FURTHER ADVANCES IN PHYSIOLOGY

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EDITED BY

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WITH DIAGRAMS

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PREFACE

THE volume now put before the reader by the editor is a sequel to "Recent Advances in Physiology," and deals with certain branches of the science other than those dealt with in that volume, the treatment of the subject-matter being, in both, on the same general lines. The aim of the editor and his coadjutors has been to write up their views on certain selected subjects which, both by their importance and interest, will stimulate the student, give him a view wider than that which the ordinary text-book can give him, and at the same time rivet his attention on subjects which have a particular application to Pathology and Clinical Medicine. While the former volume dealt mainly with problems of metabolism, secretion, and excretion, this is devoted to the consideration of certain problems concerning the circulation and respiration, the neuro-muscular system, and vision. Prof. B. Moore, writing on the relation of the heart-beat to its nutritive fluid, has developed this subject into a general consideration of the equilibrium of colloid and crystalloid in living cells. Mr. Martin Flack has discussed the present position of the myogenic and neurogenic theories of the heart-beat, and analysed the recent researches which have modified the lines of thought on this subject. Dr. Thomas Lewis has given the reader an account of the venous pulse, and those methods of investigating the cardiac cycle in man which have done so much, in the hands of Dr. James Mackenzie and others, to elucidate the different forms of heart trouble. The editor has dealt, firstly, with the wonderful advances in experimental method made possible by Carrel's surgical union of the blood-vessels; secondly, with blood pressure and its measurement in man. He has endeavoured to refute the supposed importance of blood pressure as a mechanical factor in the formation of lymph, production of dropsy, excretion of

urine, &c. Dr. Arthur Keith has contributed an account of his researches into the mechanisms of breathing, and thereby has upheld the importance of anatomy treated as a study of function. Dr. Pembrey has given an account of the subject he knows so well—the Physiology of Muscular Work—and has incorporated therein the new results which have been obtained, particularly in this country, by the study of marching soldiers. The present views held concerning the growth, regeneration, union of nerves, and the nature of the nerve impulse, have been considered by Dr. N. Alcock; while Dr. J. S. Bolton has contributed an account of the recent researches of himself and others on cortical localisation and the functions of the cerebrum, including the revolutionary views which have been put forward concerning Broca's localisation of Aphasia. Lastly, Mr. Major Greenwood has dealt with two especially interesting subjects of sense physiology—Visual Adaptation and Colour Vision. Each writer is responsible for the views he has set forth and the treatment of his subject, and the editor has done no more than select his coadjutors, write his own part, and arrange the book for the press. He hopes it may meet with as cordial a reception as the first volume, serve a useful part, and be perhaps the forerunner of still other volumes, of "more" and "most recent," and even "furthest" Advances in Physiology.

OSBORNE HOUSE, LOUGHTON,
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FURTHER ADVANCES IN PHYSIOLOGY

THE EQUILIBRIUM OF COLLOID AND CRYSTALLOID IN LIVING CELLS

By BENJAMIN MOORE

THE living cell may be regarded from the physico-chemical point of view as a machine or mechanism through which there constantly is taking place a flux of energy. The cell is continually taking energy up from its surroundings in certain forms, and redistributing this energy in other forms, but in the process it itself undergoes little or no permanent change. Certain changes, it is true, do occur slowly in the cell in the course of its life-history which have the effect of permanently altering the character of the energy discharged through it; but these structural changes are so slow that they can be put aside in the study of the cell as an energy machine acting upon the energy supply at any given moment.

If the case of the green plant cell acting as an energy transformer for light energy be placed on one side, it may be stated that the energy supplies of the cell always come to it in the form of organic compounds capable of yielding energy in the process of oxidation in the cell.

In order that the cell may be capable of oxidising these chemical compounds of organic character coming in from its environment, it is, however, absolutely essential that its own integrity be preserved; and this integrity is just as completely dependent upon the presence of the ions of certain simple inorganic salts in the cell and its surrounding fluid media, as the exhibition of the typical phenomena of cell activity is upon the supply of energy in the form of the organic compounds to the living cell. In fact, in point of time, the physiological activity of the cell is more rapidly destroyed by removing or altering the supply of

inorganic ions, than it is by interfering with the supply of organic foodstuffs. For, in the latter case, the cell can oxidise the combustible materials present in storage within it, and even use up a portion of its own intrinsic substance before its activities come to a standstill; but when the inorganic ions, forming a constitutional part of the living cell, are altered, and the equilibrium between protoplasm and ion thus destroyed, the cell activities are immediately affected, and after a short period of pathological activity everything comes to rest.

An analogy with another form of energy transformer may make this clearer. If the fires are banked under the boiler of a steam-engine the head of steam in the boiler will for a longer or shorter period keep the steam-engine going, this is comparable to stopping the organic food supply of the cell; but if there is a sudden burst in the boiler, if the cylinder blows off, or if there is a break in any essential part of the machinery, then there is a sudden stoppage of the engine, often preceded by a very brief period of excessive activity: this is comparable to interference with the inorganic ions of the cell. The inorganic ions form in fact an intrinsic and indispensable part of the cell's structure, in the absence of which it can no longer utilise its food supply, however abundant that supply may be, or suitably adapted for the nutrition of the normal cell.

These effects, although they may be demonstrated in any living tissue, are seen perhaps most typically in the case of the isolated and perfused heart muscle. If the fluid caused to flow through the heart consists of distilled water, to which organic foodstuff, in the form say of dextrose, has been added, the heart beat ceases almost instantaneously. If next the experiment be repeated upon a fresh heart, using instead a solution of pure sodium chloride in distilled water, of such concentration that it is isosmotic with the natural serum of the animal, there ensues a considerably longer period of perhaps some minutes' duration before the heart beat disappears. The sodium chloride solution, however, although possessing the proper osmotic pressure, is unable for any considerable time to preserve the heart muscle cells in normal condition. By supplying the proper osmotic concentration it has prevented the cells being suddenly broken up, but it has a zero pressure for certain ions indispensable to the heart's activity; these have slowly diffused out, and the period of the heart's action

has been determined by that moment at which the concentration in the protoplasm has reached a certain minimal value.

The most important of the ions which have been washed out of the cardiac muscle cells by the current of pure sodium chloride solution are the potassium and calcium ions. It still possesses abundance of combustible organic material to furnish the energy for its contractions, but the structural mechanism or machine for oxidation has been interfered with and the cells can no longer draw on their supply of stored energy.

That this is the true state of the case is shown by the effects of adding quite minimal traces of soluble salts of calcium and potassium to the pure sodium chloride solution, when the spontaneous beating of the heart commences and goes on for hours, and even days, in a regular and automatic manner.

The amounts of potassium and calcium salts necessary to bring out this profound difference in behaviour of the heart muscle are strikingly small, the optimum amount of potassium chloride required being only about 1 part in 10,000. More than an exceedingly minute trace must not be added or the heart will be stopped by the excess. There is only a certain range of concentration which must not be passed in either direction or the heart will not beat normally. The meaning of this range will be pointed out later.

These important experimental results were first demonstrated by Sidney Ringer in the case of cardiac muscle of the frog heart; the complete generality of their application in all cells and tissues, and the causes underlying them, are only in recent times becoming generally appreciated, but the delicate and lightly balanced labile equilibrium between the colloids of the cell protoplasm and the osmotic pressures or concentrations of the inorganic ions and other crystalloid constituents is perhaps the most important and fundamental fact in the whole of biology.

The inorganic ions are sufficient in the case of the more slowly oxidising cardiac muscle of the heart of the cold-blooded animal to maintain for lengthened periods an automatic rhythmic beat; the sufficient amount of oxygen for the oxidation being capable of being carried at the partial pressure of one-fifth of an atmosphere that the atmospheric oxygen possesses, and the combustible organic material coming from the store in the cardiac muscle cells. But in the case of the mammalian heart, the oxygen pressure

must be increased to nearly a whole atmosphere of pure oxygen by bubbling oxygen gas through the Ringer's saline heated to mammalian body temperature in a flask attached to the perfusion cannula, before a normal heart beat can be obtained. This increased oxygen pressure supplies the place of the red blood corpuscles which in the body are able to carry a sufficiency of oxygen at the lower pressure of oxygen present in the lungs. Also, in the case of the mammalian heart for a prolonged experiment, it is well, as recommended by Locke, to add dextrose to the Ringer's solution to prevent exhaustion of organic combustible material which occurs earlier in the case of mammalian muscle on account of the greater expenditure of energy which here occurs at each heart beat.

Before leaving the classical example of cardiac muscle for more general considerations, the similar action of anæsthetics may be mentioned as an example of the relationship of drugs to the cell-protoplasm.

The conditions which govern the action of chloroform upon the isolated mammalian heart have been beautifully demonstrated by Sherrington and Sowton. These observers have shown that at a fairly definite concentration of chloroform in the circulating saline the heart beat becomes affected, and if this concentration be passed the beat is stopped. If now the chloroform be cut off and pure Ringer's solution be perfused instead of it, after a short time sufficient to reduce the osmotic pressure of the chloroform in the cardiac cells below a definite limit, the heart recommences its beating, and soon becomes normal once more. The conditions of action here are obviously the same as in the case of the inorganic ions above mentioned, except that the result is reversed, and whereas in the case of the inorganic ions a certain pressure or concentration of ions was essential in order to keep the heart functionating normally, here a certain pressure of anæsthetic is required to still its activities. As soon as the osmotic pressure of the anæsthetic passes below a certain limit, the cells cease to be anæsthetised. In other words, some grouping in the protoplasm is free from the anæsthetising influence and open to continue other chemical interchanges which give rise to its activity. Within certain well-marked limits there is a certain reduced activity or anæsthesia. On one side of this is free activity or absence of anæsthesia; on the other side there is complete anchoring of proto-

plasm by anæsthetic or complete bondage from oxidising activity, resulting finally in death of the cell.

The action of chloroform upon nerve cells in the production of surgical anæsthesia is shown, by the known physiological effects connected with induction of and recovery from anæsthesia, to be similar in nature, and hence in producing safe anæsthesia we stand upon that bridge or interval of partial combination between protoplasm and anæsthetic, where there is just sufficient combination between the two to produce the stilling of activity which gives the absence of pain, but not sufficient to cause complete stilling of activity nor that degree of combination which cannot become reversible and dissociate off when the pressure of anæsthetic is lowered by discontinuing the administration and allowing the process of respiration to lower the pressure of anæsthetic in the nerve cells.

There is fortunately here, as in the case of all drugs, a degree of selective absorption by different types of cells, and the cells of the higher nerve centres are affected before other lower centres, and these again before cardiac and other forms of muscle cells. It is on this selective effect that all the benefits of anæsthesia as an accessory of surgery depend, for if the heart, for example, were affected at the same level of concentration of the anæsthetic as the higher nerve cells, anæsthesia would become impossible. Precisely at the same moment as anæsthesia set in the heart would stop beating.

In general terms it may be stated that the actions of all specific drugs depend upon this delicate selective action between the cells of different tissues, or parasitic cells, and the drugs. The problem of practical therapeutics is to find a drug or chemical combination which by its peculiar chemical conformation is capable of undergoing adsorption at a lower pressure by a specific type of cell protoplasm. This subject will be treated more in detail later on when we have considered the general conditions governing the relationships of the protoplasm to crystalloids, and to the other substances with which it is brought in contact in the cell either naturally, or as the result of disease, or in the treatment of disease.

We may now turn to a consideration of the general chemical nature of protoplasm in so far as this bears upon its power of adsorbing or combining with inorganic ions or other substances which may be present in common with it in the living cell.

The most essential and as it were the central constituents in building up the excessively complex physico-chemical aggregation which we term protoplasm or bioplasm, are the protein bodies. By means of the proteins, the fats and carbohydrates are knitted together with the variously constituted proteins themselves and with the ions of the inorganic salts to form a united system. The component parts of this system are only lightly held together, each is held in by the pressure of a free portion of it in the cell fluid, and for the life and activity of the cell it is essential that the osmotic pressure of each constituent should lie within a certain range, so that it neither becomes fixed quite permanently nor so completely liberated as to be absent from the cell when it is required for the chemical transformations which yield the supply of energy to the cell. During the molecular vibrations which accompany this labile equilibrium in which the intensities of attachment of the various constituents to the bioplasm are all the time varying, the organic oxidisable substances, viz. the proteins themselves, the fats and carbohydrates, suffer temporary molecular disruptions during which the oxygen also held in the bioplasm comes into union with them, and the oxidised products as they increase in pressure are shed off from the cell.

