of the shoulder girdle will no longer be parallel to that of the pelvis. As the lateral curve increases, the twist will tend to increase. But in addition to being a flexible rod the human spine must be regarded as a flexible rod endowed with a sense of equilibrium and adjustment. In a general way in the upright position the head must be kept over the base of support and the head pointing approximately straight ahead. This is a matter of continual and instinctive muscular effort on the part of the patient. If now a lateral curve has been acquired, the shoulders will be twisted in their relation to the pelvis and as the curve increases, the twist would naturally increase. That a twist exists in each case of lateral curve is easily seen in any case of postural lateral curvature looked down on from above in the standing position, when the shoulders can be seen to be no longer parallel to the pelvis. But the twist cannot increase beyond a certain point because of the patient's instinctive effort to keep the shoulders parallel to the pelvis. The lateral curve is a present and probably increasing factor, and to bring the shoulders again parallel to the pelvis, a compensating twist must be added to the one already existing which results in the phenomenon known as rotation and enables the shoulders to be again brought into approximate parallelism with the pelvis. To this resultant combination of two twists which results in the prominence of the ribs on one side of the spine, or of the transverse processes of the lumbar vertebrae on one side of the spine, or to both together, the name "rotation" has been applied in the nomenclature of lateral curvature.

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THE PHYLOGENY OF THE PALMAR MUSCULATURE.

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WITH 11 TEXT FIGURES.

Writing in the nineties of the nineteenth century, Leche (1893) introduces his account of the intrinsic muscles of the mammalian hand with the following words: "Da die myologische Literatur noch keine Materialien enthält, welche für eine vergleichende oder auch nur zusammenfassende Darstellung der Handmuskulatur genügt, und da ausserdem die Nomenclatur der verschiedenen Componenten dieser Muskelgruppe ausserordentlich schwankend ist, halte ich es für das Geeignetste eine rein descriptive Darstellung der wichtigeren Befunde bei den verschiedenen Säugethierordnungen zu geben." Although this indictment may not in all its particulars be as pertinent now as it was, there are still remaining for solution many questions concerning the fundamental plan of the mammalian hand muscles and their phylogenetic significance, and the following pages record an attempt to diminish the number of these.

In a previous paper (1903), in which the flexor muscles of the forearm were considered from the phylogenetic standpoint, I showed that the flexor sublimis digitorum had been evolved by the union of certain portions of the antibrachial flexor mass, which primarily terminated at the wrist joint, with the most superficial layer of the intrinsic hand musculature, part of the latter undergoing degeneration to form the terminal portions of the tendons. The profundus tendons, on the other hand, were evolved from a deeper layer of the palmar aponeurosis and the lumbrical muscles represent a layer of palmar muscles which originally arose from that aponeurosis. I did not attempt, however, in that paper, a complete reconstruction of the history of the palmar musculature, and I now propose to correct that omission as far as possible by recording the results of a comparative study of the palmar musculature of the same series of forms as were employed in the earlier paper. These results are based mainly on the study of serial sections.

I. THE PALMAR MUSCLES OF THE URODELOUS AMPHIBIA.

The muscles of the Urodele hand are arranged in four layers, for which the terminology employed by Eisler (1895) is quite satisfactory. These layers are (1) a layer of *flexores digitorum breves superficiales* (Fig. 1, *F. B. S.*) arising from the palmar aponeurosis, (2) a layer of *flexores digitorum breves medii* (*F. B. M.*) also arising from the palmar aponeurosis, (3) a layer of *flexores digitorum breves profundi* (*F. B. P.*)

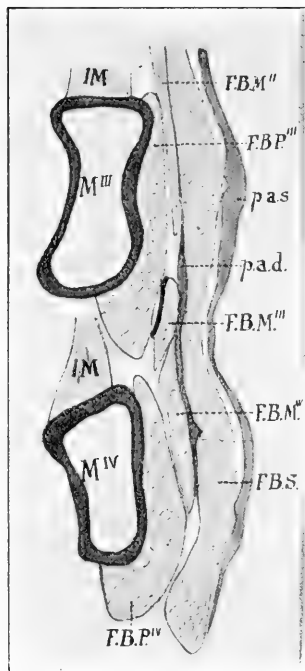


FIG. 1. Transverse section through the third and fourth metacarpals of *Amblystoma tigrinum*. *F. B. P.*, flexor brevis digitorum profundus; *F. B. M.*, flexor brevis medius; *F. B. S.*, flexor brevis superficialis; *I. M.*, intermetacarpalis; *M^{III}* and *M^{IV}*, third and fourth metacarpals; *p. a. s.* and *p. a. d.*, superficial and deep layers of the palmar aponeurosis.

arising from the carpals and metacarpals and (4) a layer of *intermetacarpals* (*Im*). A very considerable amount of similarity exists in the arrangement of the various digital slips derived from or composing each of these layers, although departures from the general plan occur in the marginal portions of some of the layers.

The *flexores digitorum breves superficiales*.—The origin of these muscles in *Amblystoma* is a curved line whose concavity is directed proximally and which is in the substance of the palmar aponeurosis, dividing this into a superficial and a deeper layer (Fig. 1, *p. a. s.* and *p. a. d.*). The muscular sheet arising from this line soon divides into portions corresponding to the digits, indeed, in some cases the portions are separate from their origin. The general plan for most of the portions may be briefly described as follows, according to what occurs in the third digit (Fig. 2). This portion divides into three slips, (1) a median one (*F. S.*) which underlies the tendinous prolongation of the palmar aponeurosis to the digit and eventually divides to be inserted into either side of the fibro-cartilage of the metacarpo-phalangeal joint, and (2 and 3) two lateral slips (*F. S'*) which also insert into the sides of the metacarpo-phalangeal fibro-cartilage, uniting as they do so with the lateral slips of the flexor digitorum brevis profundus. In the fourth digit the arrangement is essentially the same as in the third, but in the index and minimus only two slips are formed from each portion, the ulnar one being wanting in the index and the radial in the minimus.

From the ulnar border of the muscle an additional portion is separated off which becomes intimately associated with the large ulnar slip of the flexor brevis profundus minimi digiti and forms what may be regarded as an *abductor minimi digiti*. At its origin it is associated with the insertion of the flexor carpi ulnaris, indeed, the fibres of this latter muscle are to a certain extent continued directly into the abductor, additional fibres being added, however, from the ulnar carpal bone.

The *flexores digitorum breves medii* have essentially the same arrangement as do the superficiales. They arise from the dorsal surface of the palmar aponeurosis and are inserted into the fibro-cartilages of the metacarpo-phalangeal joints of each of the four digits. The slips for the medius and annulus arise together and at first form a single muscle, but later on they separate and that for the annulus divides into three slips (Fig. 2, *F. M.*, *F. M'*. and *l*) which become associated with three corresponding slips of the flexor brevis profundus and are inserted with them. The portion for the medius divides into two slips only, comparable to the ulnar and median slips of the annulus, and in the index and minimus only two slips are formed, a radial one being lacking in the index and an ulnar one in the minimus. The insertion in both these digits is, however, in association with the corresponding slips of the flexor brevis profundus.

The *flexores digitorum breves profundi* are four distinct muscles. They arise from the carpal bones and as they are traced distally each is divided into two lateral slips (Fig. 2, *F. P.*) by a median slip which arises from the palmar surface of the metacarpal (*F. P'*.), so that distally three profundus slips may be recognized in each digit. These unite, as has already been stated, with slips from the medii and superficiales to insert into the metacarpo-phalangeal fibro-cartilages. The

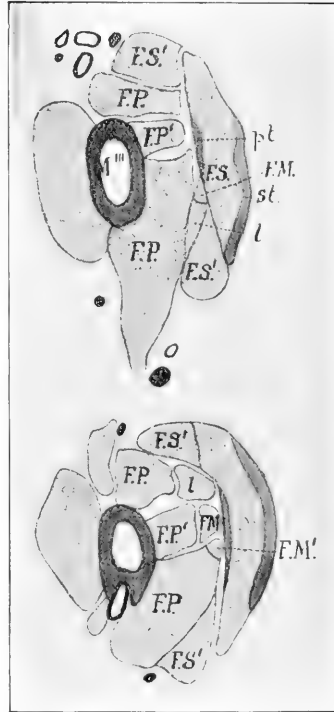


FIG. 2. Transverse section through the third and fourth digits of *Amblystoma tigrinum*. *F. M.*, flexor brevis medius; *F. P.*, flexor brevis profundus; *F. S.*, flexor brevis superficialis; *l*, one of the lateral portions of the flexor brevis medius; *pt.* deep palmar aponeurosis; *st.*, superficial palmar aponeurosis.

radial slip of the muscle of the index and the ulnar one of that of the minimus are larger than their fellows and the ulnar slip of the minimus becomes intimately associated with the ulnar portion of the flexor brevis superficialis which has been referred to above as forming the abductor minimi digiti.

The *intermetacarpales*, as their name indicates, extend across between adjacent metacarpal bones (Fig. 1, *Im*). They are consequently three in number and each has a somewhat oblique course across the intermetacarpal interval in which it lies. A muscle takes origin from each side of the fourth metacarpal and extends distally to be inserted, the one into the radial side of the fifth metacarpal, and the other into the ulnar side of the third; the third muscle arises from the radial side of the third metacarpal and is inserted into the ulnar side of the second.

In addition to these muscles, which are the hand muscles proper, there is in the third digit a strictly digital muscle, the *interphalangealis*, which arises from the palmar surface of the distal portion of the proximal phalanx and is inserted into the fibro-cartilage of the proximal interphalangeal joint of the digit.

I have endeavored in this description to be as brief as possible, since, so far as the final object in view, namely, the phylogeny of the mammalian hand muscles, is concerned, a minute account of the amphibian muscles seems unnecessary. What is of importance is a clear perception of their definite arrangement in layers, and a word seems advisable with reference to the relation of these layers to other structures. For unless definite dividing planes marked out by other structures can be recognized it will be a matter of no little difficulty to homologize the layers found in higher forms with those occurring in the group now under discussion.

In this connection one's thoughts naturally turn to the nerves as offering possible guides, and to a certain extent they do. It is not, however, in the details of their distribution to the individual muscles that they are of value in this respect, but rather in their general course and distribution. I do not intend to discuss here the significance of nerve supply in the identification of muscles; I have already in a previous paper (1903) referred to this question. I may say, however, that from what I have observed it seems clear to me that too much importance has been attached to the nerve trunks from which the various individual limb muscles are supplied. Authors have been too apt to assume that what is termed the ulnar nerve, for example, in one form is the exact equivalent of the similarly named nerve in another form, and have concluded either that equivalent muscles may have entirely

different innervations or with Gegenbaur (1889), that muscles though similar in all other respects but differing in their innervation are entirely different structures. Gegenbaur bases his conclusion on the assumption that the muscle is the end organ of a motor nerve, and, granting this and granting also that the principal nerve trunks of a limb are throughout exactly equivalent, his conclusion is logical. But there is evidence to show that the second assumption is unwarranted. In other words, the muscle may be regarded as the end organ of the nerve fibre, but that fibre need not in all cases follow the same path to reach its destination; in some cases it may follow the path marked by the ulnar trunk and in another that indicated by the median. The origin and termination of a nerve fibre are in all probability definite in their relations, but the relations of the intervening portion of the fibre may vary greatly. The nerve will follow in general the path of least resistance and this may carry it in one case into one of the larger trunks and in another into a different one, and we may thus have equivalent muscle fibres supplied from different nerve trunks, but yet by equivalent nerve fibres.

But the lines of least resistance which the main nerve trunks will tend to follow are to a marked extent definite, being largely associated in the limbs with the arrangement of the muscles in layers. Consequently, unless there be sufficient reasons to the contrary, the position of the main nerve stems may be taken as guides for the homology of certain of the muscle layers, especially in the amphibia and reptilia, in which there is great similarity in the arrangement of the main nerve trunks. It is of importance, therefore, to indicate the general arrangement of the principal nerves with reference to the muscle layers in the amphibia.

The nerves of the amphibian forearm are three in number, a *ramus profundus*, a *ramus superficialis ulnaris* and a *ramus superficialis medialis*. Of these the last is confined entirely to the forearm so far as its muscular distribution is concerned, the other two being continued into the hand. The *ramus profundus* at the wrist rests directly upon the carpal bones and as it is traced distally curves to lie between the *flexor brevis profundus III* and the *flexor brevis medius II*, later on breaking up into a number of branches which supply the muscular slips associated with the second and third digits and with the radial side of the fourth. The *ramus superficialis ulnaris* at its entrance into the hand also lies directly upon the volar surface of the carpus and is continued onward between the ulnar slips of the *flexor brevis profundus* and *flexor brevis medius*, eventually breaking up into

branches for the muscles inserted into the fifth digit and the ulnar side of the fourth.

The position of the main stems of the two nerves is therefore in the interval between the flexores breves profundi and the flexores breves medii, and there are consequently in the Urodeles two layers of muscles superficial (volar) to the nerves, namely, the flexor brevis medius and the flexor brevis superficialis, and two dorsal to them, namely, the flexor brevis profundus and the intermetacarpales.

For the separation of the layers of each of these pairs no assistance is obtainable from the nerves, but in the case of the volar pair the separation is clearly indicated by the deeper layer of the palmar aponeurosis, while the position and direction of the intermetacarpales render them readily distinguishable from the flexores breves profundi.

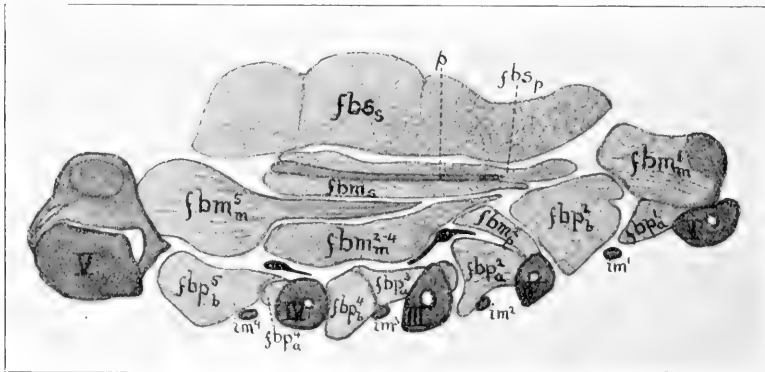


FIG. 3. Transverse section through the hand of *Liolepisma laterale*. *fbs_s*, superficial layer of the flexor brevis medius; *fbm_m*, middle layer of the flexor brevis medius; *fbm_p*, deep layer of the flexor brevis medius; *fbp_a*, muscles of the flexor brevis profundus which insert into their own digits; *fbp_b*, muscles of the flexor brevis profundus which insert into adjacent digits; *im*, ligaments representing the intermetacarpales; *p*, palmar aponeurosis which gives rise to the deep tendons to the digits.

II. THE MUSCLES OF THE REPTILIAN HAND.

I have studied the hand muscles of the lacertilia from serial sections of *Liolepisma laterale* and *Callisaurus draconoides* and also by dissection of a fully grown specimen of *Iguana tuberculata* Gray, opportunity for the examination of the last having been afforded by the courtesy of my colleague, Professor J. E. Reighard. The dissection of the iguana proved to be of very great assistance in elucidating the extremely complicated appearances presented by the transverse sections of the other

species, since, owing to the development of intersecting tendinous bands in certain of the layers, whereby they had the appearance of being composed of a number of distinct slips, and, further, owing to the lack of distinct layers of fascia separating some of the layers, it was by no means easy to recognize the true significance of some of the muscles.