As has been stated above, the inorganic ions exercise the function in the cell of favouring these chemical disruptions, for when by lowering their osmotic pressure in the cell fluid they are dissociated off from the bioplasm, the oxidation processes which form the chemical basis for the cell's activities also come to an end.

Although it is impossible at the present time to artificially synthesise any of the proteins of the cells or body fluids, and still less to build these up synthetically with the other constituents mentioned above into bioplasm, or living matter, yet we have even now obtained much insight as to the general character of the constitution of proteins, and the main plan upon which details are still to be worked out lies before us.

This knowledge has been arrived at by two different channels of approach, viz. that of studying the cleavage products of proteins in which Schützenberg was the great pioneer, followed by a host of others; and that of building together such cleavage products into bodies closely resembling in many respects the naturally occurring proteins, in which Emil Fischer is now leading the way,

and, by the synthesis of the polypeptides, has already shown the lines on which proteins must be built together.

Under the influence of hydrolytic agents, such as heating with either alkalies or acids under pressure, the proteins take up the elements of water and yield a large number of simpler organic substances; and conversely by the action of dehydrating or condensing agencies these simpler organic substances or organic radicles of the proteins can again be made to unite. In the latter direction the process cannot be carried back quite to that degree of complexity which yields the naturally occurring protein, mainly because at that level the degree of chemical association of the constituents is so delicately balanced that the chemical manipulations cause splitting off and decomposition.

The synthesised products are in fact beginning to possess that delicately balanced power of associating and dissociating which is characteristic in still higher degree of living matter, and it is for this reason that only the living cell has hitherto been able to put the finishing touches upon the delicate unions which finally yield proteins, and beyond these up to living protoplasm, where the complexity and corresponding instability reach their acme.

The organic radicles, which form the building stones, so to speak, for the structure of the protein molecules, may be divided into three classes, viz. those which are purely organic bases, those which are entirely organic acids, and a third and most characteristic class which possess both the properties of organic acids and organic bases in modified degree. The compounds of this third class are known as the amido-acids, and it is to them that the proteins owe their peculiar property of building up into such complex bodies of high molecular weights.[1] The simplest type of amido-acid contains one organic acid radicle and one basic radicle, the acid character being given by the carboxyl group (COOH) and the basic character by the amidogen group (NH_2). As the simplest example, glycocoll or glycene, which is the amido-acid of acetic acid, may be quoted. Acetic acid is $CH_3.COOH$, and is purely acid in its properties, combining with bases such for example as ammonium to form ammonium acetate ($CH_3.COO.NH_4$). If the ammonia, instead of neutralising the carboxyl group, becomes attached, with the loss of one atom of hydrogen, as the group

[1] The terms amido-acid and amino-acid have the same meaning, and are used indiscriminately in describing members of this class of compounds.

amidogen (NH_2) in the methyl group (CH_3), there is formed instead the body $CH_2(NH_2).COOH$ which is the amido-acid. The carboxyl group (COOH) being still free, the amido-acid retains acid properties, but in lessened degree, on account of the presence in the molecule of the basic group (NH_2). The presence of the basic group also at the same time confers the properties of a base, so that the amido-acid now has the peculiar property of being able to functionate either as acid or base. Thus with copper it forms a deep blue soluble compound called copper glycocoll, and when in union with other organic acids it forms well-known and important substances found in the body, for example, the compound with benzoic acid known as hippuric acid, and the compound with cholalic acid occurring in the bile as glycocholic acid.

Amido-acids possessing only one amidogen group are termed mon-amino-acids; others exist possessing two such basic groups in their molecule, and these are called di-amino-acids. A number of both classes occur amongst the products of hydrolytic cleavage of the proteins. Again, there is in the majority of cases only one acidic or carboxyl group, but there are sometimes two or more such acid groups, and then the amido-acids are referred to as mono- and di-basic, &c., as in the case of ordinary organic acids.

The most striking chemical characteristic of all these amido-acids, and that which from the point of view of protein formation interests us most at present, is that of undergoing conjugation or condensation with one another or with other organic bodies to form long chains in single series, or it may be main chains with side or branch chains arising from them.

In each union of this kind the elements of a molecule of water are eliminated, a hydrogen atom being yielded by one of the two combining molecules and a hydroxyl radicle by the other, and in the great majority of instances the union occurs between the amidogen group of one and the carboxyl group of the other.

For the reader who is not acquainted with the technical terms of organic chemistry, the nature of the process of combination to form protein, and further of proteins to form bioplasm, may be illustrated by the use of electrical terms. The amido-acid, on account of its possessing both an acidic and a basic group, may be considered as possessing a sort of polarity (indeed it does possess a kind of chemical polarity); as a result of this polarity a chemical attraction exists between acidic pole and basic pole of different

molecules, so that these tend to unite with the elimination of the elements of water above mentioned. Now it is clear, since each combining amido-acid had two free poles, that after this union has occurred there will still be left, in the new combine of double the molecular size, two opposite poles free; and if this larger new molecule is brought, under suitable conditions, in chemical contact with more molecules, that further additions of like nature can occur.

If it be remembered that a certain number of the amido-acids possess more than one basic group, or more than one acidic group, it is further obvious that it is not necessary for this process of growing to extend out in a single chain; but that branching may occur, and union of branches, so that a ramification or network can be formed in all three dimensions of space.

There is no limit but the stability of the whole chemical system to this growth proceeding until a point is reached at which, with the particular chemical agencies for union and condensation at hand, there is an equilibrium between the forces building up or synthesising and the forces tending to disrupt.

In the same way by protein unions the substances of the protoplasm or bioplasm can be formed, until new limiting conditions again fix a maximum, and, it may be added, though the agencies at work may differ in type, similarly the bioplasm can increase in aggregation until a maximum cell volume has been reached for a particular cell, and cell division becomes essential for further multiplication.

In this process of growth it will be observed that there must be left at the end of the process a number of poles of opposite type. These poles, although they are chemically saturated (for as pointed out above the elimination of the elements of water are required at each union), must still possess what has been termed residual affinity,[1] and have sufficient power to attract a group of opposite polarity and hold it very loosely attached.

[1] This residual chemical affinity is seen when compounds, saturated as regards ordinary chemical values, combine with one another, such as neutral salts with their molecules of water of crystallisation. The energy of such residual combinations is seen when dehydrated salts are dissolved in water, for this process always causes heat development although the crystallised salts after the residual combination is once completed always cause cooling when dissolved on account of energy going latent as osmotic energy from development of pressure[1] in the given volume of water. Similar heat effects are seen in dissolving alcohol in water, and in the

[1] Pressure signifies in this article osmotic pressure.

When this feeble attachment has once occurred it may become altered in different ways. First, if the growing protein aggregation has not yet reached its full size, there may be a swing into true chemical union with the elimination of a water molecule.

If chemical union does not take place, a diminution of pressure of one of the constituents may occur, causing dissociation or disruption, or conversely an increased pressure may lead to firmer attachment, increasing association at the expense of dissociation, and favouring chemical combination.

The form of union described above as "feeble union" or union by "residual affinities" is usually spoken of as *adsorption*, although often a number of processes which may be dissimilar in nature are placed together under this term.

Thus, the invisible layer of moisture that collects on the surface of glass; the adhesion of gases on the inner surface of glass vessels which are in process of exhaustion; the moisture taken up by textile fabrics; the gases occluded by certain metals such as platinum, palladium, and iron; the concentration of dyes upon the surfaces of fibres and tissues being dyed; the union or adhesion between inorganic salts or other crystalloids and colloids of various kinds—these and a great many other phenomena are variously given as examples of adsorption, and it is maintained that this process is physical in character and essentially different from chemical combination.

If extreme cases of adsorption on the one hand and of chemical combination on the other be taken for comparison, it becomes obvious at once that there exist great differences between them. Such, for example, as the hygroscopic absorption of water compared with the combination of hydrogen and oxygen to form water. In the former case the glass remains unaltered, and by heating or by drying agencies the water molecules can be removed unaltered from the surface; while in the latter case, the water is quite different in all its physical and chemical properties from

solution of free acids and caustic alkalies in water. Other examples are the union of anæsthetics such as chloroform with proteins, where the chloroform or other anæsthetic is in all cases a chemically saturated body, yet the proofs of union with protein are indisputable, there being finally obtained with sufficient pressure of chloroform actual precipitation, the precipitate containing chloroform in high percentage.

Other examples are the dyeing of tissues and fabrics by dyes, where a saturated dye combines with a saturated colloid substratum. In all such cases the best effects are obtained when the chemical sign of dye and substratum are opposite.

either of the two gases which have united with great evolution of energy to form it.

But if the comparison be made between chemical reactions and adsorptions which lie closer together, it is found that the characteristic differences become diminished in degree, there are all possible gradations, and many instances in which it is impossible definitely to say whether the union which takes place ought to be described as an adsorption or a chemical combination.

If the various criteria of a physical or chemical nature which are usually taken as decisive of whether any union is a chemical combination or an adsorption be examined critically, it is found that they one after another break down.

To take an example of interest to the biologist, it was taught for many years in all the physiological text-books that hæmoglobin formed with oxygen an easily dissociable compound. The chemical combination was said to be complete at a certain pressure of oxygen, and as the oxygen pressure fell, this compound, called oxy-hæmoglobin, dissociated off into oxygen and hæmoglobin or "reduced hæmoglobin," the dissociation occurring over a definite range of pressures. So certainly established were the facts regarding this that the proofs of the formation of the compound formed a stock question of the examination room. One of the strongest proofs of this formation of the compound oxy-hæmoglobin was supposed to be that the amount of oxygen absorbed by hæmoglobin was not directly proportional to the partial pressure of the oxygen, absorption occurring in relatively greater amount at the lower pressures and falling off rapidly to nearly a zero increment as the dissociation range was passed. So that when oxygen pressures were graphically plotted as abscissæ and amounts absorbed as ordinates, instead of a straight line, as, say, in the case of absorption of oxygen (or other inert gas) by water, a curve was obtained.

But recent research has shown that in many cases where the phenomena ought to be classed under the head of adsorption, the plotted curve of pressure (or concentration) and of amount absorbed is not a straight line but a curve, and hence the new criterion is not a simple linear relationship between concentration and amount absorbed, but that the plotted curve shall show kinks or breaks upon it, that is to say, regions at which there is a sudden change in the equation of the curve. Now the oxygen-hæmoglobin curve is a smooth curve, and for this reason it has recently been

maintained by Wolfgang Ostwald that in the case of oxygen and hæmoglobin the phenomena is one of adsorption. Yet in the case of oxygen and hæmoglobin there exists at the point where absorption is complete an exact stochiometric relationship of one molecule of oxygen to one molecule of hæmoglobin, the molecular weight of hæmoglobin being fixed by the iron determinations which can be carried out with great exactitude. Now the existence of exact stochiometric relationships is usually supposed to be one of the strongest criteria for chemical combination. Further, there is the very definite and distinctive oxy-hæmoglobin spectrum, quite definitely different from that of "reduced hæmoglobin," and the fact that other gases, such as carbon-monoxide, replace oxygen at saturation point in exactly equal volume to the oxygen required to saturate.

It would appear from this conflicting evidence that the form of the pressure absorption curve as a criterion between adsorption and chemical combination breaks down, rather than to be proved that the uptake of oxygen by hæmoglobin is adsorption and not chemical combination.

The other supposed criterion that there shall exist simple stochiometric relationships at the saturation point between the two substances uniting also breaks down in the case of unions between colloids and crystalloids for several reasons.