As pointed out in my paper on the forearm flexors (1903), the superficial aponeurosis which covers the flexor brevis superficialis in the amphibia is wanting throughout the greater part of its extent in the reptilia, so that the muscle is exposed completely on the removal of the integument. On the other hand, one finds a strong aponeurosis beneath the flexor superficialis (Fig. 3, *p*), arising from the distal edge of the volar cartilage or ossification (Figs. 4 and 5, *vc*) and passing distally to become the profundus tendons. This beyond question is comparable to the aponeurosis which separates the middle and superficial layers in the amphibia and may therefore serve as one of the orientation planes for the comparison of the muscles in the two groups, the position of the palmar nerves, which is quite as distinct and definite as in the amphibia, marking a second plane. The muscle tissue lying between these two planes may be compared with the amphibian flexor brevis medius, that immediately dorsal to the nerve layer to the amphibian flexor profundus, and, finally, more dorsally still the equivalents of the intermetacarpals should be found.

Working on this basis one at once observes that the superficial and middle layers are much more complicated than in the amphibia. It will be remembered that in that group the lateral parts of each portion of the flexor brevis superficialis unite toward their insertion with the profundus slips and that a similar fusion of the slips of the medius and profundus occurs. This condition becomes in one sense emphasized in the reptilia in that slips separate from both the superficialis and medius to form distinct muscles and, indeed, distinct muscle strata, which unite with subjacent layers at their insertions, and it is accordingly possible to recognize in the flexor superficialis a *stratum superficiale* (Fig. 3, *fbs_s*) and a *stratum profundum* (*fbs_p*), and in the flexor medius a *stratum profundum* (*fbm_p*) distinct from the rest of the layer. But this is not all, for on the development of the profundus tendons in the reptilia from the deep layer of the palmar aponeurosis, the superficial portions of the flexor medius, as I have already pointed out (1903), remain in association with these tendons, forming the equivalents of the mammalian lumbricales, and we thus have a *stratum superficiale* (*fbm_s*) as well as a deep one separated from the flexor medius, which may, accordingly, be described as consisting of three

strata. Thus the reptilian layers compared with those of the amphibia are as follows:

Amphibia.	Reptilia.
Fl. brevis superficialis	{ Fl. brevis superficialis stratum superficiale. Fl. brevis superficialis stratum profundum.
Fl. brevis medius	{ Fl. brevis medii stratum superficiale. Fl. brevis medii stratum medium. Fl. brevis medii stratum profundum.
Fl. brevis profundus	Fl. brevis profundus.
Intermetacarpales	Intermetacarpales.

The *flexor digitorum brevis superficialis*.—The *stratum superficiale* is a strong muscle arising from the surface of the volar cartilage and

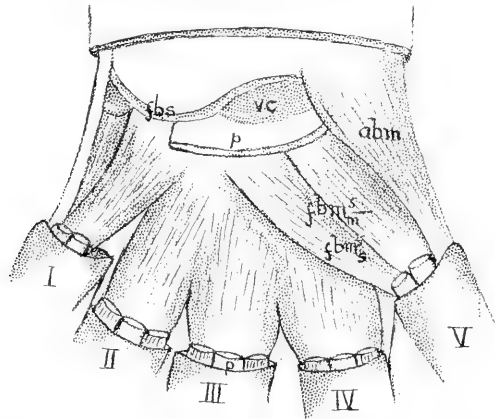


FIG. 4. The stratum medium of the flexor brevis medius of *Iguana*. $fbsm^5$, portion to the fifth digit; $fbsm^4$, portion of the stratum superficiale to the fifth digit; *fbs*, line of origin of the flexor brevis superficialis; *abm*, abductor minimi digiti; *p*, the deep palmar aponeurosis and the profundus tendons; *vc*, volar cartilage.

aponeurosis, the line of the origin (Fig. 4, *fbs*) being somewhat curved, with its convexity directed distally and prolonged much more proximally at its ulnar extremity than at the radial. Traced distally it divides into six portions, one for each of the four radial digits and two for the minimus. The portions for the second, third and fourth digits when traced distally are found to divide each into two slips which diverge to fade out in the fibrous tissue covering the sides of the metacarpo-phalangeal joint, allowing the profundus tendon to pass between them and become superficial. The portion to the pollex, however, does not divide into two slips, but passes entirely to the outer side of the joint, the profundus tendon becoming superficial to its ulnar side, while in one of the portions to the minimus, although two

terminal slips are recognizable, the ulnar one is very small, the main insertion of the muscle being into the radial side of the digit. It may be noted also that in *Iguana* this fifth portion at its origin overlaps somewhat the fourth portion, an arrangement which is, however, by no means so pronounced in *Callisaurus* or *Liolepisma*.

The second portion which passes to the fifth digit (Figs. 4 and 5, *ab. m.*) may well be termed the *abductor minimi digiti*. It is throughout its extent quite separate from the rest of the superficial sheet, except immediately at its origin which is from the ulnar prolongation of the line from which the rest of the flexor superficialis arises. In the *Iguana* the muscle wraps itself around the fifth metacarpal to a con-

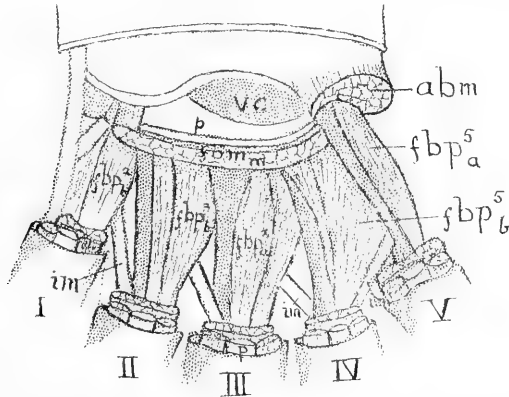


FIG. 5. The flexores brevis profundus and intermetacarpales of *Iguana*. *abm*, abductor minimi digiti; *fbp_a*, direct and *fbp_b*, oblique muscles of the flexor profundus; *im*, intermetacarpales; *fbm_m*, line of origin of the stratum medium of the flexor brevis medius; *p*, deep palmar aponeurosis which gives origin to the profundus tendons; *vc*, volar cartilage.

siderable extent, but in *Callisaurus* this is not so evident, the muscle lying rather to the ulnar side of the bone, but in both it is inserted into the ulnar side of the proximal phalanx of the digit. The muscle is more or less closely related to one of the slips of the flexor brevis profundus (Fig. 5, *fbp_a*⁵) and might on this account be regarded as possibly a portion of that layer rather than of the superficialis. I shall postpone a discussion of this possibility until the profundus layer has been described.

The *stratum profundum* of the superficial flexor I did not succeed in tracing perfectly in *Iguana*, a large slip passing to the fourth digit and a smaller one to the third being the only portions observed. In *Callisaurus* and *Liolepisma*, however, it was readily distinguished in

sections as a thin layer (Fig. 3, *fb_{s_p}*) which separated from the dorsal surface of the str. superficiale almost opposite the junction of the proximal and distal halves of the metacarpals and passed distally to each of the three middle digits, lying dorsal to the slips of the superficial stratum and becoming closely associated with the slips of the stratum superficiale of the middle flexor near their insertion.

The portion pertaining to the second digit is quite slender and lies entirely upon the ulnar side of the digit; that for the third digit is stronger, however, and forms two slips passing one to either side of the digit, and the portion for the fourth digit also divides into two terminal slips between which a thin band of small-fibred muscular tissue extends forming, when the slips unite with the subjacent slips of the flexor medius, a complete sheath for the profundus tendon.

It seems probable that a representative of this stratum also occurs in connection with the first digit, a portion of the flexor superficialis coming into relation near its insertion with the pollical portion of the flexor medius; it was not, however, quite distinctly separated from the general mass of the superficiale. In the case of the fifth digit the existence of a stratum profundum slip was much more evident, but on account of its intimate association with the minimal slip of the flexor profundus it will be more convenient to consider it later in connection with that muscle.

The *flexor digitorum brevis medius*.—The *stratum superficiale* of the flexor medius arises from the dorsal surface of the palmar aponeurosis just where it divides to form the profundus tendons; the portion for the fifth digit forms an exception to this statement, since it arises rather from the surface of the stratum medium. The stratum consists of four thin band-like portions which pass to the four ulnar digits, there being no portion for the pollex. The portion for the index is very narrow and is completely concealed by the profundus tendon; in Iguana it passes to the ulnar side of the digit, but in *Liolepisma* it divides into two terminal slips which insert into either side of the base of the proximal phalanx. The portions for the medius and annulus are broader and each divides into two terminal slips which insert into either side of the digit, the annular portion being associated throughout a considerable part of its course with the corresponding portion of the deep stratum of the flexor brevis superficialis.

The portion for the minimus (Fig. 4, *fbm_s*) differs somewhat from the other three, as already stated, in arising from the thin fascia covering the volar surface of the stratum medium. It has a very oblique direction, its origin being over the proximal portions of the second

and third metacarpals, so that in its course to its digit it crosses obliquely over the medial and annular portions of the stratum medium. It is inserted into the radial side of its digit.

The *stratum medium* (Fig. 4) is the thickest layer of the flexor medius, almost equalling the flexor superficialis in its development. It is divided by tendinous bands lying in the sagittal plane into a number of parts, several of which pass to each digit. The general mass sends a portion to each digit, that to the minimus (Fig. 4, fbm_m^s) having an oblique direction, and overlapping at its origin the portions which pass to the fourth and part of that of the third digit.

The *stratum profundum* consists of three distinct portions which arise in the fascia covering the dorsal surface of the stratum medium and pass to the radial side of the medius, index (Fig. 3, fbm_p^2) and pollex. At their origin these muscles lie distinctly in a plane palmar to that occupied by the main nerve trunks, but more distally the nerves come to lie in the same plane as the muscles, so that from sections cutting the distal parts of the muscles it would be difficult to say whether they belonged to the flexor medius or the flexor profundus. Their relations at their origins, however, clearly show their true significance.

The muscle which passes to the third digit has its origin over the ulnar edge of the third metacarpal, so that in its course to its insertion it passes somewhat obliquely toward the radial side. The same is also true for the other two muscles, that for the index arising over the ulnar border of the second metacarpal and that for the pollex over the middle line of the first metacarpal, its obliquity, however, being more pronounced than that of the other two muscles owing to its being inserted into about the middle of the radial surface of the metacarpal, instead of passing to the neighborhood of the metacarpo-phalangeal joint.

The *flexor digitorum brevis profundus*.—The flexor profundus presents some interesting peculiarities in the arrangement of its constituent muscles (Fig. 5). In the amphibia it consisted of three slips, a median and two lateral, for each digit; in the reptilia almost the same condition obtains, but the median slip, except in the case of the minimus, is greatly reduced and is associated with one of the lateral slips and, furthermore, each radial lateral slip of the four ulnar digits, instead of being inserted into the digit from which it arises, passes obliquely across an intermetacarpal interval to be inserted into the ulnar side of the adjacent digit.

In the pollex I find but one muscle that I can certainly refer to this layer (Fig. 3, fbp_a^1). It arises from the first metacarpal and inserts

into the metacarpo-phalangeal cartilage of the same digit. There is a possibility that the muscle to the pollex which I have referred to the stratum profundum of the middle flexor may really belong to the flexor profundus series, but its general relations seem rather with the medius.

The index possesses two muscles of the profundus set. One of these (Figs. 3 and 5, fbp_i^2) arises from the radial side of the base of the second metacarpal and inserts into the ulnar side of the metacarpo-phalangeal cartilage of the first digit. In *Callisaurus* this muscle consists of two fairly distinct portions, one of which has an origin both more distal and more upon the volar surface of the metacarpal than the other and probably represents the middle slip of the amphibian muscle. The second muscle (fbp_a^2) is more slender than its fellow and arises from the ulnar side of the metacarpal and inserts into the ulnar side of the metacarpo-phalangeal cartilage of the second digit.

In the third and fourth digits the arrangement is similar; the muscles which arise from the radial side of the corresponding metacarpals (fbp_i^3 and fbp_i^4) apparently include a median slip as well as a radial and extend to the ulnar side of the second and third digits respectively, while two other muscles (fbp_a^3 and fbp_a^4) arising from the ulnar and volar surfaces of the metacarpals pass to the ulnar side of the proximal phalanx of their own digits.

In the fifth digit the muscle which passes across to the fourth digit (fbp_i^5) is relatively strong and is readily recognizable, but that which passes directly to the proximal phalanx (Fig. 5, fbp_a^5) is not so easily distinguishable, being more or less concealed by and associated with the part of the flexor brevis superficialis which constitutes the abductor minimi digiti. In *Iguana* and *Callisaurus* the profundus brevis muscle was quite distinct from the abductor though completely covered by it, in *Iguana*, indeed, almost enclosed by it (Fig. 5). In *Liolepisma*, however, I was not able to separate the two muscles, which present relations recalling those found in *Amblystoma*. One would naturally be inclined to regard the amphibian arrangement as the more primitive one and that found in *Callisaurus* and *Iguana* as derived by a separation of an originally simple muscle into two portions, but although I have not been able to exclude this possibility yet I am more inclined to believe that the distinctness of the two muscles is really the more primitive and that the arrangement which occurs in *Amblystoma* and *Liolepisma* is the derived one.

My reasons for this view are based partly upon the relationship which the portion of the amphibian muscle bears to the flexor carpi ulnaris. This muscle belongs to the superficial layer of the forearm musculature,

and in *Amblystoma* is partly directly continuous with the abductor. Furthermore, the continuity of the line of origin of the abductor with that of the flexor brevis superficialis and its origin in part from the ulnar margin of the palmar aponeurosis are facts of no little importance. The distinctness of the abductor except at its origin from the rest of the flexor superficialis need have but little weight, since even in the amphibia a distinct separation of the lateral portions of the palmaris superficialis as the flexores carpi ulnaris and radialis is already in existence, and the continuity of the flexor carpi ulnaris with the abductor might well contribute to a separation of the latter. Nor does a fusion of a portion of the flexor brevis superficialis with a muscle belonging to the flexor profundus seem improbable, since there is typically such a fusion in the amphibian hand in the cases of the various slips to the digits.

Accepting then the superficial nature of the abductor we find in the reptilia an interesting rearrangement of the muscles which constitute the flexor brevis profundus as compared with the condition in the amphibia. The portion to each digit is practically reduced to two slips and, what is more important, one of these slips assumes an oblique direction, passing across an intermetacarpal space to be inserted into the digit adjacent to that from which it arises. I emphasize this arrangement of the profundus slips since it has important bearings upon the arrangement assumed by the corresponding muscles in the mammalia.

The *Intermetacarpales*.—These muscles (Figs. 3 and 5, *Im*) have entirely lost their muscular structure and have been converted into strong tendinous bands which extend obliquely across the various intermetacarpal spaces. The three radial tendons are directed ulnarly and distally, being attached at one extremity to about the middle of the ulnar side of the first, second and third metacarpals and passing to the radial side of the distal extremity of the second, third and fourth metacarpals respectively. The fourth tendon, however, has exactly the reverse arrangement, passing from the radial side of the fifth metacarpal distally to the distal end of the fourth, and, furthermore, it becomes intimately associated with the ulnar (distal) edge of the radial profundus slip of the fifth digit.

The arrangement of the nerve trunks in the reptilian hand is essentially the same as in the amphibian and does not require any detailed description.

In the preceding account I have refrained from applying to the individual muscles terms borrowed from mammalian myology, because the

differentiation and association of the various layers has not proceeded to such a degree as to allow of an accurate application of such terms. I have already, in my previous paper (1903), shown that the use of the term *flexor sublimis digitorum* in reptilian myology is incorrect, and that the same is true of the terms *interossei volares* and *interossei dorsales*, these muscles as we recognize them in the mammalia not yet being differentiated, I shall show later on. The arrangement in layers in the amphibia and reptilia is the important matter for the present study and it is to this that I have endeavored to draw especial attention in my description.

III. THE MUSCLES OF THE MAMMALIAN HAND.

In this chapter I propose to consider the muscles of the mammalian hand from the standpoint of their arrangement in layers, so as to obtain a general comparison with the condition occurring in the reptilia and amphibia, and, furthermore, I shall confine my remarks to what is found in the opossum (*Didelphys virginiana*), the cat and the mouse, reserving for a final chapter a detailed consideration of the muscles of the human hand.

Cunningham in his admirable studies of the myology of the Challenger marsupials (1878 and 1882) furnished a most important standpoint for the proper understanding of the fundamental plan of the mammalian hand musculature in recognizing its arrangement in a number of definite layers. He confines his attention to what he terms the "intrinsic" muscles of the hand, limiting that term so as to include only "those muscles which remain after the removal of the flexor and extensor tendons." In this intrinsic musculature he recognizes three layers: (1) a palmar layer consisting of the adductors, (2) an intermediate layer and (3) a dorsal layer containing the dorsal interossei and the abductores pollicis and minimi digiti.

This conception seems to me to be faulty in three particulars. It may well serve as a plan for the mammalian hand muscles, if we limit our study to that group, but to obtain a correct understanding of the mammalian muscles we must formulate for them a fundamental plan which correlates them with the musculature of lower groups of vertebrates, and this cannot be satisfactorily accomplished if we limit the term "intrinsic" as Cunningham has done. For, as I endeavored to show in my earlier paper (1903), all the muscles of the hand are primarily "intrinsic," *i. e.*, confined to the limits of the hand, and not only must the muscles which Cunningham has discussed be included

in our fundamental plan, but also the lumbricales and the tendons of the flexor sublimis which are representatives of the flexor brevis superficialis. Instead, therefore, of recognizing but three layers in the mammalian hand we must, I believe, admit at least five. These five layers I would correlate with the reptilian layers as follows:

Reptilia.		Mammalia.
Fl. brevis superfic. str. superfic.	}	Flexor brevis superficialis.
Fl. brevis superfic. str. prof.		
Fl. brevis medii str. superfic.		Lumbricales.
Fl. brevis medii str. medius.	}	Adductores.
Fl. brevis medii str. prof.		
Fl. brevis profundus		Fl. brevis profundus.
Intermetacarpales		Intermetacarpales.

I say I would recognize "at least" five layers, since there is a possibility, though it seems to be remote, that representatives of both the middle and deep strata of the flexor brevis medius may be present; this point may, however, be more satisfactorily discussed later on.

The other two exceptions that I would take to Cunningham's scheme concern his distribution of the individual muscles to the different layers. By failing to recognize the most superficial layer he has included certain marginal muscles which, I believe, properly belong to it, in his intermediate layer, *i. e.*, in the flexor brevis profundus, and others in his dorsal layer. Furthermore, his dorsal layer includes also muscles equivalent to portions of the flexor brevis profundus of the reptilian hand, there being in the mammalia an intimate association of certain slips of the flexor brevis profundus with the intermetacarpales to form the dorsal interossei. These questions again can be more satisfactorily discussed later.

The planes of separation of the mammalian layers are essentially the same as in the lower vertebrates. Although a marked rearrangement of the main nerve stems has occurred in the higher group (see my previous paper, 1903), yet, I believe, we are justified in assuming that the plane occupied by the deep branch of the ulnar nerve corresponds with that occupied by the nerve stems in the reptilia and, consequently, the two layers situated dorsal to this plane correspond to the similarly situated layers of the reptilia. Again, I have shown, I trust satisfactorily, that the tendons of the flexor profundus digitorum represent the deeper layer of the amphibian palmar aponeurosis and the profundus tendons of the reptilia and thus serve to separate, to a certain extent at least, the superficial and middle layers.

The *flexor digitorum brevis superficialis*.—In my paper on the phy-

logeny of the forearm flexors I showed that the flexor brevis superficialis of the reptilia and amphibia was represented in the mammalia partly by the terminal portions of the tendons of the flexor sublimis digitorum. Since, however, this muscle sends no tendon to the pollex, we may well expect to find some special representative of the superficial flexor in the radial side of the mammalian hand, and, furthermore, it is not unlikely that portions of the ulnar border of the sheet may have persisted and even slips of its more median portion.

That this likelihood is reality can, I think, be readily perceived by the study of a series of mammalian hands. In the opossum there is superficially in the ulnar part of the hand, in addition to the sublimis

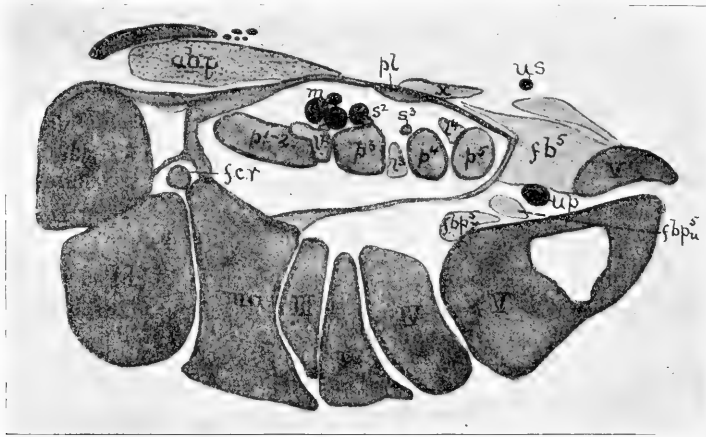


FIG. 6. Transverse section through the wrist of the opossum. *abp*, abductor pollicis; *fb*⁵, flexor brevis minimi digiti; *fbp*_r⁵ and *fbp*_u⁵, radial and ulnar slips of the flexor brevis profundus; *fcr*, flexor carpi radialis; *l*²⁻⁴, lumbricales; *m*, median nerve; *ma*, os magnum; *p*¹⁻⁵, tendons of the flexor profundus digitorum; *pl*, palmaris longus; *s*, radial sesamoid; *s*²⁻³, tendons of the flexor sublimis digitorum; *td*, trapezoid; *tm*, trapezium; *u*, unciform; *us* and *up*, superficial and deep branches of the ulnar nerve; *x*, remnant of the flexor brevis superficialis.

tendon, a well marked mass of muscle tissue, consisting of several more or less distinct slips arising partly from the sheath of the long tendons and partly from the hook of the unciform. A portion of this muscle tissue passes superficial to the superficial branch of the ulnar nerve to be lost in the fascia covering the abductor minimi digiti, and may well be regarded as representing the *palmaris brevis* of other mammals. The greater bulk of the mass (Fig. 6, *fb*⁵), however, passes between the superficial (*us*) and deep (*up*) branches of the nerve to be inserted into the outer part of the cartilage which covers the volar surface of the

metacarpo-phalangeal joint, and this and its representatives in other mammals I shall speak of as the *flexor brevis minimi digiti*, reserving until later the question as to the propriety of the use of that name.

A third portion (Fig. 6, *x*) is recognizable as a rather small slip arising from the volar surface of the sheath for the long tendons (the anterior annular ligament) close to the ulnar side of the tendon of the palmaris longus (*pl*), passing thence obliquely ulnarwards to fade out in the sheath of the tendon of the flexor profundus digitorum to the minimus. I found that the sublimis tendon of the fifth digit separates in the opossum from the palmaris longus and it seems not impossible that the slip now under consideration may represent an undegenerated portion of the flexor brevis superficialis from which that tendon has been differentiated. The probability of such an interpretation of the slip is strengthened by the fact that a small amount of muscle tissue persisted in the specimen I studied by sections (an embryo of 6.5 cm.) on either side of the sublimis tendons of the third (Fig. 7, *x*) and second digits. The presence of these slips seems to furnish strong confirmation of the views I have maintained as to the morphological significance of the sublimis tendons, the opossum in respect to the persistence of these slips as in so many others furnishing indications of a connecting link between the reptilia and the higher mammalia, in which, so far as my experience and information go, this median portion of the flexor brevis superficialis is entirely unrepresented by muscle tissue.

In addition to the muscles so far named there is a well developed *abductor minimi digiti*, whose origin is contiguous to that of the flexor brevis minimi digiti though extending a little farther proximally and whose insertion is into the ulnar side of the base of the proximal phalanx.

The muscles of the hand of the opossum have been studied with special reference to their arrangement in layers by Young (1879) and Brooks (1886^{bis}) who adopt essentially Cunningham's plan. In the identification of the individual muscles of the little finger there are certain discrepancies between these two authors, and my results, while agreeing in the main with those obtained by Brooks, differ somewhat even from his. Thus what Young has termed the abductor minimi digiti is, as Brooks has pointed out, the flexor brevis, while Young's opponens is the true abductor. Young failed to observe the slip which I have regarded as a muscular portion of the flexor sublimis, though Brooks figures it and speaks of it as the flexor brevis digitorum manus. Neither author makes mention of the palmaris brevis which might readily be overlooked in dissections on account of its thinness and its relation to the fascia.

On the radial side the flexor brevis superficialis is somewhat more strongly represented than on the ulnar. The large muscle mass which forms the thenar eminence may be regarded as consisting of three portions, recognizable both in dissections and sections: (1) a portion formed by a band (Fig. 6, *abp*) which arises from the dorsal surface of the crescentic sesamoid cartilage of the radial side of the wrist (*s*), (2) a larger and broader portion arising from the volar surface of the annular ligament, its origin extending ulnarly to the line of the profundus tendon for the index and (3) a portion (Fig. 7, *fbp_r¹*) which arises from the radial side of the sheath for the long flexor tendons

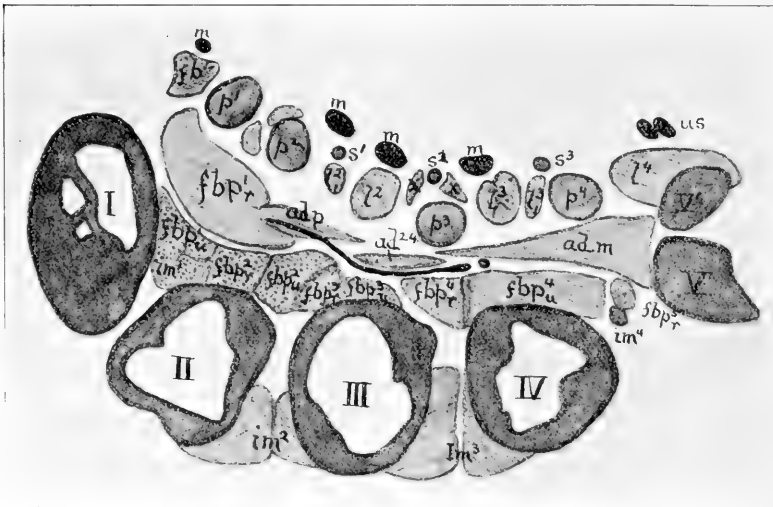


FIG. 7. Transverse section through the hand of the opossum. *ad²⁻⁴*, adductors of the second and fourth digits; *ad.m*, adductor minimi digiti; *ad.p*, adductor pollicis; *fb¹*, flexor brevis pollicis; *fbpr*, and *fbpu*, radial and ulnar slips of the flexores breves profundi; *im*, intermetacarpales; *l*, lumbricales; *m*, median nerve; *p*, tendons of the flexor profundus digitorum; *s*, tendons of the flexor sublimis digitorum; *us*, superficial branch of the ulnar nerve; *x*, remnants of the flexor brevis superficialis.

and is in contact by its volar edge with the second portion just mentioned but distinguishable from it in transverse sections by the greater obliquity at which it is cut at its origin. This third portion does not concern us now, since there is reason to suppose that it is a portion of a deeper layer and therefore belongs to a different group of muscles than the other two which, it may be remarked, insert into the outer surface of the base of the proximal phalanx of the thumb. The first portion seems to be entitled to the name *abductor pollicis* applied to it

by Young and Brooks, while the second may be termed the *flexor brevis pollicis*, although it corresponds only to the radial head of that muscle as recognized by the authors named. I shall consider the reasons for this difference in connection with the third portion of the thenar mass.

I would recognize, then, in the opossum the following representatives of the flexor brevis superficialis: (1) the abductor pollicis, (2) the flexor brevis pollicis, (3) the tendons of the flexor sublimis digitorum with their associated muscle slips, (4) the flexor brevis minimi digiti, (5) the abductor minimi digiti and (6) the palmaris brevis.

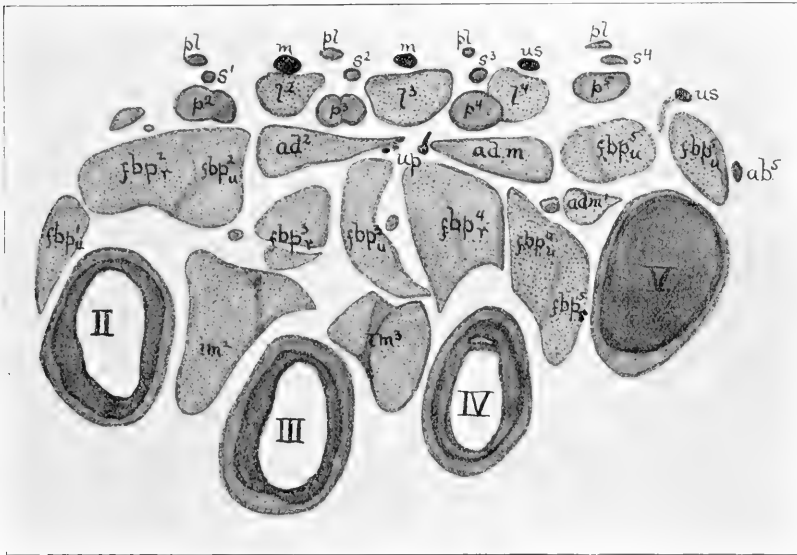


FIG. 8. Transverse section through the hand of a cat embryo of 7 cm. *ad*², adductor indicis; *ad.m* and *ad.m*¹, adductores minimi; *ab*⁵, abductor minimi digiti; *fbp*_r and *fbp*_u, radial and ulnar slips of the flexores breves profundi; *im*² and *im*³, intermetacarpals; *l*, lumbricales; *m*, median nerve; *p*, tendons of the flexor profundus digitorum; *pl*, tendons of the palmaris longus (i.e. prolongations of the palmar fascia) *s*, tendons of the flexor sublimis digitorum; *up* and *us*, deep and superficial branches of the ulnar nerve.

In the cat and the mouse there is a somewhat greater distinctness of the various muscles belonging to this layer, together with a certain amount of reduction, seen especially in the cat. Thus there appears to be no representative in that form of the flexor brevis minimi digiti and the abductor minimi digiti (Fig. 8, *ab*⁵) is much reduced in size as is also the abductor pollicis. This last muscle is represented by two slips arising one in the dermal tissue over the tendon of the palmaris

longus, the other from the radial side of the sheath enclosing the long tendons. The two slips converge to a delicate tendon which was lost in the dermal tissue over the metacarpal bone of the pollex, although in the adult it has been traced to the proximal phalanx, the muscle being that known as the abductor brevis pollicis.

It is probable that the muscle which has been termed the flexor brevis pollicis (*cf.* Reighard and Jennings, 1901, p. 184, Fig. 89a)¹ is also a derivative of the superficial flexor. It arises from the os magnum and the volar surface of the fascia covering the tendon of the flexor carpi radialis and is inserted into the radial side of the proximal phalanx of the thumb. In sections it seems to lie in a plane entirely dorsal to the long profundus tendons, but it must be remembered that it represents a marginal portion of the flexor superficialis which wraps around the margin of the hand to a certain extent. Its origin overlaps somewhat the origin of the adductor pollicis and this relation combined with the fact that it is supplied by a branch of the median nerve leads me to regard it as a portion of the flexor superficialis rather than to incline to the other possibility that it is a portion of the flexor brevis profundus.

The mouse possesses both a palmaris brevis and a flexor brevis minimi digiti (Fig. 9, *fb*²) as well as an abductor minimi digiti (*ab*⁵), all having essentially the same relations as the corresponding muscles in the opossum. The abductor pollicis is represented by two slips which arise from the crescentic sesamoid cartilage of the wrist joint and are inserted into the radial side of the first pollical phalanx and a well developed flexor brevis pollicis (Fig. 9, *fb*¹) is also present, arising from the volar surface of the anterior annular ligament as far medially as the line of the long profundus tendon for the index and passing to the outer side of the proximal phalanx of the thumb. In addition to these two muscles a third occurs in close association with the flexor brevis, consisting of a thin band lying immediately beneath the pad on the radial side of the hand, and having the same relations to it as the palmaris brevis has to the ulnar pad. It seems to owe its existence to the separation of some fibres from the flexor brevis pollicis and might be termed the *palmaris brevis radialis*.