For the appearance of absence of stochiometric relationship may be fallacious, and there may be such relationships quite definitely and true chemical union where there is apparently absorption, because the *total* mass of the colloid may not be identical or proportional to its *active* mass. For example, the crystalloid, such as a dye, may not penetrate the aggregate of the colloid, and the chemical reaction may occur on the surface of the colloid only; and since it is impossible to estimate the active mass lying on the surface and participating in the reaction, exact relative molecular masses may be involved and yet there be apparently no such relationships. Conversely, there may be no true chemical union, and yet the masses of the two substances bear quite definite molecular relationships. For, if we consider, for example, the protein molecule, with a given number of amidogen groups each chemically saturated as to valency, and yet each possessing a certain residual amount of basic affinity, and if now to this protein we add in increasing quantity a substance with weak and chemically saturated

acidic groups, then we have a definite number of anchorages, and when the saturation point of absorption is reached there must appear stochiometric relationships although there has occurred no condensation, and breaking apart would readily take place if the osmotic pressure or concentration of either constituent were reduced.

In this way a salt which crystallises with water of crystallisation has exact stochiometric relationships with the water, and yet the water and salt, which are both saturated compounds, can only be held together here by residual affinities.

To carry this short sketch of the controversy as to adsorption *versus* chemical combination into detail would lead us far beyond the limits of this article, so we may sum up with the statement that between bodies of different chemical constitution there are varying grades of affinity for union. At the one end of the scale there are the typical chemical compounds, and at the other the more physical unions [1] of a weaker type, and dependent upon the maintenance of certain appreciable pressures or concentrations of the substances uniting, which have been called *adsorptions*: but between these two there are all possible gradations, just as there are all possible stages between crystalloids and colloids.

Whether the theories and terminology of adsorption be accepted or those of the formation of easily dissociable chemical combination, or the middle view be taken that in some cases one occurs and in other cases the other, the important experimental fact which remains indisputable is that a type of union occurs which is only stable so long as a certain pressure (concentration) is maintained, and breaks up as the pressure diminishes, showing a range therefore at which association and dissociation of the union occurs in a fluctuating way accompanying variations in pressures within the range.

[1] A great deal has been written as to the mode of physical union and how it is brought about. It has been shown that any substance which lowers the surface tension at a bounding surface or interface will tend to increase in concentration at that surface. In this way the formation of surface films of protein and other colloidal solutions can be explained, similarly the formation of a layer of dye on a fabric may meet with explanation, and a great many if not all other cases of adsorption. But the question remains, why does the substance lower the surface tension? and the view is still tenable that the surface tension is lowered because of chemical affinity for the substance forming the surface, or because the conditions on the surface favour chemical condensation of the substance to form larger molecules or aggregates than in the body of the solution. Also, an attraction of residual affinities may attach the substance by adsorption, and after this anchorage true chemical union may follow.

This type of union occurs *par excellence*, and in endless variety, both as to number of substances so uniting and ranges of pressure for union and disunion in the case of colloid with crystalloid, and in particular in living cells. Also in the building up of protein and bioplasm, there occur endless varieties in the modes of grouping of the constituent radicles, which give rise to the selective affinities of the cells, and cause one cell to enter into selective union with one constituent of the plasma at a different level of pressure (concentration) from another, or to possess affinities of such a difference in order, that a substance is taken up with avidity by one cell and apparently refused altogether by another. The groups in cell and in substance entering into union with it are often so delicately arranged that the change of a single radicle alters the result entirely ; as, for example, in the action of strychnine at very low pressure upon the nerve cells of the central nervous system changing at once and practically disappearing when a methyl group is added to the strychnine molecule, or the more slightly poisonous action of piperidine passing into the most virulent action of coniine, when a propyl group (C_3H_7), in itself a harmless enough constituent, replaces one of the hydrogen atoms as a side chain.

We may now pass to the consideration of the evidence that the various organic and inorganic constituents in tissue cells and plasma are held in loose union by the bioplasm or proteins.

First, in regard to the carbohydrate material present in the blood, it has been shown that if a stream of carbon-dioxide be passed through a sample of blood, or if an anæsthetic such as chloroform or ether be added to it, and then it be subjected to dialysis, the amount of sugar passing into the dialysate is considerably increased, above the amount in the case of untreated blood. It was at first supposed that this increased amount of sugar came from the blood corpuscles, but more recent work has demonstrated that there is practically no sugar present in the corpuscles, and further a similar and equal increment in amount of sugar dialysing out can be obtained when clear serum is used for the experiment instead of whipped blood. If now a stream of air be passed through the serum in order to remove the carbon-dioxide or anæsthetic before the serum is subjected to dialysis, it is found that the yield of sugar in the dialysate has passed back again to the normal amount.

This experiment would appear to demonstrate that the sugar in the serum exists in some form of feeble union with the protein which the action of the mild acidity of the carbon-dioxide or the residual affinity of the anæsthetic is sufficient to break up, so leaving the sugar free to dialyse out.

This union of carbohydrate and protein throws a light on the glycosuria which follows hyperglycæmia. For in hyperglycæmia there is an excess of sugar above that which can enter into union with the protein, and it is this excess which is seized upon and thrown out into the urine by the kidney cells. From this point of view it is interesting to note that in the living animal, when there is more than a certain percentage of carbon-dioxide in the respired air for a given period, even though there be in the air breathed more than the atmospheric proportion of oxygen, then there invariably appears sugar in the urine in very considerable amount. Also in the case of prolonged anæsthesia, especially if the concentration of the anæsthetic administered be increased to the maximum limit, there always appears sugar in the urine, often in high percentages. The author has found as much as 11 per cent. of sugar in the urine of dogs after ether anæsthesia, and has shown that the reducing material present is undoubtedly glucose by obtaining and separating typical glucosazone crystals in abundance.

In the liver cells there is undoubtedly union between the bioplasm and the sugar before glycogen is formed. The glycogen up to a certain maximum limit at which it separates as granules can also exist in union in the cell, for considerable amounts of glycogen can be separated from the tissues long before separated glycogen can be shown by histo-chemical methods.

Similar evidence has been obtained by different authors as to the formation of unions between cell proteins and fats. By certain procedures, such as partial interference with blood supply (Bainbridge and Leathes), it has been possible to make the cells of certain organs, notably those of the liver, take on the appearances of fatty degeneration. The cells become loaded with obvious fat globules, which stain with all the usual histo-chemical staining reagents for fatty substances. It looks at first sight as if the amount of fat in the organ had been enormously increased, but the interesting point is that comparative analysis of normal liver with no appearance of fat in the cells, and of such liver cells

apparently loaded up with fat, demonstrate that the amounts of fat in the two cases are about equal.

The normal liver tissue is capable of holding 5 to 10 per cent. of fat in such form that it is quite transparent and invisible in discrete form, being in fact an integral part of the bioplasm. This can be done in no other way than by some type of union, for a fraction only of this fat in free condition would give a thick emulsion, showing obvious globules under the microscope, as it does when conditions are interfered with as above described, and the feeble union of the fat with the tissue broken up.

Similar results are seen in the chemical phenomena accompanying nerve degeneration. Again in the plasma or serum itself a certain amount of union must take place, for, from a perfectly clear serum, showing no oil globules whatever under the microscope, as much as 0·5 to 1 per cent. of fat may be taken out by organic extractives, such as alcohol and ether. Now this amount of fat, were there no agency to hold it in clear solution, would be sufficient to give a white milky emulsion. It is only when the capacity of the serum for holding fat in solution by feeble union with proteins is surpassed that the milky serum often found after a heavy fatty meal is obtainable, and this excess of fat is so soon taken into union by the bioplasm of the liver and other tissue cells, that in an hour or two no trace of any microscopically visible fat is seen in the serum or elsewhere.

In this capacity of the serum for holding in union in invisible form a certain amount of fat is found the solution of the problem of fat transference in the body from one tissue to another without any obvious carriage as an emulsion. By this power of solution of fat in bioplasm is also provided the mechanism for the oxidation of fats, for it is obvious that previously to oxidation the fat must pass into simple molecular form, and that it cannot be oxidised as globules of liquid fat.

Apart from direct oxidation to furnish energy for the cell's work, it is obvious that these lightly held unions of the organic foodstuffs furnish the means for the chemical changes in the cell which give rise to those syntheses of one organic body from another which occur in animals as well as in plants; for the synthesis of new proteins by the union of protein radicles rich in amido-acids with carbohydrate radicles; for the synthesis of fats from carbohydrates; and for the elaboration of those products

of cell activity which we know as internal secretions, lysins, antibodies, toxins, hormones, &c.

Turning now from the organic foodstuffs and the synthesised products of metabolism to the inorganic crystalloids of the cells and body fluids, we find abundant evidence of union in labile equilibrium between these and the organic constituents of the body—unions which are absolutely essential to the life and work of the cell, specific in character from one type of cell to another, and which owe their peculiar and effective functional power in the life of the cell to the very feebleness of the union which allows of interchange and reaction. So that we have stability of the whole system in the midst of and indeed as a consequence of the instability of the constituent parts.

The first evidence which may be quoted in favour of this form of union is the peculiar distribution of the inorganic salts and ions as between tissue cells and their environing fluids, the plasma and lymph.

Although the same inorganic salts are present in the cells of the tissue and in the blood corpuscles as are found in the lymph and plasma, the quantitative distribution is very different in the two cases. The cells are rich in potassium and phosphatic ions, and relatively poor in sodium and chlorides, while the converse holds in the case of the bathing fluids of the cells.

This peculiar distribution finds an easy explanation on the basis that the proteins of the cells are so constituted chemically that they possess affinities for absorbing or uniting with potassium and phosphatic ions, and have no such power for holding sodium and chlorine, while the converse holds for the proteins of the plasma. For under these conditions, with the same osmotic pressure of dissolved constituents within and without the cell, any particular ion will increase in amount in the absorbed or united form in that particular region where protein is found possessing an affinity for it.

No other view which has been put forward furnishes an adequate explanation of this peculiar distribution of the salts. The other view which has obtained most adherence is that there exist membranes with peculiar and specific properties surrounding the cells which present a varying resistance to the passage of different ions. These membranes, which recently have been regarded as

consisting of bodies called lipoids,[1] related to the fats and lecithins, are supposed to be easily permeable for some substances such as urea, ammonia, carbonic-ions, and the anæsthetics; but difficultly or almost impermeable for other substances such as the usual inorganic ions of the plasma, viz., potassium, sodium, phosphates and chlorides. As a result of this difficult permeability it is supposed that the potassium is retained in the cell, and the sodium in the plasma, while anæsthetic, ammonia, and urea, for example, rapidly pass through.[2]

There are, however, fatal objections to this membrane view, viz. first, that while it makes some attempt at an explanation of the maintenance of the *status quo*, it fails entirely to explain how that condition was originally arrived at; secondly, it inextricably confuses factors which are of value in the velocity with which equilibrium is arrived at with the final conditions of equilibrium; and thirdly, it fails to explain the phenomena of cell interchange and the rapid physiological effects upon the cells of variations in the concentration of the ions in the external medium.

If the cell is almost impermeable to potassium ions, for example, it is difficult to see how it has become fully charged with them, and to many times the amount that these are present in the nutrient fluid outside.

Again, however poor the permeability, if there is no union between constituents within or without and the ion in question, it is obvious that when equilibrium has finally been attained, the concentrations at the two sides must be equal. Variations in permeability can only alter the time required to reach equilibrium, and not the final conditions of accumulation on the two sides corresponding to the equilibrium.

Further, anæsthesia cannot, as has been suggested by the upholders of the membrane theory, arise from greater solubility of the anæsthetic in the membrane, because that would only delay

[1] The text merely refers to lipoids regarded as semi-permeable membranes. Using lipoid as a generic term to include the class of the lecithides and other forms of compound fats, there is no doubt that these play an important rôle in the life of the cell by means of their power of entering into combination or absorption with organic poisons and toxins. But this is entirely different from a membrane action, being a formation rather of easily dissociable unions of the kind shown in the text to exist between bioplasm and organic bodies.