I have not been able to distinguish any structures in the mammalian hand which could with certainty be looked upon as representatives of a stratum profundum of the flexor brevis superficialis such as occurs

¹ I refer to this work alone of those that have been written on the anatomy of the cat, since it does not seem necessary to enter into an extended discussion of the myology of this form and this is the latest extended work on the subject.

in the reptilia. Certain possible elements of such a layer will be discussed later in connection with the lumbrical muscles.

The *flexor digitorum brevis medius*.—As I have already stated, the stratum superficiale of this layer is represented by the lumbricales, arising from the tendons of the flexor profundus digitorum and passing to the four inner digits.

In the reptilia it was noted that the portion of this stratum which passed to the minimus inserted only into the radial side of that digit, while the portions to the annulus and medius divided to pass to either side of the proximal phalanges. In the opossum (Fig. 7) one finds an

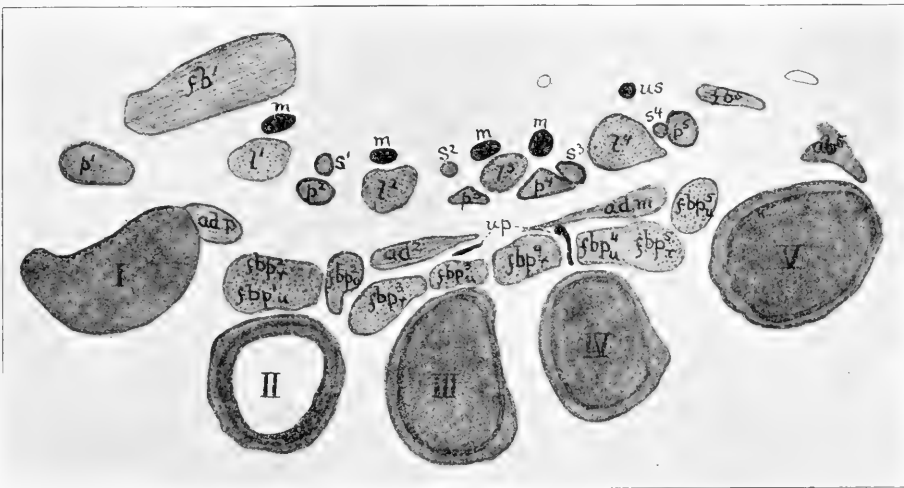


FIG. 9. Transverse section of the hand of a new-born mouse. *ab⁵*, abductor minimi digiti; *ad.m*, adductor minimi digiti; *ad.p*, adductor pollicis; *ad²*, adductor indicis; *fb¹*, flexor brevis pollicis; *fb⁵*, flexor brevis minimi digiti; *fbp_r*, and *fbp_u*, radial and ulnar slips of the flexores breves profundi; *l*, lumbricales; *m*, median nerve; *p*, tendons of the flexor profundus digitorum; *s*, tendons of the flexor sublimis digitorum; *np* and *us*, deep and superficial branches of the ulnar nerve.

interesting suggestion of a similar arrangement, the lumbricals to the medius and annulus each consisting of two distinct portions, one large portion (*l²* and *l³*) which inserts into the radial side of the proximal phalanx of its digit and a smaller one (*li²* and *li³*). The smaller portion of the third lumbrical arises from the radial side of the fourth long profundus tendon and passes distally, retaining its independence throughout its entire course, to be inserted into the sheath enclosing the long tendon just where the sublimis tendon spreads out to allow its passage; the corresponding portion of the second lumbrical arises

from the ulnar side of the profundus tendon to the index and is inserted into the ulnar side of the sheath of that tendon. The first lumbrical in *Liolepisma* has also two insertions, but in *Iguana* it passes only to the ulnar side of its digit; in the opossum it has only one portion which passes to the radial side of the index. It may be stated that von Bardeleben (1902) mentions incidentally the occurrence of two portions in the lumbricals of certain mammals.²

I was not able to detect any indications of a doubling of any of the lumbricals in either the cat (Fig. 8) or the mouse (Fig. 9), in both of which the muscles present the usual mammalian relations. The fact that we have a bilateral insertion for the second and third lumbricals in the lacertilia inclines one to the view that the doubled condition of the corresponding mammalian muscles may be a relic of the reptilian arrangement. There is, however, another possibility, namely, that the smaller slips of the mammalian muscles represent persistent portions of a stratum profundum of the flexor brevis superficialis. In *Callisaurus* slips from this stratum pass to the second, third and fourth digits, and these slips are associated at their insertions with the sheaths of the corresponding profundus tendons. It is not at all impossible that the smaller slips of the second and third lumbricals of the opossum may represent the corresponding portions of the stratum profundum of the reptilian flexor brevis superficialis, the portion to the third digit being indistinguishable.

Which of these two views may be the correct one the material I have had for study does not determine. The nerve supply of the various slips, so far as my observations go, throws no light on the question.

We come now to the consideration of the *stratum profundum*³ of the flexor brevis medius, being the first of the three layers described by Cunningham and that which is constituted by the adductor muscles of the mammalian hand. The arrangement of these muscles in the opossum has been well described by Young (1879) and Brooks (1886^{bis}), but on comparing their descriptions a slight difference in the limitations of one of the muscles is noticeable, a portion of the muscle recognized by Brooks as the adductor pollicis, namely, its ulnar head, being regarded by Young as a portion of his flexor brevis pollicis, *i. e.*, of the intermediate layer of the pollical muscles. My observations lead me to agree with Young on this point, the relatively thick muscle

² Von Bardeleben refers to certain observations of his own upon this point which I have not been able to consult.

³ I use this term here in a strictly mammalian sense. The stratum is probably equivalent to the str. medium of the reptilian hand.

bundle which forms the radial border of Brooks' adductor having its origin from the fascia covering the first and second metacarpals decidedly proximal to the origin of the adductor and being overlapped, furthermore, on its ulnar border by the adductor. In accordance with Young's description of the adductors then, there is a large fan-shaped adductor pollicis (Fig. 7, *ad p*) and a similar adductor minimi digiti (*ad m*) which arise mainly from a median fibrous raphe in the line of the middle metacarpal and insert into the ulnar and radial sides respectively of their digits. In addition there are two other adductors (*ad²⁻⁴*), much less extensively developed, arising from the dorsal surface of the adductor raphe and inserting into the ulnar and radial sides respectively of the second and fourth digits.

In the cat the correct interpretation of the deeper muscles of the hand is rendered difficult by the flexor brevis profundus elements being pushed volarly so that some of them come to lie in apparently the same plane as the adductors and are, furthermore, traversed near their volar surface by the deep branch of the ulnar nerve, thereby seeming to be partly epineural structures. If, however, these two peculiarities be taken into consideration, an arrangement of the various portions of the flexor brevis medius and profundus essentially similar to what occurs in the opossum and the mouse can be made out.

It is the profundus portion for the index (Fig. 8, *fbp_r²* and *fbp_u²*) which is especially obtrusive in the way mentioned, occupying a position so far volar as to separate the adductor pollicis from the adductor indicis. The former of these muscles arises from the surface of the os magnum and is inserted into the ulnar side of the proximal pollical phalanx, while the latter (Fig. 8, *ad²*) arises in continuity with the rest of the adductor layer from the fascia covering the volar surface of the carpal bones and the bases of the metacarpals and is inserted into the ulnar side of the base of the proximal phalanx of the index. In addition to these two muscles there are two others belonging to the adductor layer; they arise together and are closely associated throughout the greater part of their course, the more ulnar one (*ad m¹*), however, inserting into the radial side of the shaft of the fifth metacarpal, while the more radial one (*ad m*) passes to the base of the proximal minimal phalanx. I suspected at first that the more radial of these muscles belonged to a different layer than the other, but the evidence available makes it preferable to regard the two together as equivalent to the adductor minimi digiti of the opossum whose insertion has been partly extended proximally upon the metacarpal.

In the mouse three muscles may be recognized as belonging to the

adductor layer: (1) an adductor pollicis which arises from the fascia covering the first metacarpal and is inserted into the ulnar side of the proximal phalanx of the pollex (Fig. 9, *ad p*), (2) an adductor indicis (*ad i*) and (3) an adductor minimi digiti (*ad m*), both of which arise from the fascia covering the bases of the third and fourth metacarpals and are inserted into the proximal phalanges of their respective digits. No separation of the adductor minimi digiti into two portions, as is the case in the cat, occurred.

Of the stratum profundum of the middle flexor which occurs in the reptilia I have found no representative in the mammalian hand if the identification of the adductor minimi digiti of the opossum with a part of the stratum medium be correct. It is to be noted, however, that superficial to the adductor there is clearly to be seen in sections a very thin layer of muscle tissue, separated from the surface of the adductor by a narrow but quite distinct layer of areolar tissue. Its fibres are directed less obliquely than those of the adductor and, becoming tendinous, it fades out in the fascia beneath the profundus tendon of the fourth digit. It is possible that this muscle really represents a portion of the stratum medium and that the adductor represents the stratum profundum. I have been able, however, to find no corresponding muscle toward the radial side of the hand in the opossum and it seems hardly possible that the adductor minimi digiti represents a different layer for the adductor pollicis when their general similarity and their origin from a common median raphe are considered. In the higher mammals studied I have found nothing which corresponds to this muscle.

But instead of regarding it as part of the stratum medium another interpretation is possible for it, and that is that it represents in a diminished condition the more superficial radial slip of the portion of the median flexor which passes to the fifth digit in the Iguana (Fig. 4, *fbm*^s). Its relations to the remaining portions of the stratum medium are essentially the same as those of the reptilian muscle and there seems to be no obvious reasons for not regarding it as identical with the latter.

I conclude, therefore, that the deep stratum of the reptilian flexor brevis medius is unrepresented as a distinct stratum in the mammalian hand.

The *flexor digitorum brevis profundus* and the *intermetacarpales*.— We come now to the epineural muscles of the mammalian hand, those which correspond to the flexores breves profundi and intermetacarpales of the lower vertebrates and to the intermediate and deep layers

of Cunningham's scheme. It must be pointed out that while the two layers taken together correspond with Cunningham's two layers, individually the layers of the two sets are quite different. I shall not discuss this point here, however, but reserve it for the concluding chapter, and, in the meantime, would merely point out that the flexores breves profundi and intermetacarpales are so intimately associated in the mammalia that it is not feasible to discuss them separately.

In the opossum and other marsupials Young, Brooks and Cunningham have recognized in their intermediate layer a series of flexor muscles corresponding to the various digits, each muscle being composed of two slips which pass to the ulnar and radial sides of a proximal phalanx. Such a condition recalls, it is true, the amphibian arrangement of the profundus layer, but it must be remembered that the reptilian arrangement is quite different, one of the two slips of certain muscles transferring its insertion to an adjacent digit, and I believe that in the mammalian hand there has been a similar transference of some of the slips.

In the opossum I find on the ulnar side of the hand two muscles belonging to the flexor brevis profundus, one (Fig. 6, fbp_u^5) arising from the fascia enclosing the long tendon to the fifth digit and being perforated close to its origin by the deep branch of the ulnar nerve, and the other (Figs. 6 and 7, fbp^5) taking its origin from the base of the fifth metacarpal and lying to the radial side of the first. The ulnar muscle passes directly distally and inserts into the base of the proximal phalanx of the minimus, while the other passes obliquely across the interval between the fifth and fourth metacarpals and unites with the intermetacarpal of that interval and with the ulnar slip of the flexor brevis profundus of the fourth digit to be inserted into the proximal phalanx of that digit. The ulnar muscle I take to be the radial slip of the portion of the intermediate layer passing to the minimus as described by Young and Brooks, but they seem to have overlooked the radial muscle, although it is evidently identical with the slip which Cunningham has described in *Thylacinus* and *Phalangista* (1882) as a palmar slip entering into the formation of the fourth dorsal interosseous. The ulnar minimal slip which these authors recognize in the fifth digit belongs, I believe, to the abductor mass and therefore to an entirely different layer from the radial slip.

The muscles referred by the same authors to portions of the intermediate layer passing to the annulus medius and index are identical with those which I take to be the flexores breves profundi of the same digits (Fig. 7, fbp^4 , fbp^3 and fbp^2); they arise in pairs from the

bases of their metacarpals and are inserted one into either side of the base of the proximal phalanx of the same digit. In the case of the pollex, however, the arrangement of the slips is similar to that occurring in the minimus, one of them (Fig. 7, fbp_u^1) passing across the intermetacarpal interspace to be inserted into the radial side of the base of the proximal phalanx of the index, uniting with the radial slip of the flexor brevis profundus of the index and with the first intermetacarpal, while the other (fbp_r^1) passes directly distally to be inserted into the ulnar side of the phalanx of the thumb. In this digit, as in the minimus, the oblique muscle has been overlooked by Young and Brooks, or rather has been considered to be a part of their dorsal layer, while the other is identical with the ulnar slip which they ascribe to the thumb. Their radial slip is, I believe, a portion of the flexor brevis pollicis and, consequently, belongs to the flexor brevis superficialis.

The intermetacarpals are distinctly muscular, thus differing from those of the lacertilia which are throughout converted into ligaments. The second, third and fourth intermetacarpals (Fig. 7, im) arise each by two heads from the sides of adjacent metacarpals near their dorsal surfaces and converge to a tendon (im^4) which passes distally in the intermetacarpal space and finally bifurcates to be inserted into the adjacent sides of the neighboring proximal phalanges, the radial branches of the third and fourth tendons uniting with the tendons of the flexor brevis profundus slips inserted into the corresponding phalanges, while the ulnar branch of the second tendon similarly unites with the radial slip of the flexor brevis profundus of the third digit. What I take to be the first intermetacarpal (im^4) differs from the others in that it arises by a single head from the first metacarpal and is situated more volarly than its fellows. It passes obliquely across the first intermetacarpal interval to unite with the ulnar slip of the flexor brevis profundus of the pollex and the radial slip of the same muscle of the index and inserts with them into the proximal phalanx of the index.

In the cat an arrangement of the flexor profundus muscles comparable to that occurring in the opossum is readily discerned, but the intermetacarpals are not in all cases so distinctly separated from the muscles with which they unite. In the fifth digit one finds the ulnar muscle dividing into two slips (Fig. 8, fbp_u^5) which are inserted into either side of the base of the proximal phalanx; the radial muscle (fbp_r^5), however, passes across to the proximal phalanx of the annulus. This digit, the medius and the index each possesses two slips, those of the annulus and medius having undergone a distal recession so that they arise from the shafts

of their metacarpals instead of from their bases, and those of the index having assumed a volar position so as to lie, as has already been pointed out, in the same plane as the adductors. The thumb possesses two muscles of the flexor profundus set, an ulnar one which passes across the intermetacarpal space (*fbp*¹) to be inserted into the index and a radial one which is inserted into the proximal phalanx of its own digit. The first and fourth intermetacarpals I was not able to distinguish, they being probably intimately united with the muscles with which they insert. Those of the second and third intermetacarpal spaces (*im*² and *im*³) are fairly distinct, but less so than in the opossum, and are more volar in position.

In the mouse (Fig. 9) the general arrangement is practically the same as in the two forms already described and need not be discussed in detail. The intermetacarpals are even less distinguishable from the slips of the flexor brevis profundus with which they are associated than are those of the cat.

IV. THE MUSCLES OF THE HUMAN HAND.

In considering the musculature of the human hand it will probably conduce to clearness if, instead of discussing it from the standpoint of the fundamental layers, the various muscles be taken up in sequence.