[2] The questions of cell permeability, and the arguments for the membrane view, may be found in detail in Hamburger's *Osmotischer Druck und Ionenlehre*. For the reasons given in the text they have not been stated at length.

the arrival of the anæsthetic at the active part of the cell until the lipoid membrane had first been saturated with anæsthetic.

For this reason also greater solubility of any constituent in the cell substance itself will not explain the greater amount or concentration of any particular substance or ion in the process of secretion or excretion. Such greater solubility would serve to fill the cell up with it *and keep it there*, but would not hasten passage through the cell, and after the solubility in the cell substance had been satisfied, diffusion would then go on until the free concentration on the secretion side equalled the concentration on the lymph side, but not a fraction beyond this point.

With regard to increased or specific solubility in the cell substance as an agency in statically loading the cell up with a given constituent or ion, as distinct from passing it out again in heightened concentration in a secretion, it may be admitted that this would explain the accumulation; but this on closer examination is essentially the same view as that of union or adsorption with the protein, except that the adsorption or combination view goes a step further and attempts to give a basis for the increased or specific solubility.

Even in the simpler case where a substance in solution divides itself in different concentrations between two solvents which do not mix with each other,[1] giving rise to the quotient of distribution, it is obvious that there is an equilibrium between the concentrations in the two media depending upon the relative affinities (or residual affinities) of the molecules of two solvents respectively for the molecules of the solute or dissolved substance.

One may therefore quite justly assign the unequal distribution of the various ions in cell and environing fluid respectively to different solubilities in the two media; apart from membrane action which is out of the question unless the somewhat absurd hypothesis be made that the accumulation remains and resides in the membrane. But knowing the nature of the constitution of the protein constituents, and that these must possess residual affinities or absorptive powers, it appears feasible to go a step further and assign the distribution and different solubility to the formation of unions between protein or bioplasm and the ions.

On this view the cell of any tissue or the blood corpuscle is a

[1] As, for example, an organic acid dividing itself between water and ethylic ether.

system in equilibrium regarding ions with its surrounding medium, and the equilibrium is maintained by the pressure of each particular ion, acting independently, in the surrounding medium. Also variations in concentration of any of the ions will cause reaction and variation in the equilibrium of the whole, and may cause such disturbances as will alter the distribution of other ions and soluble substances, and so cause variations in the character and types of reaction of the protein or bioplasm.

Two chief factors determine the equilibrium between each ion and the cell; one of these is the concentration of the ion, the other the constant of association or adsorption between the cell substance and the ion. This constant changes its value specifically from one ion to another with a constant type of cell or bioplasm; and with the same ion kept constant varies from type of cell to type of cell, so giving rise to the specific picking out of particular cell types by particular ions or other bodies.[1]

In addition to these chief factors, there is some evidence that certain ions can replace each other, or in other words compete for the same vacant places in the protein or bioplasm. This is known as the antagonistic action of drugs. Usually the ions so replacing must be of the same order of valency, a monad being unable to take the place of a dyad, but one dyad can replace another, and especially two dyads in the same periodic group of elements are interchangeable. For example, one heavy metal can take the place of another, and even the paradox is arrived at that the poisonous action of one of these heavy metals is decreased by the

[1] This might be put in simple mathematical form thus: if C_1 be the concentration of the protein or other substratum in a given cell, C_2 the concentration of the ion to be absorbed in the medium outside (lymph), and C_3 the concentration of the substance adsorbed, then $C_3 = KC_1C_2$, where K is a constant dependent on the chemical and physical affinities of ion or other substance for each other, and hence having a different value when either ion or type of protein is changed. If now we keep the same ion, as in the distribution of any naturally occurring ion in the body, or in the action of any given drug which can only be given so that it is free to act on all cells in the body, then for a different cell using small letters we can write as before $c_3 = kc_1c_2$ where the suffixes show the same meaning as before. But now C_2 and c_2 the concentration of the ion or drug in the circulating medium is the same in both cells, and hence if we want to get the relative concentration in the two types of the cell we have $\frac{c_3}{C_3} = \frac{k}{K}\frac{c_1}{C_1}$, and further if we take it that the protein concentration is the same in the two cells, we finally have $\frac{c_3}{C_3} = \frac{k}{K}$, or the relative distribution is in proportion to the affinities between ion or drug and particular type of protein.

simultaneous presence of another, so that instead of there being an additive effect of the two poisons, one balances the other and protects in part from its action, so that the lethal dose of either is increased.

The ions of the inorganic salts at the same time that they are in a loose type of union with the proteins, possess a freedom of movement which shows itself in their giving to the solution in which they exist in common with the colloidal proteins many of the more important physico-chemical properties of a saline solution. For example, in the case of the blood serum, the depression of freezing point is almost the same as that of an equal amount of salts dissolved in distilled water, showing that here every ion in the solution has its full effect in producing osmotic pressure notwithstanding its adsorption by the serum proteins. Again, the electrical conductivity is practically the same as that of an isosmotic solution of the saline constituents alone in distilled water, showing that any adsorption which may be present does not interfere in the least with the movements or velocities of the ions in the electrical field. Yet there is other evidence that the salts of the serum are in union of some type with the proteins, and that the amount of salts in the serum as regulated by the kidney cells is dependent upon the combining power of the proteins.

One fact that gives a clear indication of this is the titration value for the serum in presence of one of the more stable coloured indicators, such as methyl orange or "di-methyl." It has been pointed out earlier in this article that the proteins can act either as acids or bases, or as it is termed are *amphoteric* to indicators. Thus, blood serum is *acid* to phenol-phthalëin, and must have *alkali* added to it to produce the pink colour denoting alkalinity; at the same time it is *alkaline* to methyl orange or di-methyl, and requires the addition of much *acid* before showing the acid colour of the indicator.

The actual reaction of the serum is almost that of exact neutrality in the sense of physical chemistry, that is to say, the concentrations of hydrogen ion and hydroxyl ion are about equal. Now although it is essential that the colour of an indicator for acid and alkali should change before the ratio of the concentrations of the two ions becomes a high one, no indicator used in practice actually does change exactly at the chemical or exact neutral point, and the turning point is different for each one. Hence it is that blood

serum *appears* to be acid when tested by phenol-phthalëin, and appears to be alkaline when tested by methyl orange, &c. Not, as is too often stated, because it is at the same time acid and alkaline, for that is absurd, but that its actual position in reaction lies very nearly at the neutral point, and just short of that slight degree of alkalinity which shows the alkaline colour to phenol-phthalëin on the one hand, and just short of that degree of acidity which gives the acid colour to methyl orange. Now these two points lie very close together, for if instead of the serum we take distilled water and add the two indicators phenol-phthalëin and methyl orange in traces to it, then a single drop of dilute alkali will develop the alkaline colour of the phenol-phthalëin, and on the other hand a single drop of dilute acid will show the acid colour of the methyl orange.

In the case of the serum, however, the result is quite different, for very considerable amounts of alkali must be added before it turns alkaline to phenol-phthalëin, and proceeding in the opposite direction still larger amounts of acid must be added before acidity to methyl orange is realised. The reason for this is that the proteins, which can figure either as acid or base according to whether there is excess of alkali or acid respectively in the solution, must first be satisfied before the indicators are affected; and as the amount of protein is large, so the amount of acid or alkali required before it is neutralised and the acidity or alkalinity can commence rapidly to run up and affect the coloured indicator, is very considerable.

This is a factor of great importance to the life of the cells, which cannot bear any appreciable degree of either acidity or alkalinity, and are protected from such variations by the very delicate regulation of the reaction by the amphoteric proteins.

The regulating action of the proteins upon the reaction of the serum has been mentioned here, however, because it gives a strong indication that the proteins are in union with the inorganic salts. If a clear sample of serum be titrated with methyl orange or "dimethyl" as an indicator, an alkalinity equivalent to the very high figure of 0·17 to 0·18 normal is obtained. This alkalinity is chiefly due to proteins, for if the salts of the serum be separated off by dialysis or incubation and titrated to the same indicator, the alkalinity now amounts to only 0·03 to 0·04 normal. Subtracting these amounts due to inorganic constituents from the higher figure, we obtain the result that the combining power of the serum pro-

teins alone for acid is equivalent to about 0·14 normal.[1] Now the interesting point about this figure is that it coincides almost exactly with the *total* osmotic concentration of all the salts naturally occurring in the serum or plasma. The depression of freezing point of mammalian sera is on the average equivalent to that of a 0·9 per cent. solution of sodium chloride, and the molecular weight of sodium chloride being 58, this corresponds to a 0·15 normal solution.

In addition to this direct evidence from the chemical side, there are certain physiological correspondences between amounts of protein and crystalloid in the blood which must be obeyed, or otherwise the excess of salt in the plasma is removed by the kidneys. This action comes into operation as soon as the plasma salts exceed the amounts which can be loosely held by the proteins.

The salts in cells are held more firmly adsorbed or combined than is the case in the plasma, as is shown by effects on the electrical conductivity and by the difficulty of dialysing the salts from the cells.

Thus it is found that although the osmotic concentration of the salts in the red blood corpuscles is nearly the same as in the plasma, as shown by the depressions of freezing points,[2] yet the electrical conductivity of the separated corpuscles is only one-fourteenth to one-seventeenth of that of the separated serum. Part of this difference is mechanical and due to the envelopes of the corpuscles rendering the conducting fluid non-homogeneous; but even after removing this factor by laking, the conductivity of the laked corpuscles still remains only at one-fifth to one-sixth of that of the serum. This difference is undoubtedly due to the attachment of the ions to the hæmoglobin interfering with the ionic velocities, for on dialysing against distilled water and then reducing the volume of the dialysate to such a degree as to represent the original concentration of the salts before dialysis, it is found that the conductivity of the free salts in the dialysate has undergone a further increase above that which they possessed when in union with the hæmoglobin, and now lies at about one-half the value in the serum. Even dialysis, however, is unable to detach the phosphates from the hæmoglobin, and the above

[1] The amount of this combining power of the protein may be better appreciated by some if it be stated as equivalent to about 0·51 per cent. of hydrochloric acid.

[2] *Vide infra.*

conductivity of one-half is chiefly due to chlorides detached in the process of dialysis. It is only after incineration and making up to original volume that the conductivities of corpuscles and serum become practically equal.

The following table illustrates these interesting changes in conductivity accompanying detachment of colloid and crystalloid in two experiments on separated blood corpuscles and serum. The figures give specific conductivity multiplied by 10^5 to save decimals.

Treatment to which subjected.	Sample I.		Sample II.	
	Serum.	Corpuscles.	Serum.	Corpuscles.
1. Fresh	1705	95	1519	109
2. Frozen solid and thawed (corpuscles laked) . .	1602	310	1468	237
3. Dialysed and volume reduced to original . .	1843	891	1623	754
4. Incinerated and ash made up to original volume .	1608	1677	1697	1655

That the phosphates are more firmly held than the chlorides, so that the union persists even in presence of a very low concentration of phosphatic ions in the fluid, is shown by the following analysis for chlorides and phosphates in the dialysates of corpuscles and serum respectively, and in the two cases after incineration. The figures also illustrate the very different distribution of chlorides and phosphates in corpuscles and serum respectively.

	Serum Percentages.		Corpuscle Percentages.	
	Cl.	P_2O_5.	Cl.	P_2O_5.
Dialysis . . .	0·3657	0·0197	0 1331	0·0329
Incineration . .	0·3373	0·0219	0·1704	0·1708

Even the chlorides are more strongly held in corpuscles than in serum, the figure on incineration being considerably higher than after dialysis, 0·1704 as against 0·1331, instead of being slightly lower, due to volatilisation with organic matter, as in the case of the serum, 0·3373 as against 0·3657. In the serum the phosphate figures are almost equal by the two methods, but in the corpuscles the evidence of union is clear, only 0·0329 per cent. dialyses out of the 0·1708 shown to be present by incineration. These figures are completely confirmed by freezing point determinations.

This experimental evidence is interesting as showing that the special affinities existing in each case between protein and ion

demand very different pressures or concentrations to preserve the equilibrium.