1. The *palmaris brevis* occupies a characteristic position with reference to the superficial branch of the ulnar nerve, being the only muscle which lies volar to it. Throughout the series of forms studied this relation is constant and affords a simple clew for the identification of the muscle, which, be it noted, is in the opossum closely associated with the flexor brevis minimi digiti. It is evidently a portion of the flexor brevis superficialis.

2. The *flexor brevis quinti digiti*.—The significance of this muscle has been discussed by Brooks (1886), with the conclusion that it really belongs to the adductor set, *i. e.* to the flexor brevis medius. Brooks has evidently been deeply influenced by Cunningham's views as to the layers of the palmar musculature, and his assignment of the muscle under discussion to the adductor layer may be taken as meaning that it is an element of a hyponeural layer, *i. e.* of a layer volar to the deep branch of the ulnar nerve. I have shown that in addition to the palmar (adductor) layer, which was the only hyponeural layer recognized by Cunningham, there are really two others to which that term may be applied, namely the lumbrical layer and the flexor brevis superficialis layer, and it seems highly probable that the flexor brevis quinti digiti

belongs to this last layer. Its exclusion from the adductor layer seems certain from its relations in lower forms, in which it is evidently a muscle arising volar to the profundus tendons instead of dorsal to them, and there seems to be no reason for supposing that this superficial origin has been secondarily acquired. I regard the muscle, therefore, as a second member of the flexor brevis superficialis.

It is unfortunate that by the application of the terms flexor brevis to their intermediate layer the English authors have introduced a certain amount of confusion into the nomenclature of the hand muscles, a confusion which becomes very evident in the perusal of Brooks' paper (1886). For finding that the flexor brevis quinti digiti is not a member of the intermediate layer he prints its name throughout in inverted commas and reserves the title of "the true flexor brevis minimi digiti" for what he regards as the ulnar slip of the intermediate layer. It seems far preferable to reserve the designation flexor brevis for muscles which belong to the superficial layer, since, in the first place, this layer has long been spoken of in the lower vertebrates as the flexor brevis digitorum, and, in the second place, we have for the members of the intermediate layer the long-established term interossei.

3. The *abductor quinti digiti*.—This muscle has been referred by Cunningham to his dorsal layer and regarded as the most ulnar dorsal interosseus. It seems to me that the relations of the muscle in the lower vertebrates strongly negative such a supposition and show it to be a derivative of the most superficial sheet of the hand musculature. For I take it that the mammalian muscle is the equivalent of the abductor minimi digiti of the lacertilia, the continuity of whose origin with that of the flexor brevis digitorum is so striking.

It is interesting to note that in the forearm the deeper layers of muscles, represented by the flexor profundus and the pronator quadratus, do not extend laterally beyond the lines of the radius and ulna, and that the deepest layer is more limited laterally than is the middle one. It is from the superficial layer, that farthest from the bones, that the marginal muscles, the flexores carpi radialis and ulnaris, are derived. Such an arrangement is just what might be expected, for it would seem natural that the layer farthest away from the bony axis should wrap itself to a certain extent around the axis at the sides, while the closer the relations of the layers to the bones the more their lateral extension would be limited. We may expect to find this same condition obtaining in the hand as well as in the forearm, and when in addition to this *a priori* argument we have that derived from the continuity of origin of the abductor with the flexor brevis digitorum, strong evidence is

afforded for the reference of the former muscle to the same layer as the latter one.

Furthermore, it is worthy of remark that the occasional fusion of the abductor with flexor brevis quinti digiti in man, noted by Macalister and Le Double (1897) speaks in favor of a close phylogenetic relationship between the two muscles.

4. The *opponens quinti digiti*.—This muscle also stands in intimate relationship with the flexor brevis, with which, as Le Double states, it is in general more or less related, and it may also unite with the abductor. I regard it as part of the flexor brevis superficialis and probably a derivative of the abductor quinti digiti of the lower mammals. Brooks (1886) refers it, in part at least, to the adductor layer, but this may probably be interpreted to mean merely that it is not to be considered part of the epineural musculature, the reason for such an interpretation being that which has already been adduced in speaking of the flexor brevis quinti digiti.

5. The *flexor brevis pollicis*.—This muscle has been the subject of a good deal of discussion, which has resulted in the establishment of the fact that, as usually understood, the muscle is really a compound structure, including elements from different layers; the exact significance of the different elements is yet open to discussion, however.

The description of the muscle given by Albinus has served as the basis for the accounts given in many and especially the English text-books, even the most recent of these, with the exception of that edited by Cunningham (1902), adhering to the original limitations of the muscle. According to this there is recognized in the muscle a *cauda prior vel exterior*, the outer head of the English texts, and a *cauda posterior vel inferior*, the inner head, which is again composed of three divisions. A very different view was that of Cruveilhier, who limited the term flexor brevis pollicis to that portion of the muscle which inserts into the outer side of the thumb and referred the rest to the adductor. Henle (1871), again, following Sömmering, regarded the outer head as part of the abductor and the greater part of the inner head as belonging to the adductor, confining the term flexor brevis to a small slip which divides to be inserted into both the ulnar and the radial side of the proximal phalanx and corresponds to the second and third divisions of the inner head of the English texts. Furthermore, Henle called attention to the existence of a deeper head arising mainly from the first metacarpal and inserting into the ulnar side of the proximal phalanx of the thumb, regarding it as the true first palmar interosseus, thus recognizing four of these muscles instead of the usual three.

In 1887 Flemming reconsidered the question as to the proper significance of the various parts of Albinus' muscle and arrived at a conclusion somewhat similar to that of Cruveilhier, namely, that the term flexor brevis should be applied to the outer head only, the entire inner head being regarded as a portion of the adductor. To this view Cunningham (1887), on the basis of his earlier work (1878 and 1882), took exception. As already pointed out, he applied the term flexor brevis to the muscles constituting his intermediate layer and regarded each of these muscles as being typically two-headed. Accordingly, while admitting the correctness of the reference of the entire inner head of the flexor brevis pollicis of Albinus to the adductor, he maintained that the true flexor brevis was represented not only by the so-called outer head but also by the interosseus primus volaris of Henle, these two slips constituting the radial and ulnar heads, respectively, of the pollical portion of the intermediate layer. This same view he had already advanced in an earlier paper (1882^{bis}), and it is that presented by Patterson in the recently published text-book edited by Cunningham (1902).

Gegenbaur in his *Lehrbuch der Anatomie* (5th Ed., 1892) adopts essentially the view of Flemming and Cruveilhier, but in a paper published in 1889 he takes the position that the variation in the nerve supply of the muscle described by Brooks (1886) indicates that the muscle is a variable one and is not equivalent in all cases, portions of it present in one individual as indicated by the nerve supply being absent or replaced by portions of other muscles in other individuals.

There is thus a very considerable amount of difference in the limitations set to the muscle by different authorities. I believe, for reasons that have already been set forth in speaking of the flexor brevis quinti digiti, that the term flexor brevis pollicis should be reserved for that portion of the muscle as described by Albinus which is derived from the flexor brevis superficialis, and the portion which has that origin is the so-called outer head. Cunningham is, I believe, in error in referring this head to his intermediate layer; it seems to me clearly equivalent to the flexor brevis pollicis of the mouse, for instance, and this is undoubtedly a derivative of the flexor brevis superficialis, as is shown as well by its origin as from its supply by the median nerve.

On this point, then, my results are in accord with those of Flemming, and I am in agreement both with that author and with Cunningham in regarding the inner head as a portion of the adductor. What, then, is the interosseus primus volaris of Henle? Why, it is evidently just what Henle named it; it is the equivalent in man of the slip of the flexor brevis profundus which arises from the first metacarpal and inserts

into the proximal phalanx of the thumb, and is the radial counterpart of the palmar interosseus of the fifth digit, as I hope to show later on.

The interosseus primus volaris is frequently indistinguishable from the deeper portions of the flexor brevis pollicis (*sens. lat.*), being possibly incorporated with it, although from the fact that in a human embryo of 6 cm. which I examined the slip (Fig. 10, *fbp_r*) was exceedingly small and showed evident indications of degeneration I am inclined to believe that the failure to distinguish it may frequently be due quite as much to its great reduction as to its fusion with the adjacent adductor. But if we suppose that it does frequently become incorporated in that muscle or at all events is included in the flexor brevis pollicis as limited

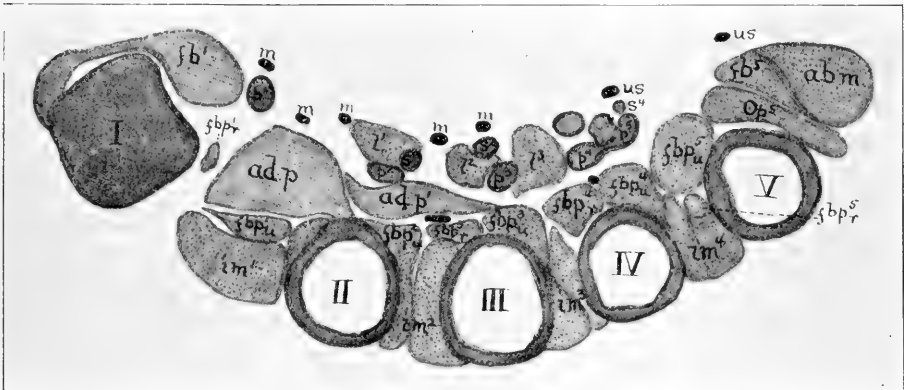


FIG. 10. Transverse section through the hand of a human embryo of 6 cm. *abm*, abductor minimi digiti; *ad.p*, caput obliquum and *ad.p^t*, caput transversum of the adductor pollicis; *fb^l*, flexor brevis pollicis; *fb⁵*, flexor brevis quinti digiti; *fbp_r* and *fbp_u*, radial and ulnar slips of the flexores breves profundus; *im*, intermetacarpals; *l*, lumbricales; *m*, median nerve; *op⁵*, opponens quinti digiti; *p*, tendons of the flexor profundus digitorum; *s*, tendons of the flexor sublimis digitorum; *us*, superficial branches of the ulnar nerve.

by those who adhere to Albinus' conception of the muscle, then the flexor in this sense is really composed of elements from three different layers, namely, the superficialis, the deeper stratum of the medius and the profundus.

6. The *abductor pollicis*.—The abductor pollicis does not seem to exist as a distinct muscle in the lower vertebrates I have studied; the mammalian muscle has appeared within the limits of that phylum and I believe, contrary to the opinion of Cunningham, that it is derived from the flexor superficialis. The *a priori* reasons which indicated an origin of the abductor quinti digiti from this layer holds also in the case of the

abductor pollicis and is strengthened by the origin of the muscle from the volar surface of the annular ligament, by its not unfrequent confusion with the flexor brevis pollicis (*sens. str.*) and by its nerve supply from the median.

7. The *opponens pollicis* is clearly allied very closely to the abductor and in all probability has the same derivation. Its occasional intimate union with the flexor brevis pollicis (*sens. str.*) is important in this connection as is also its supply from the median.

8. *The lumbricales*.—The equivalency of these muscles to the superficial stratum of the flexor brevis medius of the reptilia has already been noted. In the two hands from different human embryos which I studied I found the lumbricales possessing their usual origins, *i. e.* the first and second from the radial sides of the profundus tendons of the second and third digits, and the third and fourth from the adjacent sides of the third and fourth and fourth and fifth tendons, the muscles making their appearance in sections just at the point of separation of those tendons from the common tendon. In none of the muscles could any certain existence of doubling be distinguished. In the embryo of 6 cm. the four muscles were inserted into the radial side of the proximal phalanges of the four inner digits, but in one of 4.5 cm. the third lumbrical divided just before its termination into two equal slips which were inserted respectively into the ulnar side of the proximal phalanx of the third digit and the radial side of the corresponding phalanx of the fourth digit.

The recent observations of Kopsch (1898) and Reinhardt (1902) have shown that the insertion of the third lumbrical into the adjacent sides of the third and fourth digits is of frequent occurrence, Kopsch finding it in 47 out of 110 cases examined (42.7 per cent) and Reinhardt in 43 cases out of 100. A satisfactory explanation of this variability has not yet been advanced. Von Bardeleben (1900) has suggested an association of the double insertion with a nerve supply of the muscle from both the median and the ulnar nerves, and in another place (1901) he has also suggested its possible reference to the doubling of the muscle seen in some of the lower mammals. As regards the first suggestion it may be noticed in the first place that it is rendered very plausible by the fact that Brooks (1887) found in twenty cases a double supply of the muscle in nine; Brooks' paper, however, contains no statements as to the mode of insertion of the muscle in the various cases, and, furthermore, I have been able to determine with certainty that in the embryo with a double insertion mentioned above, the muscle is supplied by a twig from the deep branch of the ulnar and by that alone.

The second suggestion would therefore seem to be the more satisfactory one; but, again, there are difficulties in the way of its being regarded as altogether sufficient. It is true that we find double lumbricales or a double insertion for them in the marsupials and monotremes, and it might be supposed that there is fundamentally a similar condition in man, sometimes persisting to the adult condition, but more usually giving place to a single insertion. The finding of a double insertion of the third lumbrical in an embryo of 4.5 cm. and but a single insertion in an embryo of 6 cm. is suggestive, but it completely loses weight when it is noted that in the younger embryos studied by Lewis (1902) this lumbrical had but one insertion. Furthermore, it is noticeable that while in the lower mammals it is the second and third lumbricales which are doubled, the second muscle in man is remarkably constant in possessing but one part, and, furthermore, a double insertion occasionally occurs in the fourth muscle in man, Kopsch and Reinhardt each recording ten cases of this nature, while Kopsch records four cases and Reinhardt one of a single insertion of the muscle into the ulnar side of the fifth digit.⁴

It would seem, then, that neither of von Bardeleben's suggestions satisfy the requirements of the case, nor does there seem to be any morphological explanation of the variation at present available. May it not be, after all, that there is no such explanation required, what is required being rather a physiological explanation?

For, as has been seen in comparing the muscles of the amphibia, reptilia and mammalia, the shifting of an insertion from one digit to the adjacent side of another is by no means an uncommon phenomenon. In other words, there is not that morphological isolation of the digits from one another which we are apt to imagine; the hand develops as a whole rather than as a series of independent radiating units and the transference of a muscle from one digit to another is consequently a simple matter.

9. The *adductor pollicis*.—This seems to be the only representative of the deeper stratum of the flexor brevis medius which exists in the human hand. Its limitations have already been discussed in considering the flexor brevis pollicis and as a result of the conclusions then reached it is necessary to regard the muscle as consisting of two portions which have been termed the adductor obliquus and the adductor transversus. This nomenclature implies, however, the existence of two distinct muscles,

⁴ This last argument is based upon the arrangement of the muscles which I have found in the Virginian opossum. If in other forms a doubling of the fourth lumbrical should occur, then the argument would lose its value.

and it would seem more satisfactory and more in harmony with the results of comparative anatomy to speak of only one adductor pollicis, regarding it, however, as consisting of a *caput obliquum* and a *caput transversum*.

10. The *interossei*.—From what has been said in connection with the *flexor brevis pollicis* it will be seen that I am in accord with Henle in his contention that there are really four palmar *interossei* present in the human hand, that to the thumb, however, being frequently unrecognizable either from its small size or on account of its incorporation with the oblique head of the adductor.

Recognizing the identity in number of the dorsal and palmar *interossei*, it remains to consider their mutual relationship and their equivalents in the lower vertebrates. Ruge (1880) in his paper on the development of the deep muscles of the human foot, considered briefly the *interossei* of the hand and, by showing that these muscles resembled in their development their homologues in the foot, established the important point that the dorsal *interossei* were in reality portions of the palmar musculature, their final dorsal position being secondary. He went, however, even farther than this and regarded the dorsal *interossei* of the foot as in all respects equivalent to the palmar *interossei*; in other words, he regarded them both as derivatives of the same fundamental layer, considering Cunningham's assignment of them to different layers as erroneous. It seems to me, so far as the *interossei* of the hand are concerned, that the correct position is an intermediate one between those held by these two authors. I believe that the *interossei* really represent two fundamental layers but that there has been a considerable amount of union between the two layers to form the dorsal *interossei*, these muscles consisting of elements from the *flexor brevis profundus* combined with the *intermetacarpales*.