We can now understand why so little phosphate is required in the Ringer's solution; the union of the phosphates is so strong that it is not possible to run the phosphate concentration down to such a level as rapidly to disintegrate the phosphatic ions of the cardiac tissue. The merest trace given off from the heart to the perfusing fluid suffices to stop further loss. The level for calcium and potassium, though low, is somewhat higher, and traces sufficient to preserve equilibrium must be added, or these ions break free from the cardiac cells, producing irregularity of function. Finally, the sodium and chlorine ions are but loosely held, and hence as much as 0·7 to 0·9 per cent. of sodium chloride must be present to preserve the equilibrium and normal conditions of physiological activity.

The facts as to the constitution of the colloidal material and its relationship with electrolytes and other crystalloids which have been given above, and the interpretation put upon those facts, are intended to demonstrate that the living cell is a peculiarly constructed energy machine or energy transformer, dependent for its activity upon a delicate labile equilibrium giving stability as a whole, and yet a weakness of union causing disruption and oxidation of parts, and so furnishing energy. The view put forward is intended as a reaction from that view which complacently regards all the work of the cell and peculiarity in its constitution as being due to the physical properties of inert membranes.

The attempt has been made to show that something is required more than membranes and osmotic pressure to explain the peculiar distribution of electrolytes in cell and nutrient medium, and going further to give a basis for the understanding of the peculiar energy exchanges of cells. It has been sought to invoke the peculiar chemical constitution of protein and bioplasm, and the varying equilibria of these with the materials brought in from the nutrient media at varying pressures, giving rise to transient stages of association and dissociation, and an accompanying play of energy changes.

It is not intended in doing this, however, to suggest that membranes and variations in osmotic pressure play no part in the cell's work or in preserving the integrity of the cell, nor to depreciate work upon osmotic conditions in cell life. Because there are other factors to be reckoned with, it does not follow that osmosis is to

be neglected. In fact a wider appreciation of the phenomena of union between the bioplasm and crystalloid constituents widens rather than narrows our conceptions of the cell as an osmotic centre, by allowing us to regard the cell as a chamber with varying osmotic properties, both of contents and wall, rather than as heretofore as a more or less fixed solution, bounded by a membrane of fixed properties also, and resembling a semi-permeable copper-ferrocyanide wall.

The rigorous conception of the cell as analogous in all respects to a fluid medium holding crystalloids simply in solution and bounded by a semi-permeable wall is most pernicious in biology, for there are no experimental facts to warrant such a view, but rather, as has been shown above, quite the reverse.

The whole chemical structure of the cell and that part of it which is physiologically active *is* the osmotic machine, and needs no membrane permeable or impermeable in order to exhibit the usual osmotic phenomena of shrinking or swelling, leading finally to disruption. In some cases membranes in the narrower sense of the word are demonstrable surrounding the cell mass, and in other cases which form the vast majority, no such coarsely structural membranes exist; but in all cases the nature of the bioplasm is so differentiated chemically as to form a dividing surface readily permeable to the solvent, and this is all that is required, in addition to the varying unions or holding powers between the cell colloids and crystalloids, to establish an osmotic cell. As an example of what is meant here we may instance the swelling of fibrin, connective tissue, and gelatine under the imbibition of water. Between gelatine and water there is no structural membrane with semi-permeable pores, yet the gelatine takes in water in a truly osmotic fashion, and the pressure developed, if the swelling and uptake of water are resisted, is very high.

It is hence necessary to get our minds rid of the preconceived idea derived from too closely drawn analogies with experimentally constructed osmotic cells that the cell membrane is responsible for the osmotic behaviour of the whole cell.

If instead of this we take the view, which is supported by experimental facts, that the bioplasm holds the crystalloids in loose union in the cell, so that they cannot for the time escape or diffuse out, and yet admits of a degree of molecular freedom to the crystalloids, so that they still attract water molecules by residual

affinity, then we arrive at a conception which is capable of linking together the osmotic properties of the cell, not merely in a statical but in a dynamic way, and gives a basis for understanding the variations in osmotic effects which accompany cell activities from one phase to another.

With the view of an inert semi-permeable membrane of fixed properties, not sharing the varying changes in chemical constitution associated with life, or in other words not possessing the properties of bioplasm outlined above, all that can be arrived at is a continual tendency in one direction to a fixed equilibrium.

The other view, that the osmotic properties are developed by the bioplasm itself in its varying unions with crystalloids, gives room for that up and down play of properties which is the outstanding characteristic of living matter.[1]

For example, a circulating hormone, a drug substance or a nerve impulse arriving at a given set of cells in a tissue, may activate the cells by momentarily disrupting unions between bioplasm and crystalloids or the reverse, and so may cause an uptake or a giving out of water accompanied by certain crystalloids free in excess to or from the cell, or may alter water distribution in varying parts provoking muscular contraction or other form of protoplasmic movement.

Similarly molecular movements of radicles attached to the bioplasm may be induced, causing changes in molecular arrangement and synthesis of new bodies within the cell. Further, the osmotic pressures and concentrations of the crystalloids and other bodies so set free need obviously bear no immediate relationship to the concentration of these substances in the plasma outside the cell, and so the very varying concentrations of secretions may be understood in a way that cannot be realised on any basis of pure osmosis or filtration.

The experimental facts of cell life, both in regard to the taking up and giving out water and substances in solution, furnish a clear demonstration that neither osmosis nor any other physical hypothesis which leaves out the peculiar and varying chemical constitution of bioplasm can yield an explanation of absorption, secretion, or excretion.

[1] It is interesting to note that serum proteins exactly at their neutral point show no osmotic pressure whatever, but addition of minute amounts either of acid or alkali at once gives rise to an osmotic pressure which up to certain limits increases with amount of acid or alkali added.

The whole of the experiments lend support to the view that the living cell exists in a periodically or phasically varying *osmotic equilibrium* with its surroundings, and not in a state of osmotic equality with them. The cell by its unions with crystalloids preserves a distinct osmotic condition within its bounds different from that in the surrounding fluid media from which its nutrient materials are taken up. This is particularly well seen when the medium without is subject to considerable and accidental variations. Even in those cases where the outer medium is practically constant, as in the extreme case, for example, of blood corpuscle and plasma, although there appears to be an existence of osmotic equality within the cell, and without, yet this is due to the peculiar conditions having induced a close coincidence of the two sets of osmotic phenomena, and the existence of an equilibrium and not an equality may be easily shown by suitably varying the conditions. So that even in these extreme cases what we have to do with is not really equality of osmotic pressures, but an equilibrium which happens to simulate equality from the presence of reducing conditions; the equality disappears as soon as these reducing conditions are disturbed.

When the corpuscles of whipped blood are separated as completely as possible from the serum by means of the centrifuge, and the depressions of freezing point of the corpuscles and of the serum separately determined, it is found that the freezing point of the serum lies on the average at 0·02° to 0·03° C. lower than that of the corpuscles. This difference, small as it is, is constant in its occurrence, and corresponds to a difference in osmotic pressure of approximately 200 to 300 m.m. of mercury. If the corpuscles after separation from the serum are thoroughly shaken up with saline solutions weaker and stronger than the serum, or as they are termed, hypo- and hyper-tonic solutions, it is always found, on again separating corpuscles and saline by means of the centrifuge, that the depression of the freezing point of the saline is greater than that of the corpuscles, no matter whether the saline employed was hypotonic or hypertonic. The differences become in these cases much greater than the natural differences between corpuscles and serum. These results show that there is established, as the concentration of the saline is varied, an equilibrium for each strength of saline, but not an equality, there always being a negative osmotic difference within the corpuscle.

In other types of cell these differences in osmotic pressure within and without the cell become enormously greater. Thus, in plants, the root sap which carries up the electrolytes from the earth for the nutrition of the growing cells is exceedingly dilute, the depression of freezing point being only about one-fifth part of that of the cell juice. Similarly, in the secretion of sweat and saliva the concentration of inorganic ions, as shown both by freezing point methods and by direct chemical analyses, is only a small fraction of that of the plasma or lymph. In other cases, such as absorption by the intestinal cells and secretion by the kidney cells, the osmotic pressure on the side remote from the lymph may lie either above or below that on the lymph side, but nearly always differs widely from it. It has been shown that either distilled water or hypertonic salines can be taken up by the intact intestinal mucosa; and the Δ (*i.e.* freezing-point depression) of the urine may be many times greater than that of the plasma, or may after ingestion or intra-venous injection of much water be a mere fraction of the Δ of the plasma.

Whether the tremendous pressure differences corresponding to these differences in Δ really exist within the cells must remain indeterminate so long as we possess no knowledge as to the degree to which the crystalloids of the secretion are adsorbed while the secretion is passing through the cell and is in contact with the bioplasm. By alternating or periodic dissociation and combination between colloid and crystalloid in the actively secreting (absorbing or excreting) cell, the pressures would appear and disappear alternately; and if by the action of the nerve supply or any stimulating substance the bioplasm is thrown into any such rhythmic activity of adsorption and re-separation, there would follow an easy explanation of the passage of both water and crystalloid through cells, in any concentration. For the concentration would depend solely on the uptake of crystalloid by the cell colloid, before the next explosion, disrupting colloid and crystalloid, threw the crystalloid free in the cell and determined, by the osmotic pressure developed thereby in the cell, the flow of secretion.

It would appear that in nerve and muscle at the period of activity only, and in injured tissue (which is excited or active tissue), there exists in reality a detachment of potassium ions from the colloid which does not exist before or after the active period (Macdonald).

It has been already pointed out that for each constituent passing into union with the bioplasm there exists an optimum concentration or osmotic pressure of solution in the nutrient medium of the cell which alone is compatible with normal physiological activity; or rather it might better be put that there is a range of suitable concentrations with a minimum and maximum which must not be passed in either direction.

This point is particularly well illustrated in the case of the respiratory gases. For both oxygen and carbon-dioxide there are well-marked limits of pressure which are required to be satisfied in order that the processes of respiration and oxidation in the tissues may proceed in a normal fashion.

Since the energy for all tissue activity is derived from the oxidation of organic bodies it is obvious that there must be a minimal pressure of oxygen below which life is impossible, but it is not so obvious that there is an upper limit of oxygen concentration at which life becomes equally impossible. Yet it is found that when warm-blooded animals are exposed to a pressure of about three atmospheres of pure oxygen, death occurs in a few minutes after violent convulsions (Bert). Short of this excessive pressure, exposure to over one atmosphere of pure oxygen for a longer period leads, as shown by Lorrain Smith and L. Hill, to a pneumonic condition of the lungs.

If pure oxygen at atmospheric pressure be breathed for a shorter time interval, the tissues become charged with oxygen at a higher pressure than normal, and Hill and Flack have shown that for a short period afterwards muscular work can be done at a more rapid rate in such forms of exercise as sprinting, hill-climbing, and working against resistance. After exhaustive muscular exertion also the breathing of oxygen diminishes the dyspnœa and sense of fatigue.

On proceeding in the direction of testing the effects of percentages of oxygen less than the atmospheric, it is found that the results obtained depend upon the type of mammal experimented with, and upon the state of quiescence or activity of the animal. As the percentage of oxygen decreases the will and energy to do work diminish, and at a partial pressure of about half that present in the atmosphere any attempt at muscular work has to be abandoned, and the mental processes also become most sluggish.

The earlier experiments on the absolute minimum amounts of

oxygen required to support life in animals in a state of quiescence were vitiated by the simultaneous accumulation of carbon-dioxide from the respiration of the animals.

When means are taken to exclude this source of error by absorbing the carbon-dioxide with soda-lime as rapidly as it is formed, it is found that animals (rabbits) can be kept alive for as long as forty hours on a respiratory mixture containing as little as 5 to 6 per cent. of oxygen. With slightly less than 5 per cent. of oxygen, death occurs very rapidly.

These results, considered together, show that there is a minimum concentration of oxygen necessary for sufficient oxidation to support life; that as the pressure rises the degree of combination or union between bioplasm and oxygen increases, quickening the oxidation processes in the tissues; that an optimum of activity exists somewhere above the normal amount present in atmospheric air; and that still higher up embarrassment occurs from too high pressure, causing firmer union between the oxygen and bioplasm.