For the sake of avoiding repetition of details I would refer back to what has been said in the previous chapter regarding the representatives of these layers in the mammalia I have studied and merely state that the *intermetacarpals*, though less evident than in the opossum, are yet much more distinct in the human hands I studied than in either the cat or the mouse, as may be seen from the inspection of the adjacent figure (Fig. 10, *im*).

I believe the significance of the mammalian *interossei* to be as follows: The *flexor brevis profundus* is represented by a series of paired slips for each digit inserted into the opposite sides of the proximal phalanges, except in the cases of the first and fifth digits in which one of the slips is inserted into the adjacent side of the second and fourth digit, respec-

tively, along with the radial (or ulnar, as the case may be) slip of that digit. Furthermore, the first and fourth intermetacarpals become associated with the combined muscles so formed, the three portions thus associated constituting the first and fourth dorsal interossei. The second and third intermetacarpals unite with the flexor brevis profundus slips of the third digit to form the second and third dorsal interossei, and the flexor brevis profundus slips of the first, second, fourth and fifth digits which do not unite with intermetacarpals form the palmar interossei. A diagram (Fig. 11) will, I trust, make this description clear and at the same time demonstrate the significance of the mutually complementing arrangement of the two sets of interossei.

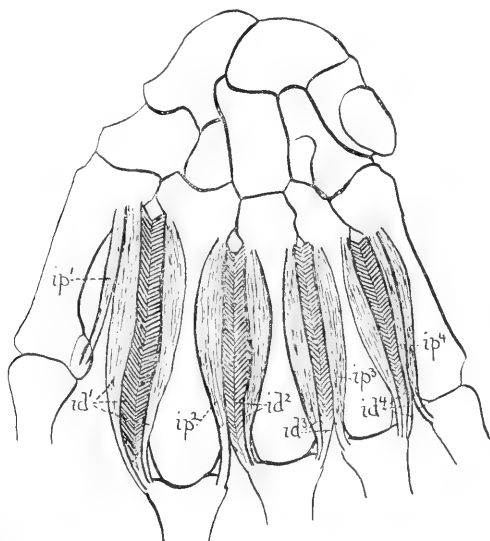


FIG. 11. Diagram showing the composition of the interossei of the human hand. *id*, dorsal interossei; *ip*, palmar interossei.

V. SUMMARY.

It is difficult and tedious to follow a lengthy description involving reference to a number of separate structures even when an abundance of illustrations accompanies it. Owing to my results having been based very largely on the study of the serial sections it would require an undue number of figures to demonstrate all the points to which reference has been made in the preceding pages, and hence, I fear, only those who are especially interested in the subject will have the patience necessary for the thorough perusal of what I have written. And yet it seems that the

importance of obtaining a correct idea as to the fundamental significance of the mammalian hand musculature is sufficiently great to interest all students of vertebrate morphology in the questions discussed. I have, therefore, endeavored to state in a series of propositions the main conclusions which I have expressed both in this paper and in a preceding one (1903) so far as it concerns the hand musculature.

1. In the urodele amphibia the volar hand muscles are arranged in *four* distinct layers which may be named the flexor brevis superficialis, flexor brevis medius, flexor brevis profundus and intermetacarpales.

2. In the lacertilia the number of these layers is increased to *seven* by the subdivision of the flexor brevis superficialis into a stratum superficiale and a stratum profundum, and of the flexor brevis medius into a stratum superficiale, a stratum medium and a stratum profundum.

3. In the mammalia the number of clearly recognizable layers is *five*, the str. profundum fl. brevis superficialis and the str. profundum fl. brevis medii of the lacertilia being apparently wanting.

4. In the mammalia the greater portion of the flexor brevis superficialis has degenerated to form the palmar portions of the tendons of the flexor sublimis digitorum, marginal portions of it persisting, however, to form the abductor and opponens pollicis, the abductor and opponens quinti digiti, the flexor brevis pollicis, the flexor brevis quinti digiti, the palmaris brevis and, in some cases, a palmaris brevis radialis.

5. The palmar portions of the flexor profundus digitorum are derived from a layer of fascia which, in the lower forms, intervenes between the flexor brevis superficialis and the flexor brevis medius, the str. superficiale of the fl. brevis medius arising in these lower forms from this fascia.

6. The str. superficiale of the fl. brevis medius gives rise to the mammalian lumbricales.

7. The str. profundum of the fl. brevis medius gives rise to the mammalian adductors.

8. The flexor brevis profundus in the mammalia consists of paired slips for each digit. Certain of these slips remain distinct and form the palmar interossei; the remainder unite with the intermetacarpales to form the dorsal interossei.

9. The term flexor brevis as applied to muscles of individual digits (pollex and minimus) is appropriately limited to muscles derived from the flexor brevis superficialis.

10. The flexor brevis pollicis as defined by Albinus is composed of elements derived from both the flexor brevis superficialis and the str. profundum of the flexor brevis medius. Only the outer head which is de-

rived from the flexor brevis superficialis is entitled to be known as the flexor brevis pollicis.

11. The interosseus primus volaris of Henle is correctly so named, and there are typically four palmar interossei in the human hand.

12. The derivation of the palmar muscles of the human hand from the various layers may be tabulated as follows:

Flexor brevis superficialis.—Palmaris brevis, abductor quinti digiti, opponens quinti digiti, flexor brevis quinti digiti, abductor pollicis, opponens pollicis, flexor brevis pollicis.

Flex. brevis med. str. superficiale.—The lumbricals.

Flex. brevis med. str. profundum.—The adductor pollicis.

Flex. brevis profundus.—The interossei volares, the interossei dorsales (in part).

Intermetacarpals.—The interossei dorsales (in part).

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PROCEEDINGS OF THE ASSOCIATION OF AMERICAN ANATOMISTS.¹

SIXTEENTH SESSION.

*Columbian University Medical School, Washington, D. C.,
December 30 and 31, 1902.*

At its general business session, the association adopted the following recommendations made by the executive committee:—

1. To accept the invitation tendered by the American Association for the Advancement of Science to form an affiliation with that association and to elect a delegate to its Council. Such affiliation impairs in no degree the integrity of the Association of American Anatomists and does not bind this association to meet with the American Association for the Advancement of Science, unless it deems it expedient.

2. To omit the session in connection with the Congress of American Physicians and Surgeons in May of 1903.

3. To omit from the program abstracts of papers presented at the meetings.

4. That newly elected members must qualify by payment of dues for one year within thirty days after election (By-Laws).

5. That any change in the constitution of this association must be presented in writing at one meeting in order to receive consideration and be acted upon at the next meeting; due notice of the proposed change to be sent to each member at least one month in advance of the meeting at which such action is to be taken.

The following amendment to Article V of the constitution was proposed at this meeting and will receive consideration at the next annual meeting:—Candidates for membership must be persons engaged in the investigation of anatomical or cognate sciences and shall be proposed in writing to the executive committee by two members, who shall accompany the recommendation by a list of the candidate's publications, together with the references.

¹These proceedings should be bound at the end of Vol. 2.

II Proceedings of the Association of American Anatomists

On motion of JAMES PLAYFAIR McMURRICH it was voted, "That a committee of three be appointed to select topics for cooperative investigation."

Committee: Chairman, JAMES PLAYFAIR McMURRICH, *University of Michigan*; WILLIAM KEILLER, *Department of Medicine, University of Texas*; WARREN H. LEWIS, *Johns Hopkins University*.

The following officers were elected:

CHARLES S. MINOT, Boston, member of the executive committee (*five years*); JOSEPH A. BLAKE, New York City, delegate to the Executive Committee of the Congress of American Physicians and Surgeons; SIMON H. GAGE, Cornell University, delegate to the Council of the American Association for the Advancement of Science.

Nineteen new members were elected.

TREASURER'S REPORT FOR THE YEAR 1902.

Receiver from Dr. Lamb (late treasurer).....	\$123.51	
Received from annual dues	517.25	
Total	\$640.76	\$640.76
Expenditures for the year 1902.		
Postage	\$ 17.00	
To American Journal of Anatomy for subscriptions		
to Vol I,	286.50	
Printing	73.80	
To expenses of American Secretary of the Madrid		
International Medical Congress	25.00	
Type-writing	9.20	
Express, telegrams, etc.,	20.53	
Total	\$432.03	\$432.03
Balance in hand, Dec. 31, 1902		\$208.73

ABSTRACTS OF PAPERS PRESENTED.

ON THE HISTOLOGY OF THE GLANDS OF BRUNNER. By ROBERT R. BENSLEY. *Hull Laboratory of Anatomy, University of Chicago.*

This paper presents the results of a comparative study of the glands of Brunner in Mammals. It was shown that the failure of Schaffer, von Ebner, and others to obtain positive results with Mayer's mucin stains in the glands of Brunner, was due to too close an adherence to Mayer's formulae, which, as that author expressly states, stain different mucins with different degrees of facility. The writer has found that by increasing the strength of Mayer's muchametein fivefold, a positive

result may be obtained with perfect certainty in the glands of Brunner of a large number of mammals. A similar positive result may be obtained with Mayer's mucicarmine by using the undiluted freshly prepared stock solution. Photographs were exhibited illustrating the results of these methods in the glands of Brunner of the human subject.

The question of the similarity of the glands of Brunner and the pyloric glands was discussed from the standpoint of the relative specialization of the stomach. It was pointed out that this similarity was greatest in those animals, *e. g.*, Carnivora, Insectivora, etc., in which the stomach is primitive, and that specialization of the stomach is accompanied by increase in the differences between the two groups of glands.

An account was given of the peculiar condition in the Virginian opossum, in which the ducts of the glands open on defects of the mucous membrane of the intestine, where the villi and glands of Lieberkühn are wanting and the epithelium is of the gastric type.

Finally the changes in the glandular cells due to physiological activity were described and compared with those observed by Maximow, Krause, and others in mucous glands from other sources.

THE DIFFERENTIATION OF THE SPECIFIC ELEMENTS OF THE GASTRIC GLANDS OF THE PIG. By ROBERT R. BENSLEY. *Hull Laboratory of Anatomy, University of Chicago.*

It is possible by the use of the more discriminative staining methods, devised in recent years, to demonstrate the exact time of appearance of the several kinds of glandular elements of the gastric glands. The appearance of zymogen granules may be demonstrated by the neutral gentian method devised by the writer, that of mucous secretion, by the muchaematein solution of Mayer, as modified by the writer, and that of the parietal cells, by the strong stain certain of their cytoplasmic elements take in iron alum haematoxylin, as demonstrated by Zimmermann. The hypoblast of the pyloric region and of the lesser curvature distal to the cardiac orifice is the first to exhibit secretory activity, all the cells of the region exhibiting in a 6 cm. pig a well defined mucigenous border stainable in muchaematein. As in lower vertebrates the pyloric glands develop from an element which is already a mucin secreting cell. The parietal cells may be distinguished as early as 7.5 cm. pigs and show almost from their inception distinct intracellular ductules which develop apparently as enfoldings of the surface of the cell. These ductules are therefore actually portions of the free surface of the cell and not merely channels excavated in the cell by the outflowing secre-

tion. An interesting fact confirming the hypothesis of the writer as to the aberrant nature of the cardiac glands is the occurrence of parietal cells in the cardiac sac of the foetal pig, although none are present in the adult. Zymogen granules I found by means of the neutral gentian method for the first time in the 21 cm. pig in the cells at the bottoms of the rudimentary glands.

THE NATURE OF THE GRANULE CELLS OF PANETH. SIDNEY KLEIN
(Communicated by ROBERT R. BENSLEY). *Hull Laboratory of Anatomy, University of Chicago.*

The granule cells of Paneth, which are, in the majority of the mammals in which they have been found, confined to the deep ends of the glandulae intestinales of Lieberkühn, occur in the opossum intermixed with goblet cells and cylindrical epithelial cells on the sides of the villi. This fact shows clearly that the theory of Bizzozero that the Paneth cells are young elements which grow up the sides of the intestinal gland and become gradually transformed into typical goblet cells is incorrect. The granules of the Paneth cell do not, under any conditions, stain with mucicarmine or muchaematein, but, on the contrary, stain intensely in iron alum haematoxylin and in the neutral gentian method recommended by Bensley for staining zymogen granules, in both of which the mucigen granules of the goblet cells remain unstained. Furthermore the granules of the Paneth cells give, when tested by MacCallum's modification of Lilienfeld and Monti's reaction for phosphorus, a distinct positive result. These facts indicate that the Paneth cells are serous cells engaged in secretion of a product chemically distinct from that of the goblet cells, probably an enzyme.

THE DEVELOPMENT OF THE FRAMEWORK OF THE SUBMAXILLARY GLAND. By JOSEPH MARSHALL FLINT. *Hearst Anatomical Laboratory, University of California.* AMERICAN JOURNAL OF ANATOMY, Vol. II, No. 1.

ON THE DIFFERENTIATION OF MUSCULAR TISSUE WHEN REMOVED FROM THE INFLUENCE OF THE NERVOUS SYSTEM. By ROSS G. HARRISON. *Anatomical Laboratory, Johns Hopkins University.*

The following experiments were made to determine whether a stimulus from the nervous system (*formativer Reiz*, Herbst) is necessary to initiate the differentiation of striated muscle tissue.

The medullary cord, the rudiment of the ganglion crest inclusive, posterior to the second or third trunk segment, was cut out of frog embryos (*R. sylvatica*, 3.7 mm., and *R. palustris*, 2.9 mm. long) in which no histological differentiation in the nervous or muscular systems had

taken place. The greater part of the mesoderm of the trunk was left intact, although a small portion of the myotomes was necessarily removed with the cord. The embryos were kept alive until the yolk was absorbed. Aside from the defect caused directly by the operation, i. e. the absence of the dorsal fin, the dorsal part of the musculature and the total absence of the spinal cord and ganglia, the development was normal. No voluntary movements in the trunk or tail of the embryos were observed nor was there any response to mechanical stimuli applied to these regions. Sections show that the differentiation of the trunk and tail musculature, which has no connection whatever with the nervous system, is normal. Muscle fibrillæ with cross striations and the sarcolemma are normally developed. Moreover the grouping of the fibres into muscles, as shown by the shape and size of the myotomes and the existence of the primary abdominal muscle, is also normal. The only pathological feature observed was the somewhat excessive vacuolization of the muscle fibres, due no doubt to the suspension of function.

A second series of experiments was made, in which embryos of the same stage as used above were allowed to develop in solutions of acetone-chloroform,¹ 0.02-0.03 per cent in strength. Embryos reared in these solutions develop almost normally though more slowly than those kept in water. They were never observed to make any voluntary movements, nor did they respond reflexly to mechanical stimuli, owing to the action of the drug upon the nerve centres. At the close of the embryonic period, when the yolk had been absorbed, the larvae were put into fresh water. After the expiration of ten minutes larvae of *R. virescens* had recovered sufficiently to react to stimuli and in a quarter of an hour were able to swim and to carry on respiratory movements. Larvae of *R. palustris* require a considerably longer time for their recovery. Sections of larvae, killed without being allowed to recover, show normal morphological differentiation of musculature and nervous system.

The first series of experiments, in which the influence of the nervous system was removed by operation, shows conclusively that the normal differentiation of muscular tissue is absolutely independent of stimuli from the nervous system. The second series, where the nerve influence was suspended through the action of a drug, while not conclusive in itself, corroborates this result. It shows, moreover, that complex nervous and muscular mechanisms may develop without a functional stimulus and that they may be ready to perform their function as soon as the inhibition is removed, although in the frog normally the development of these functions is a gradual one.