A very parallel set of results are obtained in the case of carbon-dioxide. Here it might be thought that since carbon-dioxide is a waste product of the oxidation process, the best possible condition would be its complete removal; but it has been clearly shown by Haldane that a definite minimal percentage of carbon-dioxide is required for the regulation of the respiratory exchange, and that when the percentage is reduced by artificial ventilation, the subject passes into apnœa or suspension of breathing until the amount is brought back towards normal in the lungs and tissues. The normal amount of carbon-dioxide in the alveolar spaces lies between 4 and 5 per cent., and if it rises or falls but slightly from the normal, corresponding changes take place in the respiratory rhythm and depth which tend to restore the balance once more.

It has further been shown by Henderson that excessive and prolonged ventilation of the lungs by artificial means leads by lowering of the carbon-dioxide concentration to irregularity of the heart beat, and finally, if pushed, to *delirium cordis* and death of the animal. Short of this limit, stoppage of the positive ventilation has the effect of restoring the heart to regular rhythm.

Passing in the opposite direction, and observing the effects of increasing amounts of carbon-dioxide, administered in artificial

mixtures containing as high, or higher, amounts of oxygen as are present in atmospheric air so as to avoid asphyxiation from deficiency of oxygen, it is found that carbon-dioxide has directly poisonous effects upon the bioplasm. Thus, with 12 to 15 per cent. of carbon-dioxide and 20 to 25 per cent. of oxygen, it is found that animals become somnolent, and, as above stated, that the urine contains glucose, while with 20 to 25 per cent. of carbon-dioxide, even in presence of excess of oxygen, death rapidly occurs.

The same effects are seen upon isolated tissues. Thus Waller has shown that the first effects of minimal traces of carbon-dioxide is to increase the excitability of nerve, while larger doses diminish excitability, and finally all excitability disappears. Similar results are found in unicellular organisms and in ciliary movements.

All these results point to varying degrees of union and corresponding stability or instability of union between carbon-dioxide and bioplasm.

Exactly similar results are everywhere evident in the application of various drugs in therapeutics, in the action of the toxins of disease, and in the action of antiseptics. There is the same stimulating action seen, followed by paralysing action as the concentration is increased and the union between bioplasm and drug becomes more stable and complete.

One of the most striking results here is the adaptation between drug and different types of cell, due to molecular variations in the structure of the two reacting bodies causing them to possess higher affinities and unite at lower concentrations. For this reason one type of cell takes up a drug and robs the other cells of it, lowering the pressure in these other cells and the plasma, so that the particular type of cell becomes loaded up at a pressure which scarcely causes any uptake in other cells.

On such a basis it is easy to understand why all mercury salts produce the same specific action in syphilis, the result being due to the free mercury ion and not being affected by the anion of the salt used except in so far as this quantitatively alters the degree of ionisation, and hence the concentration of mercury ion. Similarly, the ferric ion in all iron salts stimulates the production of erythrocytes in anæmia. So too quinine, and the alkaloids generally, furnish a basic ion affecting specific cells of the organism in each case, or of pathogenic foreign organisms present in it, for which at different stages they possess special affinities.

The same specific action due to different detail in structure of bioplasm, which we see exemplified in the picking out action of drugs in the multicellular organism, is seen, and from the same cause, in the action of different drugs upon different stages of the same parasitic organism.

For example, quinine only attacks the malarial parasite when it is breaking forth from the erythrocyte. Again, the drug atoxyl acts on the ordinary motile form of the trypanosome, but rapid recurrence shows that it does not destroy the latent bodies, while mercury is shown, by the prolongation in the period of recurrence which it causes when given after atoxyl, to attack the latent bodies, although it has no action whatever on the ordinary motile stage.

The closer and more detailed study of the conditions of the formation of these unstable unions between bioplasm and the dissolved substances of its natural and artificially varied environment must furnish the key to many of the intricate problems both of physiology and of practical medicine; and it may perhaps be added that these subjects, whether studied in the laboratory or by the bedside, form one organic whole, for the subject of study in both is the living cell in all its wealth of reaction to changes in its environment.

THE HEART

By MARTIN FLACK

From time immemorial the heart has been the object of great, although perhaps not altogether scientific interest. In recent years many points relating to its anatomy and physiology have occupied the attention of investigators, so that the literature upon these subjects has become very large and in many respects intricate. In the following remarks the subject will be treated under these headings :—

A. The microscopic anatomy of the heart.
B. The morphology of the vertebrate heart.
C. The nervous elements of the vertebrate heart.
D. The heart as a muscle.
E. The site of origin and mode of conduction of the excitatory wave of the heart.
F. The movements of the heart in situ.

A. The Microscopic Anatomy of the Heart

The heart musculature must not be regarded as being built up of a number of separate cells fixed together by a cement substance. It is really a network of cells, intimately fused on all sides, or as it is sometimes termed a syncytium (Kölliker, M. Heidenhain).

In fresh and in well-prepared fixed preparations there is no trace of division of the musculature into short mononuclear segments or cells. The muscle fibre is seen to pass many nuclei without the appearance of a division or cement line between them —indeed in the heart of mammals such small segmented portions are hard to find, and seem only to occur in the circular bands of muscle at the heart orifices and in the musculi papillares.

According to M. Heidenhain, the muscle fibres of the heart are about one-third thinner in diameter than those of voluntary muscle. They possess nuclei, sarcoplasm, fibrillary substance, and

sarcolemma. The nuclei lie at regular intervals inside the fibre; they are elliptical in shape, 7–16 μ long, 5–9 μ broad, and possess a well-marked chromatin network and a nucleolus. At both poles of the nucleus is situated a mass of granular protoplasm, the sarcoplasm. This sarcoplasm is more richly developed than in voluntary muscle, and contains strongly refractile basophile granules which in the adult are frequently yellow or yellow brown. Their presence, so far as is known, denotes nothing abnormal.

Running out from the central sarcoplasm between the bundles of fibrils to the periphery of the fibre there is a very delicate protoplasmic membrane, the sarcolemma, often richly impregnated with fine granules. It is perhaps not so well developed as in striated muscle, and differs in not being of a chitinous nature.

The contractile substance of the heart muscle fibre is made up of a number of bundles of fibrils, the sarcostyles. These are somewhat prismatic in shape, and lie at the periphery of the fibre; the centre being occupied by the nucleus and the sarcoplasm (Kölliker). The sarcostyles exhibit longitudinal and frequently transverse striation; the former being due to its composition of fibrils; the latter to the presence of singly and doubly refractile substances within the fibril. When the sarcolemma running between the fibrils is well marked, the transverse striation is masked.

There is an intimate fusion between neighbouring fibres—a number of fibrils from one fibre becoming detached and passing uninterruptedly into its neighbour. From this it will be seen that only the small amount of protoplasm situated around the various nuclei can be looked upon as being discontinuous and in any way comparable to the original cells (the myoblasts) from which the heart is developed. These cells appear to have become fused together to form a syncytium, and in this a common network of fibrils has been laid down.

The question then arises that, if the lines formerly described by von Eberth as separating the cells of cardiac muscle from each other, do nothing of the kind, what is their function? Von Eberth thought they were a cement substance binding the cells together, and called them "cement lines" in consequence. This view has been given up. The lines do not separate cells since the fibrils pass through them (v. Przewosky, v. Ebner, M. Heidenhain). In many places, too, it can be seen, particularly in a fresh preparation, that the so-called line does not always go completely across

a fibre—it may only go part of the way across, or it may go across in step-like fashion.

According to v. Ebner these lines represent a dying phenomenon —a thickening of the fibre due to an abnormal contraction during death. Eppinger regards them as pathological in origin. M. Heidenhain, on the other hand, believes that they are really present in the normal fibre, and have a special function to perform in regulating the growth of the fibre. He therefore terms them "Schaltstücke" ("regulators"). In the human heart they are 1–1·7 μ thick, and consist of separate parallel perpendicular rods. As we have said, they do not necessarily go right across a fibre. The intervals at which they occur are by no means regular: the pieces shut off by them may be of any length, and cannot be looked upon in any way as cells.

To sum up, the heart muscle, according to the more recent investigations, is to be regarded as a syncytium in which a common network of fibres has been developed.

B. The Morphology of the Vertebrate Heart

The study of the comparative anatomy of the vertebrate heart greatly facilitates a proper understanding of the most recent anatomical work on the mammalian heart—namely, the isolation of the auriculo-ventricular bundle. It aids us also in estimating the significance of the many facts known about the heart, and also in arriving at the probable value of the theories held in regard to its working. Furthermore, the study of the comparative anatomy is undoubtedly very helpful in bringing out points about which research is still required and also in determining the lines of such research.

The Primitive Vertebrate Heart.—Figure 1 is a generalised diagram of such a heart. It consists of five chambers—(*a*) The sinus venosus; (*b*) the auricular canal; (*c*) the auricle; (*d*) the ventricle; (*e*) the bulbus cordis. These parts are all in free muscular continuity; there is no break at any of the junctional lines (1.1, 2.2, 4.4, 5, in Fig. 1).

This is a point of interest, since in tracing the representatives of these primary divisions in the mammalian, and especially in the human, heart, it will be of service to ascertain whether this muscular continuity between the different chambers still exists.

The Sinus Venosus in the Human Heart.—The sinus venosus is of importance in primitive vertebrate hearts, because it is here that many authorities have observed the origin of the heart rhythm (Gaskell, MacWilliam, Engelmann). This fact makes it essential for us to know what parts represent the sinus venosus in the

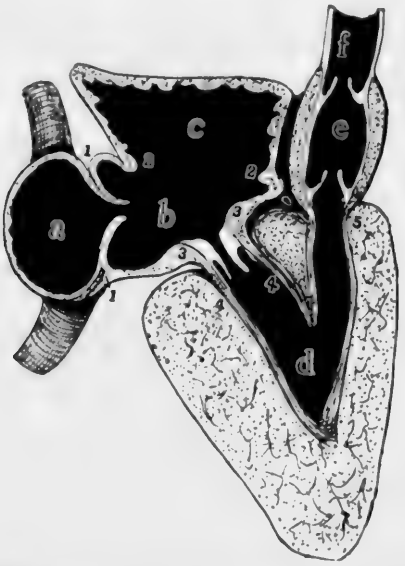


FIG. 1.—A generalised type of vertebrate heart—combining features found in the eel, dogfish, and frog (Keith); *a*, sinus venosus and veins; *b*, auricular canal; *c*, auricle; *d*, ventricle; *e*, bulbus cordis; *f*, aorta; 1–1, sino-auricular junction and venous valves; 2–2, canalo-auricular junction; 3–3, annular part of auricle; 4–4, invaginated part of auricle; 5, bulbo-ventricular junction.

mammalian heart, since in them one might expect the heart rhythm to arise.

The sinus venosus is represented in the mammalian heart by four remnants:—(1) The termination of the superior vena cava (the right duct of Cuvier). (2) The coronary sinus (the left duct of Cuvier). (3) A stratum submerged beneath auricular tissue at the tænia terminalis. (4) The remnants of the venous valves, *i.e.* the Thebesian and Eustachian valves.

This does not represent a large amount of tissue, and it is difficult to trace in the mammalian heart. I would, however, draw attention to the occurrence in all mammalian hearts examined of a remarkable remnant of primitive fibres persisting at the sino-

auricular junction—that is, where the superior vena cava joins the tænia terminalis of the right auricle (beneath *a*, Fig. 4). This corresponds in position to the right venous valve of the sinus venosus of the primitive heart. The remnant has been termed the "sino-auricular node." It is interesting because it is in close muscular connection (1) with the outer wall of the auricle; (2) with the interauricular septum. In the latter fibres pass from the node down the septum to another remnant of primitive fibres at the base of the septum known as the auriculo-ventricular or A-V node. To this we shall refer again, but it is worthy of note that the two nodes, identical in structure, and therefore probably in function, are in muscular connection with each other.

The sino-auricular node has a special blood supply, and the nerves in the neighbourhood come into intimate relationship with it (Keith and Flack).

The Auricular Canal of the Human Heart.—It will be seen that in the simple form of vertebrate heart (Fig. 1) the auricular canal consists of three parts :—

(1) A basal part opposite the auricle.

(2) An annular part or "auricular ring" (3.3).

(3) An invaginated or intraventricular part (4.4).

The basal part is the ventral wall of the primitive cardiac tube. The auricle (*c*) has developed from the dorsal wall alone, leaving the ventral wall unspecialised. The basal wall is therefore continuous with—

(*a*) The sinus venosus.

(*b*) With the ostium of the auricle.

(*c*) With the auricular ring.

Does this continuity persist in the mammalian heart? In this heart the basal wall has become profoundly modified owing to the formation of an interauricular septum and a vestibule to the left auricle. Both these structures have been developed from the primitive basal wall.

The "auricular ring" is that portion of the auricular canal interposed between the auricle and the ventricle (3.3, Fig. 1), and in these hearts is of comparatively appreciable dimensions. In the mammalian heart, however, it is represented by a small but nevertheless important remnant. This is submerged in the auriculo-ventricular groove at the junction of the auricles and ventricles. The shape of "the ring," however, has become

modified owing to the extension of the bases of the ventricles backwards under the basal wall of the auricular canal. By this means the mesial fold has come to rest at the base of the interauricular septum on the right side just about the top of the interventricular septum. Most of the fibres representing the auricular part have become indistinguishable from the other auricular tissue, but the circular fibres of the auriculo-ventricular groove may be held to represent them. However at the spot referred to above, namely, at the base of the interauricular septum on the right side, a portion of the ring has remained undifferentiated. This is the node of tissue termed the "auriculo-ventricular or A-V node," and which is similar in structure to the "sino-auricular node."

The invaginated portion of the auricular canal is of interest, since in the lower type of heart (Fig. 1, 4.4) it forms a muscular connection between the auricular and ventricular portions of the heart. Has this invaginated portion any homologue in the mammalian heart, since if it have then a muscular connection must exist between the auricles and ventricles of the mammalian heart? For a long time this question was answered in the negative. The anatomists taught that in the mammalian heart the auricles were absolutely separated from the ventricles by fibrous tissue, so that no such muscular connection could exist. In 1893, however, His, jun., described a muscular connection between the auricles and ventricles. Stanley Kent also in the same year came to the conclusion that the auricle and ventricle were connected by muscle. Recently in 1904 Retzer and also Bräunig corroborated the observation of His in certain mammalian hearts, but not in all. Tawara in 1905 published a most elaborate and accurate account of this muscular connection, its extensive nature and its connection with the Purkinje fibres. Both he and other observers have found it in all the mammalian hearts examined, so that now there appears to be no doubt that such a muscular connection exists in all mammalian hearts. Keith and the writer have shown that, as might be expected, it is the homologue of the invaginated portion of the auricular ring. As later we shall have occasion to refer to this muscular connection, it will perhaps be well to describe it in some detail.

The Muscular Connection between Auricle and Ventricle in the Mammalian Heart. The Auriculo-Ventricular (A-V) Bundle.—This connection is sometimes called after His,

who first described it, the bundle of His; but it is perhaps simpler to term it the auriculo-ventricular or A-V bundle. The bundle, as first shown by Tawara, consists of four portions:—

(1) The auriculo-ventricular or A-V node.
(2) The main bundle.
(3) The septal divisions, right and left.
(4) The terminal ramifications.

These divisions can be followed in some hearts better than in others; for instance in the hearts of the sheep and ox it is a matter of great ease, since the fibres constituting the bundle are much paler than those of the surrounding musculature, and therefore easier to dissect out. These hearts, therefore, are recommended for preliminary dissections of the bundle. Microscopically also the fibres of the bundle present a greater contrast to the rest of the musculature in these hearts, so that the course and structure of the bundle are more easily followed through a series of sections, a matter of considerable difficulty at first in the human heart where the fibres are less differentiated.

Taking the human heart, however, as a type, it may be said that the auriculo-ventricular node lies, as described above, at the base of the interauricular septum on the right side (3, Fig. 2). It is in close connection (1) with the fibres of the interauricular septum and thus indirectly with the sino-auricular node; (2) with the right auricle proper by means of the circular fibres of the A-V groove. A good guide to its position is the coronary sinus (8, Fig. 2). The node lies below and to the right.

Arising from the A-V node is the main bundle (2, Fig. 2). This rides along the top of the interventricular septum below the pars membranæa septi—a spot easily found in the human heart by holding the organ up to the light. The knife may be safely entered through this spot, and the isolation of the bundle thereby facilitated. At this point the main bundle divides into its right and left septal divisions (Fig. 2). These divisions turn downwards on the interventricular septum, and make for the septal groups of musculi papillares. On the right side the division is in the form of a fairly fine cord, and may run part of its course embedded in the tissue of the septum; but it usually becomes superficial as it approaches the septal group of musculi papillares, and it can be invariably found in that position (Fig. 2, 4). On the left side close inspection of the septum will

reveal this division of the bundle as a delicate flattened ribbon of fibres passing downward directly beneath the endocardium. The ribbon soon breaks up into smaller strands which pass to the musculi papillares situated on the septum (4, 6, Fig. 3).

Arising from the groups of musculi papillares in either chamber are the terminal ramifications of the bundle. They frequently, especially on the right side, take the form of small moderator bands, and pass out to all parts of the ventricular wall. Here

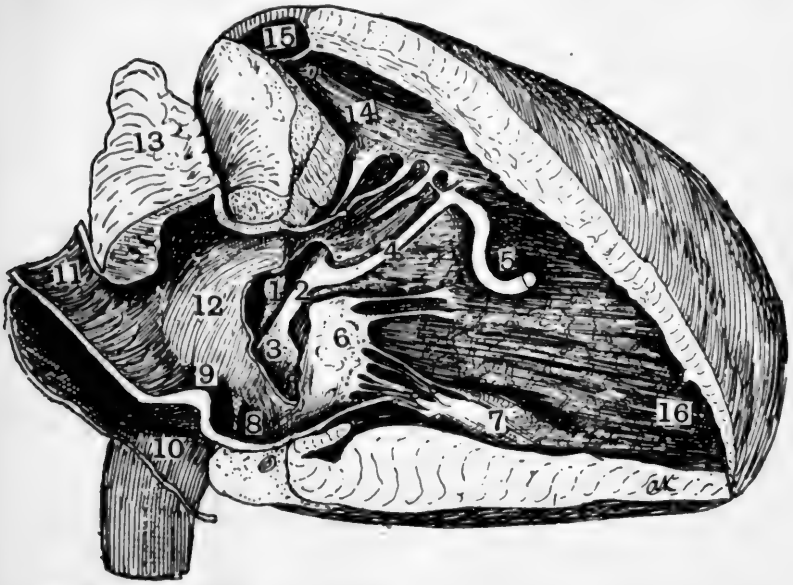


FIG. 2.—Right auricle and ventricle of calf (Keith). 1, Central cartilage; 2, main bundle; 3, A-V node; 4, right septal division; 5, moderator band; 8, orifice of coronary sinus.

they can be seen as delicate trabeculæ passing from one part to another. Eventually they fuse with the ventricular musculature.

With regard to the microscopic appearances of the various parts of the bundle, Tawara in his book gives drawings of them for the sheep's heart. In such hearts they are quite easy to recognise. The chief points to be noted are—(1) The peculiar branched cells of the A-V node. (2) The large pale cells of the main bundle with their large nuclei. (3) The peculiar Purkinje cells found in the septal divisions, and their terminal ramifications (especially in a so-called moderator band).

In the human heart the different portions of the bundle are not so easy to recognise microscopically. With a little practice, however, the bundle can be traced through a series of sections in its course

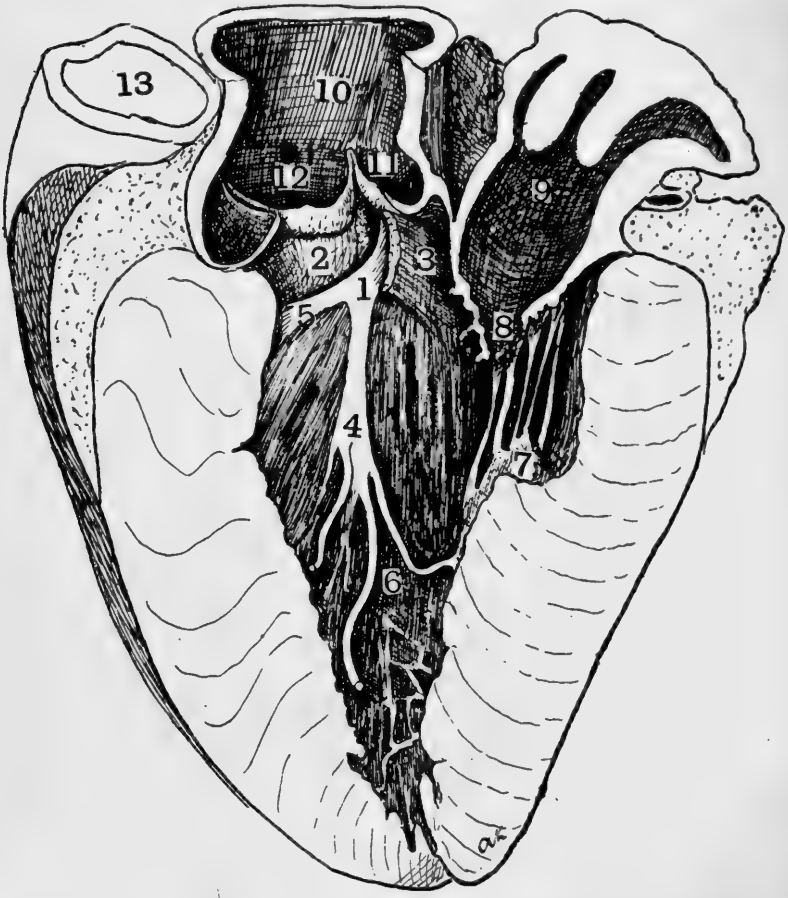


FIG. 3.—Left ventricle of calf (Keith). 1, Left septal division of A-V bundle; 2, 3, subaortic musculature divided to show passage of bundle from right side of heart; 4, 5, branches of left septal division; 6, free muscular "moderator" bands containing prolongations of bundle; 9, left auricle; 10, aorta; 13, pulmonary artery.

from auricle to ventricle. It will be found that the node is made up of closely interwoven fibres and a certain amount of fibrous tissue. The main bundle is completely separated from the remaining musculature by fibrous tissue, and is made up of paler

staining fibres with larger nuclei. The septal divisions are recognised by similar differences. In the moderator band of a human heart true Purkinje cells are not usually found, but the terminal ramifications can be easily seen. The greatest help in tracing the bundle is a knowledge of its course as determined by repeated dissections. This having been obtained, the "lie" of a section will be more readily appreciated, and the probable site of the A-V bundle located.

The Auricles of the Human Heart.—In the primitive heart

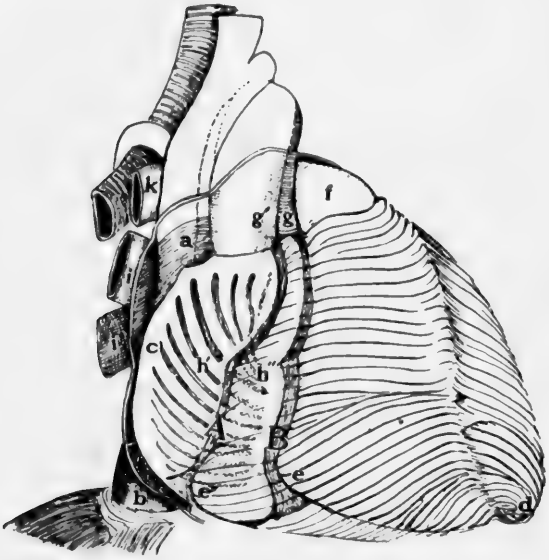


FIG. 4.—To show the antagonistic action of the musculatures of the right auricle and ventricle (Keith). A, the position of the A-V groove at the end of auricular systole; B, its position at the end of ventricular systole.

depicted in Fig. 1 it is seen that the common auricle is a well-marked outgrowth from the dorsal wall of the auricular canal. Its ostium is indicated by a ring of thick circular musculature (Fig. 1, 2.2). In the mammalian heart the development of the basal wall of the auricular canal has led to a separation of the two parts of the true auricle, namely, the appendices of the right and left auricles. Their original continuity, however, is still preserved by a ridge of musculature passing from the right auricle in front of the termination of the superior vena cava to the left auricle.