¹Known commercially in the United States as chloretone.

VI Proceedings of the Association of American Anatomists

THE TERMINAL ARRANGEMENT OF THE BRONCHI IN THE CAT. By
WILLIAM S. MILLER. *University of Wisconsin.*

THREE CASES OF A PANCREATIC RESERVOIR OCCURRING IN THE
DOMESTIC CAT. By WILLIAM S. MILLER. *University of Wisconsin.*

In 1815 Mayer figured and described a pancreatic reservoir in the cat. This reservoir was connected by means of a long duct with the duct of Wirsung. In 1879 Gage of Cornell figured and described a second case of a pancreatic reservoir also in the cat. In this case the duct coming from the reservoir bifurcated into two short divisions, one of which entered the duct of Wirsung, the other the main duct of the splenic division of the pancreas. In the three cases which I report, in each instance the duct coming from the pancreatic reservoir opened into the duodorsal division of the *ductus pancreaticus*. In all five cases thus far described the pancreatic reservoir has occupied a position close to the gall bladder and its duct has throughout its course run nearly parallel to the *ductus choledochus*.

THE LYMPHATICS OF THE LUNG OF NECTURUS (Demonstration). By
WILLIAM S. MILLER. *University of Wisconsin.*

The lungs of *Necturus* consist of two elongated, cylindrical bodies which are connected anteriorly with the short, wide pharynx. In the abdomen they are situated one on either side of the body cavity and are attached to the stomach by a thin loose mesentery which extends nearly the entire length of each lung.

The pulmonary artery runs along the medial side of the lung, giving off branches, at nearly right angles to its course, which break up into a capillary network. The pulmonary vein arises from this network by short radicles and runs along the lateral side of the lung. The pulmonary veins coming from each lung unite in the midline and form a single trunk which runs along the ventral side of the short *ductus pneumaticus* and enters the heart.

There is present in the walls of the stomach a network of very large lymphatics which unite to form near its cephalic end a prominent vessel which is situated in the midline and passes dorsal to the single trunk formed by the union of the pulmonary veins. The lymphatics of the lung are connected with this network.

The lymphatics can be divided into two groups:—

- a) Lymphatics of the pulmonary artery.
- b) Lymphatics of the pulmonary vein.

Along the pulmonary artery the lymphatics form three main trunks

which are connected with each other by numerous branches, thus forming a complete network about the artery. From this network lymphatics pass to the branches of the pulmonary artery. These are usually two in number, one on each side of the arterial twig, and are connected by short branches.

The network of lymphatics about the branches of the pulmonary artery extends across the intervening part of the lung to the venous radicles which they now accompany. In this manner two, rarely three, main trunks are formed which follow the course of the pulmonary vein. These trunks are connected by short branches but the network thus formed is not so compact as that about the artery.

The lymphatics of the lung of *Necturus*, therefore, consist of a closed system of vessels intimately associated with the blood vessels; a condition similar to that present in the lungs of higher vertebrates.

ON THE MORPHOLOGY OF SUDORIPAROUS AND ALLIED GLANDS.
By G. CARL HUBER. *University of Michigan.*

ON THE PRESERVATION OF SUBJECTS FOR DISSECTION BY INJECTION WITH FORMALIN AND CARBOLIC ACID SOLUTIONS AND STORAGE BY IMMERSION IN SIMILAR SOLUTIONS. By WILLIAM KEILLER. *Medical Department of the University of Texas.*

The body is to be injected if possible within 24 hours after death unless the weather be cold, when it may be better to let post-mortem rigidity pass off. During injection the arms are to be fixed in full abduction, the forearms supine, the fingers extended by fixing the fingers by means of large iron staples to a board passing behind the shoulders. After the preservative injection is finished the board is to be removed and not reapplied for the colored injection. The apparatus is a set of T-tubes, size to fit the common carotid artery, a 5-gallon bucket with stopcock, swivel, rope and pulley to run it up to the ceiling, 15 feet of three-eighth inch bore red rubber tubing, tongs to suspend the body from the ceiling by the external auditory canals and rope and pulley for the same.

Nearly 10 gallons of fluid are to be used, the first 5 gallons with the body lying on the floor, the second 5 gallons or as much over the first 5 gallons as the body will hold while suspended from the ceiling. For hardening a body to be used as a His' model with movable viscera use recipe 1; for dissecting purposes use recipe 2; for operative surgery use recipe 3. The body can be stored indefinitely in the solution, recipe 4. For arterial colored mass use recipe 5, injecting not less than a week after the preservative.—

VIII Proceedings of the Association of American Anatomists

R 1. FOR SECTION AND SPECIAL DEMONSTRATION OF VISCERA IN SITU.

Formalin	2.5
Carbolic acid	2.5
Glycerin	10.0
Water	q. s. to 100.0

R 2. FOR ORDINARY DISSECTING PURPOSES.

Formalin	1.5
Carbolic acid	2.5
Glycerin	10.0
Water	q. s. to 100.0

R 3. FOR OPERATIVE SURGERY.

Formalin	1.0
Carbolic acid	2.5
Glycerin	10.0
Water	q. s. to 100.0

R 4. FOR STORAGE TANKS.

Formalin	1.0
Carbolic acid	2.0
Water	q. s. to 100.0

Glycerin to the amount of 2½ per cent will be an advantage but is not necessary.

R 5. COLORED INJECTION MASS.

A. Potassium bichromate	3 ounces.
Water	1 pint.
B. Lead acetate (commercial)	6% ounces.
Water	1 pint.
C. Gelatin (commercial)	4½ ounces.
Water	1 pint.

Dissolve A, B, and C in separate stone jars immersed in a large fish kettle and raised very nearly to boiling point. Strain the gelatin solution through fine wire strainer into a vessel capable of holding 2 quarts; add to this while hot, the hot bichromate solution (also strained), stir well and add gradually, while hot, the acetate of lead solution (also straining it). Inject while hot with a brass anatomic syringe, using about as much force as you can exert with the hand. The fluid should be so hot that you require to protect with a cloth the hand holding the syringe. Each body will require about a pint. The bodies do not require to be warmed and will be ready for dissection after 24 hours. Bodies so prepared if protected on the tables by oiled cloth will keep indefinitely. The perineum is to be dissected after the legs are removed, the long pudendal nerve and internal pudic vessels and nerves being carefully kept intact. The knees and hips can be made moveable by frequently moving them before and during the injection.

THE ANATOMY OF THE HUMAN INSULA IN ITS RELATION TO THE
SPEECH-CENTERS; ACCORDING TO RACE AND INDIVIDUALITY.

By EDWARD ANTHONY SPITZKA. *Anatomical Laboratory, Columbia University.*

The insula, probably the purest association area in the brain, seems to be most intimately concerned with the speech-faculties. The purpose of these investigations was to ascertain the form, size and surface-markings of the insula in the brains of various races and in those of **known** or distinguished men. Thus far, the race-brains in the series were those of 4 Eskimos, 2 Papuans, and 1 Japanese. The distinguished or **known** individuals were Dr. Edouard Seguin, his son Dr. E. C. Seguin, W— A—, a New York Assemblyman, an Anatomist, a **Palaeontologist**, General Morphologist, a Physician and a Cerebral Morphologist. The brief descriptions by Waldschmidt of the insulae of two Freiburg professors, by Rüdinger of those of H. V. Schmid and Wulfert; and by Wilder of the exposed insulae of Chauncey Wright, seem to be the only references in the literature.

The author's investigations included the making of drawings, wax and plaster models or casts, and careful measurements, for purposes of comparison. The number of specimens is far too small for generalization, yet the following may be tentatively proposed: a. The insula is, on the whole, somewhat of an index of the degree of development of the general cerebral surface, particularly of those parts which are more or less in juxtaposition with it. This is especially demonstrable in the redundancy of the preinsula in persons noted for their powers of speech. (The significance of this redundancy of the pre- or post-insular region, as the case may be, in its relation to the greater or lesser development of neighboring somaesthetic and sense-areas, seems strongly emphasized in the form of the insulae of the cetacea and proboscidea.) b. The two insulae in the same brain usually exhibit a common type; and there seems to be a difference of type according to race. When there is any notable difference between the two sides, it is practically always in favor of the left insula, so far as size, massiveness and complexity of configuration are concerned.

c. The exposure of the insula has already been noted by the author in the **two** Seguin brains, and Wilder has observed it in the brain of Chauncey Wright. This feature has been explained elsewhere. In the race-brain series, the insula is exposed on both sides of two Eskimos (Atana and Avia) more so on the left than on the right side.

The author would urge the necessity of obtaining for further study the brains of men notable for their oratorical powers, as well as of

members of lower races whose language is of the simplest kind; of studying the relations of the insula to the lenticular nucleus, claustrum, and the mass of the paraclaustral lamina of white fibres; and lastly, of obtaining the brains of left-handed persons for the purpose of seeking a commensurate redundancy of the right insula as compared with the left.

THE DISTRIBUTION OF BLOOD VESSELS IN THE LABYRINTH OF THE EAR OF THE DOMESTIC PIG. By GEORGE E. SHAMBAUGH. *Hull Laboratory of Anatomy, University of Chicago.*

(Read by title.)

The circulation of the labyrinth of the pig's ear was studied by means of celloidin casts of the labyrinth. Injections of a large number of embryos were made, of sizes measuring from 2.5 cm. in length to the foetus at full term. The complicated system of vessels found in the foetus at full term was interpreted in part by the study of the more simple arrangement found in the younger embryos. The arterial blood is supplied to the labyrinth by a single vessel which reaches the labyrinth through the meatus acusticus internus. Its terminal branches anastomose freely with each other before giving off the vessels which supply the various parts. The venous blood is collected in a single large trunk which leaves the labyrinth along with the canaliculus cochleae.

A COMPARISON OF HUMAN AND ORANG HEARTS, WITH LANTERN SLIDES. By J. RALPH HARRIS. *Washington, D. C.*

(Read by title.)

SINUSES OR AIR CHAMBERS IN COMMUNICATION WITH THE NASAL FOSSAE. By DANIEL KERFOOT SHUTE. *Columbian University, Washington, D. C.*

NOTES ON THE EARLY DEVELOPMENT OF RODENTS. By THOMAS G. LEE. *University of Minnesota.*

Spermophilus tridecemlineatus exhibits in its preplacental development certain remarkable and important conditions which differ from those of any other mammal yet described. The ovum enters the uterine cavity in the morula stage usually surrounded by a zona pellucida; it rapidly differentiates an ectodermal trophoblast layer and an inner cell mass which forms the germinal ectoderm and endoderm. The uterus has a characteristic T-shaped lumen, the lateral portion or *placental chamber* next the mesometrium, the vertical portion consisting of the long *intermediate portion* which terminates in the *fixation chamber* at the antimesometrial portion.

The blastocyst passes into the fixation chamber, the trophoblast develops at the anti-embryonal pole a syncytial enlargement, the *fixation mass* which perforates the uterine epithelium and spreads out between the surrounding epithelium and the mucosa; this mass soon develops root-like processes which project into the vascular mucosa. This condition continues while the blastocyst is increasing in size and forming a decidual cavity at the expense of the intermediate portion; as this cavity is developed, the lateral trophoblast of the blastocyst causes a destruction of the lining epithelium; finally a zone of trophoblast surrounding the germinal area is brought in contact with the margin of the placental chamber, and thus is begun the formation of the true placenta. As this stage is reached, the blastocyst becomes entirely separated from the uterine mucosa of the fixation chamber by degeneration of the root-like processes of the fixation mass. The trophoblastic covering of the germinal area (Raubert's layer) has now disappeared and then follows a folding over of the marginal trophoblast and borders of the germinal area to form the amniotic cavity; the united trophoblast (serosa) extends into the placental chamber and causes destruction of its lining epithelium which up to this time has been unaltered. Where the uterine mucosa comes in contact with the trophoblast there are developed vascular channels which penetrate the trophoblast, and the allantoic outgrowth of the embryo has spread out as a disk on the underside of the trophoblast and gives rise to vessels which penetrate it.

Fiber zibethicus shows in its early development the so-called inversion of layers and presents a number of interesting facts in comparison with the other described Muridae.

A detailed description of the preplacental stages of *Spermophilus* is now in press, and a paper now in preparation will figure and describe the formation and structure of the true placenta of *Spermophilus*, *Fiber* and other hitherto undescribed rodents.

NOTES ON THE VARIATION IN ORIGIN OF THE INTERNAL CAROTID OF THE HORSE. By GRANT S. HOPKINS. *Department of Veterinary and Comparative Anatomy, Cornell University.*

The origin of the internal carotid artery was noted in fifteen cases—on both sides in eight of them, on one side only in the remainder. In eight cases the internal carotid originated as commonly described, namely, as one of the terminal branches of the common carotid. In the remaining seven, the relation of the internal carotid to the occipital and external carotid varied considerably. In three specimens it originated from one to eight centimeters posterior to the occipital; in three others, it and

the occipital originated from a common trunk of varying length in the three specimens, of which the longest was sixteen centimeters. In one specimen the occipital and internal carotid, on the right side, were given off as commonly described, but on the left side the internal carotid originated five centimeters posterior to the occipital.

A STUDY OF THE HISTOGENESIS OF THE PIG'S ADRENAL. By R. H. WHITEHEAD. *Medical Department, University of North Carolina; Hull Laboratory of Anatomy, University of Chicago.*

The anlage of the cortex is first detected in embryos about 8 mm. long. In passing from older to younger stages this anlage gradually approaches the coelomic epithelium, and finally, in the embryo of 8 mm., lies in contact with the epithelium immediately lateral to the attachment of the mesentery. It is very difficult to detect any difference between the cells composing the two structures, and the conclusion is drawn that the anlage of the cortex is probably derived from the coelomic epithelium, either by rapid invagination, or by the wandering of cells into the mesenchyme.

The medulla is first found in embryos of from 30 to 35 mm. At this stage it lies spread out as a mantle around the periphery of the cortex. The cells composing it are identical in appearance with those which compose the adjacent anlagen of the sympathetic ganglia; and the mantle is in direct continuity with the ganglia by means of connecting strands of cells which enter along the dorso-medial aspect of the adrenal, in which region the capsule is, in large measure, wanting. Collections of cells pass from the mantle in between the cortical rows to reach finally their adult position around the central vein in the way described by J. M. Flint.

THE DERIVATION AND SIGNIFICANCE OF CERTAIN SUPERNUMERARY MUSCLES OF THE PECTORAL REGION. By GEORGE S. HUNTINGTON. *Anatomical Laboratory, Columbia University.*

The primate pectoral region offers peculiar conditions both as regards the ontogeny of the pectoral muscles and the development of the ventral thoracic wall. As the direct result of these conditions a number of anomalous supernumerary muscles are encountered in this region, united into a group by their derivation from the muscular sheet of the Pectoralis and by the common etiological factors apparently responsible for their production. These variations possess a very definite morphological character, and one of the members of the group, the Sternalis, occurs in a remarkably constant percentage. The variant muscles are

not of reversional significance, since they cannot properly be homologized with divisions of the Pectoralis normally encountered in the mammalian series, notwithstanding the wide range of complexity which the Pectorales present in the mammalian orders below the primates.

The group is again subdivided, according to the position occupied by the variant in reference to the plane of the Pectoralis major, into:

- A. *Supernumerary muscles placed superficially to the Pectoralis major.*
 - 1. Sternalis.
 - 2. Infraclavicularis.
- B. *Deep supernumerary muscles in the interval between the Pectoralis major and minor.*
 - 1. Chondro-coracoideus ventralis (Pectoralis minimus).
 - 2. Tensor semivaginae articulationis humero-scapularis (Gruber).
 - 3. Some forms of the Præclavicularis.

In attempting to define the derivation and significance of these variations the following etiological factors deserve consideration:

- 1. The relation between the variant muscles and coexisting deficiencies in the plane of the Pectoralis major, especially conditions indicating that the variant represents a portion of the normal muscle atypically displaced.
- 2. Innervation of the variant.
- 3. The peculiar type of development followed by the pectoral group, as determined by Mall and Lewis, together with the development and fusion of the sternal bar in the formation of the ventral thoracic wall.
- 4. Atypical cleavage of the Ecto- and Entopectoralis, resulting in the production of the intermediate supernumerary pectoral muscles.
- 5. The possible significance of some superficial pectoral slips as remnants of the thoraco-humeral panniculus.

Conclusions.—1. The components of both the superficial and deep group of variants are frequently associated with defects in the muscular plane of the Pectoralis major.

2. The innervation of all the muscles here considered is probably uniformly by branches derived from the anterior thoracic nerves.

3. The superficial group develops in consequence of ontogenetic disturbances in the normal migration of the pectoral mass, and may be further influenced by faulty development in the closure of the ventral thoracic wall. The atypical widening of some of the intercostal spaces, adduced by Eisler as the main etiological factor in the production of the Sternalis, does not obtain uniformly.

4. Certain instances of Sternales, occurring in direct combination with additional supernumerary muscles, of undoubtedly pannicular origin, may possibly represent reversions of the cuticular muscle. More probably, however, they are to be interpreted as examples of coincidence of several etiological factors simultaneously operative in the same individual.

5. The muscles forming the deep group result from faulty processes in the cleavage of the pectoral mass, while their secondary attachments yield the subvarieties noted.

THE EVOLUTION OF THE FLEXOR SUBLIMIS DIGITORUM. By JAMES PLAYFAIR McMURRICH. *University of Michigan*. AMERICAN JOURNAL OF ANATOMY, VOL. II, No. 2.

NOTES ON THE HISTOGENESIS OF THE STRIATED MUSCLE IN NECTURUS. (Communicated by LEVELLYS F. BARKER.) By ALBERT C. EYCLESHYMER. *Harvard Embryological Laboratory and Hull Laboratory of Anatomy, University of Chicago*.

The myoblasts in the earliest stages (5-7 mm.) form a more or less complete syncytium; i. e. there are cytoplasmic strands connecting the ends of myoblasts in adjoining myotomes. After the septa are formed through the ingrowth of the mesenchyme these strands are no longer discernible.

The myoblasts in all stages correspond precisely in length to the respective lengths of the myotomes from which they are taken. It is therefore improbable that in this form a number of myoblasts, in adjoining myotomes, unite to form a single muscle fibre as observed by Godlewski in the rabbit.

The first change in the myoblast preparatory to fibrillation is an accelerated absorption of yolk granules in either end of the myoblast which gives rise to clear, yolk-free zones. In the clear zones which have thus arisen, longitudinal striæ are soon differentiated. These striæ are first formed on the notochordal side of the myoblast and in the 7 mm. embryo converge in such a manner that they take on a somewhat conical or brush-like arrangement. The bases of these cones, or brushes, spread over a considerable portion of the end of the myoblast while their apices lie on the notochordal margin.

These striæ are the beginnings of the fibrillæ proper, but at first show no transverse markings whatever. *Pari passu* with the absorption of yolk granules these cones of fibrillæ rapidly extend, each toward the other until, in the 8 mm. embryo, they have united and have given rise to a continuous tract on the notochordal side of the cell. The entire tract

taking on the general form of an hour-glass. At this time the isotropic and anisotropic bands are differentiated throughout the entire length of the fibrilla.

Since one observes the fibrillæ divided throughout variable portions of their extent and since their number at either end of the myoblast is greatly in excess of that at the level of the centre of the myoblast, one is led to infer that the mode of increase is longitudinal division.

The cytoplasmic network, if such it may be called, is exceedingly variable, not only in different myoblasts, but also in different portions of the same myoblast. Instead of a network one finds a granular matrix filled with vacuolar spaces which are highly variable in both form and size. The appearances lead one to doubt the existence, in the living cell, of a cytoplasmic network.

That such a network, if it be present in the living cell, bears any definite relation to the fibrillæ is very doubtful. Its meshes must undergo marked transformation during the absorption of yolk granules, changing from the enormously large meshes, which contain the yolk-spheres, to the exceedingly minute meshes containing the fibrillæ or groups of fibrillæ. Again in conformity to the conical grouping of fibrillæ, the meshes of such a network must converge toward the notochordal side, or in other words, as the fibrillæ divide and subdivide the meshes must do likewise. This is highly improbable; moreover were it true, we should expect to find the smallest meshes at the ends of the myoblast, but this is not the case.

Those who believe in the existence of a cytoplasmic network maintain that certain transverse markings of the fibrilla are due to the transverse strands of this meshwork. The fibrillæ when first formed present no transverse markings.

The observations on *Necturus* lead one to conclude that the fibrillæ form independently of the so-called cytoplasmic network; the differentiation of the transverse striations being due to certain portions of the fibrilla taking up chromatin or at least a phosphorous-holding nuclein as pointed out by A. B. Macallum.

ON THE RELATION OF THE THIRD FOETAL SYSTEM OF TREPINSKI TO THE DIRECT CEREBELLAR TRACT. By LEWELLYS F. BARKER.
Hull Laboratory of Anatomy, University of Chicago.

The report referred to the study of two cases of Dr. Sanger Brown's series of hereditary ataxia, and especially to the degeneration of areas in the posterior funiculi which correspond closely to the region occupied by the fibres of the third foetal system of Trepinski, associated with de-

generation of the direct cerebellar tract (Fasciculus spinocerebellaris dorso-lateralis) in the lateral funiculi. Corresponding to the very extensive degeneration of the direct cerebellar tract there is almost total disappearance of the cells of the nucleus dorsalis. The association of the two systemic degenerations indicates a probable functional relation between the third foetal system of Trepinski, the nucleus dorsalis and the direct cerebellar tract.

The results reported in the paper will be incorporated in a larger report upon the whole subject to appear later.

AN ANOMALOUS VENA CAVA INFERIOR. By DANIEL G. REVELL. *Hull Laboratory of Anatomy, University of Chicago.*

The case was observed in the anatomical department of the University of Toronto.

The vena cava inferior was absent excepting a slender vessel which extended from the vena iliaca communis dextra to the V. renalis dextra. Its place was taken *postrenally* by a persistent V. cardinalis sinistra; *prerenally* by the V. hemiazygos (V. azygos minor inferior) and the cranial half of the V. azygos (V. azygos major). There were two hepatic veins, which passed through two openings in the diaphragm and opened separately into the heart.

A full description will be published elsewhere.

THE MESAL ASPECT OF THE LEFT HEMICEREBRUM WITH SELECTED HUMANS AND REPRESENTATIVE OTHER PRIMATES. By BURT G. WILDER. *Cornell University.*

The brains exhibited were from two mathematicians and philosophers; two educated women; a lawyer and politician, afterward a drunkard and pauper; an unknown mulatto and an ignorant black; an insane woman, an idiot, and a murderer; an orang, gorilla, and chimpanzee. There was presented a table including the foregoing with other orangs, a gibbon, two other idiots, and a mathematical teacher. The table gave the ratios to the length of the left hemicerebrum of (a) the width of the precuneus; (b) the height from the "central eminence" (just cephalad of the dorsal end of the central fissure) to the tip of the temporal lobe; (c) the height from the central eminence to the cut surface left by removing the olfactory tract; this, the "olfactory ratio" was found less variable than the "temporal;" in either case the plane coincides very closely with the general location and direction of the central fissure.

Certain results of the comparison are noteworthy, but the main object of this paper is to emphasize the need of rendering the study of the fissures both more general and more perfect.

Amongst the means to this end are: (a) Early familiarity with cerebral topography. (b) Preserving the brains, especially of the rarer Primates, even at the sacrifice of the skulls. (c) Insuring the identification of such brains by preserving also the entire animals or characteristic parts under the same number. (d) Preserving the brains of Foetuses and of orderly and educated persons, particularly of blood-relations. (e) Employment of the most perfect methods of removal, preservation, preparation, and study, including a simple and correlated terminology. (f) Beginning with the mesal aspect rather than with the lateral or dorsal. (g) Providing that those best qualified by nature and training for the elucidation of the many and complex fissural problems should devote themselves thereto continuously for considerable periods.

REASONS WHY ORDERLY, EDUCATED AND FAIRLY PROSPEROUS
WHITES SHOULD LEAVE THEIR BRAINS FOR SCIENTIFIC
PURPOSES, WITH SUGGESTIONS FOR FORM OF BRAIN BEQUEST.

By BURT G. WILDER. *Cornell University.*

From the nature of the case most of the human brains hitherto preserved or studied have come either from individuals recognizably defective in respect to senses, intellect, character, or capacity; or from individuals notably superior or peculiar; or from members of other races than the white. Descriptions have tacitly or expressly assumed the existence of a normal or standard condition. Such a standard cannot be claimed to exist at present. Its determination is very desirable with reference to both defectives and the eminent; likewise with reference to other races, particularly the black; likewise for the sake of formulating the distinctions between the human fissural pattern and that of the other Primates.

There are suggested certain improvements in the Form of Bequest hitherto employed by the writer.

Of brains of orderly educated persons there are now preserved in the Neurologic Department of Cornell University thirteen, nine male and four female. There have been bequeathed seventy, forty-seven male and twenty-three female. Of the total number, eighty-three, seventeen are or have been physicians and thirty-three have had other degrees. Fourteen are or have been college professors and five teachers in schools. The speaker deprecated the recent publication in the daily press of sensational items and erroneous, even preposterous, statements, opinions and

expectations ascribed to him. In particular he wished it understood that no person ever has been asked to bequeath his brain to him or to any organization or institution represented by him.

QUERIES AS TO THE HUMAN ANKLE-JOINT AND THE PERONEUS TERTIUS. By BURT G. WILDER, *Cornell University.*

Has a rudiment of the peroneus tertius been recognized outside the human species? What are the latest statistics as to its presence in the several races of man? The conditions that permit apposition of the soles of the feet in climbing or for prehension are obviously useful with arboreal forms; but with man at his present stage of evolution do they confer any advantage commensurate with the disadvantage of the liability to sprain the ankle with inversion of the sole? If not, must not the existence of these conditions be regarded as purely phylogenetic rather than teleologic. Referring to the address of C. S. Minot as president of the American Association for the Advancement of Science, 1902 (*Science*, July 4, 1902), if the remarks on p. 5 as to the preservation of "only such structures and functions as are useful or have a teleological value" apply also to conditions as determined by structures, then either the designated conditions of the human ankle have a present use that is not apparent, or else they constitute an exception to the rule.

DEMONSTRATIONS.

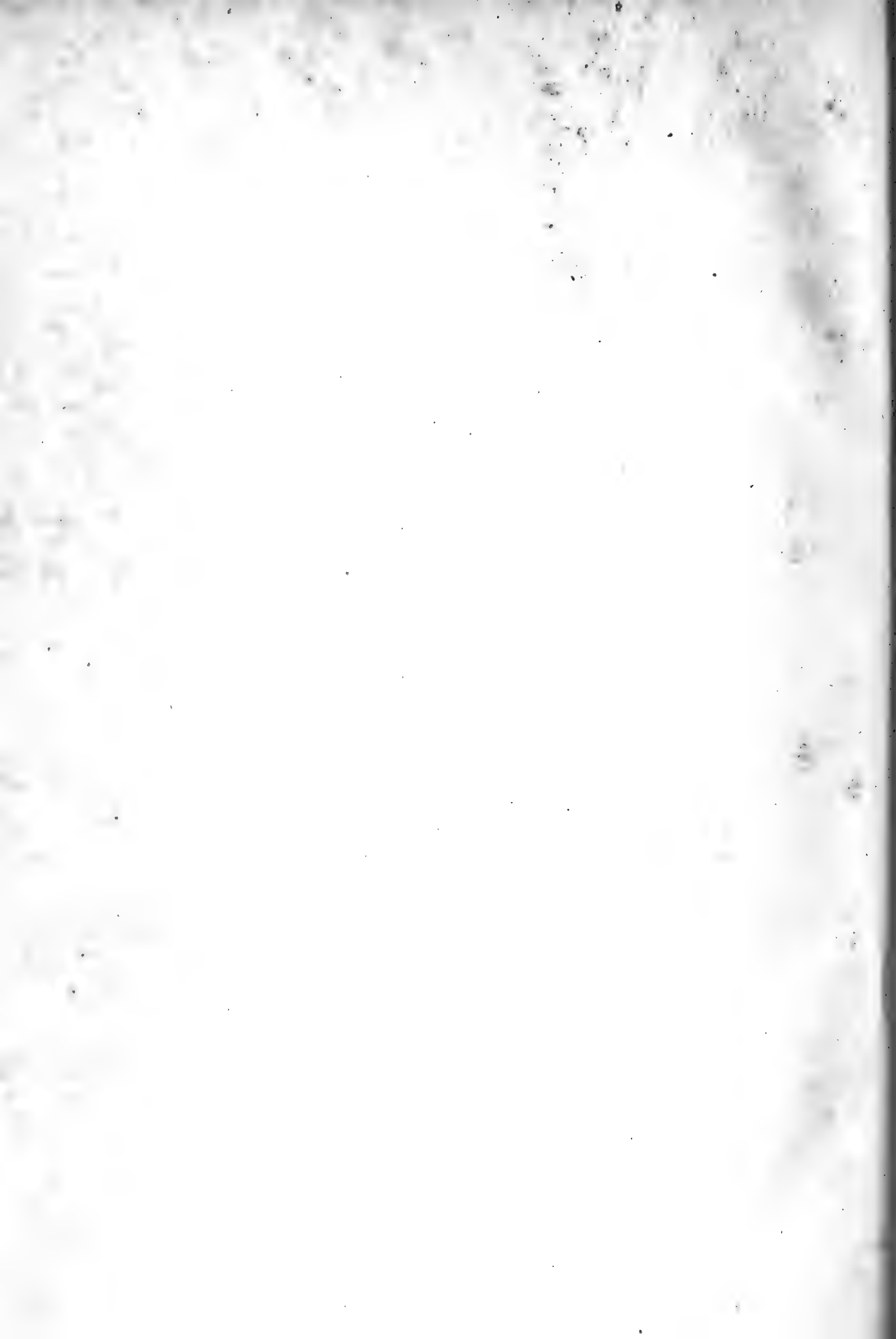
1. Dr. Charles R. Bardeen: *a.* The effect of fatigue on muscle nuclei (P. K. Gilman). *b.* Nerve and muscle preparations. *c.* Students' charts made during dissection.
2. Dr. Ross G. Harrison: *a.* Specimens illustrating the differentiation of muscular tissue when removed from the influence of the nervous system. *b.* Specimens illustrating the development of the lateral line and wandering of the skin in the amphibian embryo.
3. G. Carl Huber: *a.* Models of sudoriparous and allied glands. *b.* Photograph of a new apparatus for making wax plates for reconstruction after the method of Born.
4. Dr. William Keiller: Specimens illustrating the state of preservation of material injected by formalin and carbolic acid solutions, also wet and dry museum preparations.
5. Dr. Abram T. Kerr: Corrosion preparations.
6. Dr. Henry McE. Knowler: A demonstration on illustrations for anatomical publications.
7. Dr. William S. Miller: *a.* Models illustrating the terminal arrangement of the bronchi in the cat. *b.* Specimens illustrating pancreatic bladder in the cat. *c.* The lymphatics of the lung of *Necturus*.
8. Dr. Burton D. Meyers: Specimens illustrating the partial decussation of the optic fibres in the chiasm of some mammals, and the commissuræ on the floor of the third ventricle.

9. Dr. Florence R. Sabin: Gross and microscopic preparations of developing lymphatics.
10. Dr. Edward A. Spitzka: Drawings and plaster models, illustrating the anatomy of the human insula in its relation to the speech-centres.
11. Dr. Mervin T. Sudler: Photographs of the lymphatic system and topographical dissections as made in the anatomical course of the Cornell University Medical College.

G. CARL HUBER,
Secretary-Treasurer.







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