The right auricle of the human heart, therefore, consists of musculature from three sources—(1) Sinus venosus. (2) Auricular canal. (3) Auricle proper.

The left auricle is composed of musculature from—(1) The auricular canal. (2) The auricle proper. (3) Possibly sinus venosus. All these parts are in the freest muscular continuity.

The Ventricles of the Human Heart.—The main mass of these is true ventricle, although, as we have shown above, the invaginated

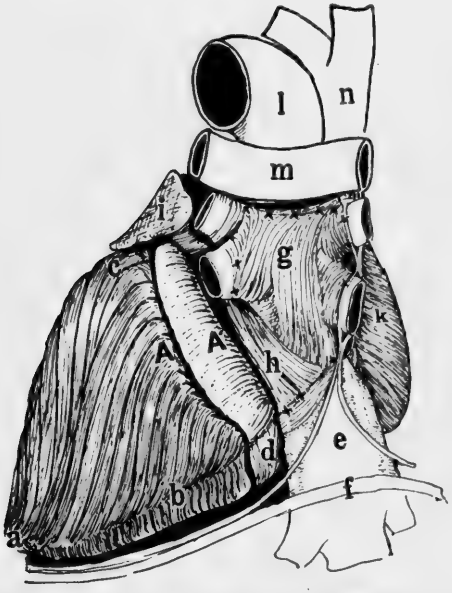


FIG. 5.—The heart from behind, showing the arrangement of the musculature of the left auricle and ventricle (Keith). A', the auricular base of the left ventricle in systole of the auricle; A, its position in ventricular systole.

portion of the auricular canal (4.4, Fig. 1) is represented by the A-V bundle. The single ventricle of the primitive heart is a diverticulum from the ventral wall of the primitive cardiac tube. The double chamber of the mammalian heart is homologous with it. The question of how the septum arose has, however, been differently answered. The old idea was that the interventricular septum grew up from the apex and thus divided the common cavity. This view is undoubtedly incorrect. What really happens is that the two ventricles are developed side by side from the

ventral wall of the primitive tube. The fusion of their adjacent walls forms the interventricular septum. The top part of this septum, therefore, represents the part of the primitive tube which has been least disturbed by the evolution of the ventricles. Now it is particularly interesting to note that it is at this point only in the mammalian heart that the invaginated portion of the auricular canal has persisted in the form of the A-V bundle. This point alone proves the mode of development of the interventricular septum. Further, not only has the bundle been subjected to the least possible amount of disturbance by this process of development, but in the adult heart it is undoubtedly better protected here than in any other possible situation (Keith and Flack). From this one infers that the A-V bundle is likely to vary but little in its course and must have a very valuable function to perform, since it is so well guarded both during development and in its final form.

The Bulbus Cordis.—In Fig. 1 it will be seen that a fifth chamber exists in the primitive vertebrate heart, the bulbus cordis. This chamber is generally supposed to be absent in the mammalian heart, but the recent researches of Greil and of Keith render it probable that this is not the case. The infundibulum of the right ventricle is the homologue of this portion of the heart. Of the original musculature of the bulbus probably but little if any is left, it having become replaced entirely or for the greater part by that of the ventricle proper. There is therefore, as in the primitive form, the freest muscular continuity in this part of the mammalian heart. This being so, we see that as in the primitive cardiac tube we have in the mammalian heart free muscular continuity from one end of the organ to the other—from the representative of the sinus venosus to that of the bulbus cordis.

C. The Nervous Elements of the Vertebrate Heart

The vertebrate heart is undoubtedly very rich in nervous elements. As considerable stress is laid by some observers upon this fact, it is important to ascertain as far as possible their distribution. These elements may be classified as (*a*) ganglion cells; (*b*) nerve fibres and nerve endings. The ganglion cells are usually regarded as the more important, since, as we shall see, the automaticity of the heart is credited to them by some physiologists.

Since, however, Apathy and Bethe make a similar claim for nerve fibres, their distribution has now an added significance.

The nerve endings in the heart are both sensory and motor. There is some doubt about the exact distribution of the sensory fibres. It is held by some physiologists that they do not supply the heart at all but only the aorta; others, however, believe that they end as tree-like expansions very like those in fascia and tendons, in both the epicardium and endocardium. According to Smirnow, all the sensory fibres run in the depressor branch of the vagus, since after section of this nerve in the cat no sensory nerve endings can be detected.

The motor nerve endings come from both the vagus and the sympathetic nerves. Gerlach states that the motor nerves accompany the fibrous tissue among the heart muscle and finally end as a delicate peri-muscular layer embracing the muscle fibres. Heymann and Demoor claim that every heart fibre is surrounded by a nervous network right down to the apex of the heart.

In regard to the ganglion cells of the heart, Dogiel has divided them into three types. The differences between the types are mainly in the shape and size of the nucleus, the length of axon and the number and form of the dendrites. The distribution of the ganglion cells is a matter of prime importance. It is certain that the auricular part of the heart is rich in these cells, which are often arranged in groups corresponding to Remak's, Ludwig's, and Bidder's ganglia in the frog's heart. These are respectively situated at the sino-auricular junction, on the interauricular septum and round the A-V groove. The distribution of ganglion cells in the ventricle is a vexed point. Dogiel and his pupils find that they undoubtedly occur in the upper third of this chamber. The lower two-thirds is, usually speaking, ganglion-free. This is true for the hearts of such animals as the sheep, calf, dog, sucking pig, duck, turkey, and chicken (Kasem-Beck). Ganglion cells have also been found in the ventricle of the rabbit and ape (Vignal), and of the mouse (Berkley), and in the ventricle and bulbus of the frog (Dogiel).

Yet against this view such authorities as Engelmann, His, Krehl and Romberg state that the ventricle contains no ganglion cells either in warm-blooded or cold-blooded animals. In many cases it appears to turn upon the interpretation placed upon certain histological appearances. For instance, Engelmann claims

to have proved that cells which Löwit termed nervous, were really not nervous but endothelial. Another investigator, Schwartz, concludes that the so-called ganglion cells seen in the endocardium and epicardium of the ventricle are really akin to if not actually mast-cells. Recently also Bethe claims to have demonstrated by his methylene-blue method that ganglion cells exist at the apex of the ventricle. He admits that they differ slightly from what is regarded as the normal type of cell, but he believes that they are true ganglion cells. As a critic says, many people would call this ganglion cell a connective tissue cell.

The question of the distribution of both ganglion cells and nerve fibres is therefore in a somewhat chaotic state. More work is required—it is of the greatest importance to know whether every muscle fibre has a nerve network surrounding it, and also whether ganglion cells exist throughout the heart. Lastly, it may be asked—Do nerve fibres exist in the A-V bundle? The question must be answered in the affirmative. It is said to contain nerve fibres and a few ganglion cells. Fredericq does not believe that nerve fibres actually pass through the bundle, and brings as proof evidence which we quote later on. He also states that he has histological proof of this, but I have not been able to find this piece of work.

D. The Heart as a Muscle

The chief properties of the heart should be studied on that part of the heart which contains no nerves. From what has been written in the previous section it will be obvious that this is a matter of no little difficulty. In determining these properties, however, most experiments have been made upon the apical part of the ventricle, on the assumption that this contains no nervous tissue. Although we shall have occasion to refer from time to time to the property of automaticity possessed by the heart, we shall not in this section discuss in which tissue, muscular or nervous, that property resides, but shall leave it until later, when we shall consider this question together with the mode of conduction of the excitatory wave which arises as the result of this property of automaticity.

The properties of cardiac muscle may be studied either when the heart is at rest or when it is beating. We shall consider the

former condition first, since it corresponds more closely to the conditions under which the other forms of muscle are studied. The heart may be reduced to this state of rest by four methods :—

(1) By placing it in physiological saline and waiting for it to cease beating, the cardiac muscle being excitable for a variable period after such stoppage. This method is more appropriate for the hearts of warm-blooded than of cold-blooded animals, since the latter may continue beating for days under these conditions.

(2) By shutting off the part of the heart possessing the greatest automatic power. This is done in the Stannius ligature experiment, more usually on the frog's heart, in which a ligature is tied round the sino-auricular junction. The same result can also be obtained by cutting away the more automatic parts of the heart—in other words, by making a ventricle preparation only.

(3) By stimulating the vagus most hearts can be reduced to a standstill.

(4) By certain drugs, such as muscarine, a like condition is obtained.

It must be stated, however, that under conditions 3 and 4 the normal properties of cardiac muscle are greatly altered, and therefore the methods are unsuitable. Preference must therefore be given to methods 1 and 2.

The preparation being obtained, it is found that cardiac muscle, like other forms of muscle, possesses the properties of excitability and contractility. It responds to a single stimulus by a single contraction. The stimulus may be either mechanical, thermal, chemical, or electrical. The last is most commonly chosen, but it is interesting to note with regard to the chemical stimuli that the heart muscle responds to the stimuli for muscle but not to those for nerve. Thus ammonia, dilute lime water, dilute mineral acids when applied to the apex of a frog's ventricle excite contraction or a number of contractions. These, according to Kühne, do not excite motor nerves. The potent nerve stimulant, glycerine, on the other hand, fails to excite a single contraction from such a preparation.

Different parts of the heart possess different degrees of excitability. This power of excitability, moreover, does not run parallel with the degree of automatism possessed by the same part of the heart. As an instance, the heart of the embryo chick at three days possesses great automatic power, but only a small

degree of excitability to artificial stimuli; later the automatism, especially that of the ventricle, decreases, while its excitability notably increases. Similarly the auricle possesses at this time a greater power of automatism than the ventricle, but the ventricle is the more excitable of the two chambers (Fano). The power of contractility also varies in different parts of the heart, being greatest in the ventricle, the part of the cardiac tube developed for propulsive work. But in dying this power is preserved longer in the auricle than in the ventricle, the parts of the right auricle around the superior vena cava and round the coronary sinus being the last to lose this property.

The muscle curve obtained as the result of the application of a stimulus corresponds to that of an ordinary muscle. There is the period of delay, the period of contraction, and the period of relaxation. In point of time it approaches more nearly to that of smooth muscle; the latent period is well marked, and the period of contraction is considerably slower than that of the sartorius or of the gastrocnemius of the same animal. As with smooth muscle, the heart appears to be more easily stimulated by gradual than by momentary shocks.

As with skeletal muscle, the contraction of the heart can be recorded under two conditions, namely, the isotonic and the isometric. This has been done more especially by O. Frank. The conditions in the heart, however, are not directly comparable with those in the skeletal muscle. In the latter, under isotonic conditions the actual shortening of the muscle under a constant weight is measured; in the heart, owing to the anatomical arrangement of its fibres, it is impossible to do this. The isotonic curve is therefore obtained by measuring the alteration in the size of the cavity of the ventricle which occurs as the result of this shortening of the fibres. This is done by introducing a sound into the ventricle and connecting it with a tambour. The isometric curve of skeletal muscle is obtained by preventing the muscle from shortening while the change in its tension is measured. The allied condition is brought about in the heart by causing it to contract against an insuperable obstacle, such as a tap introduced into the circuit. The tension of the ventricle wall alters under these conditions, but the length of the fibres remains the same. This alteration in tension is measured by a manometer inserted between the ventricle and the insuperable obstacle.

The skeletal muscle can also be studied under the combined condition, namely, when "after-loaded." Here the condition of the muscle is isometric while altering in tension to overcome the load, and isotonic after this load has been overcome and the muscle begins to shorten. A similar state of affairs prevails in the heart. The ventricle contracts under isometric conditions upon its load of blood until the semilunar valves open, thenceforward under isotonic conditions whilst its fibres shorten and its load is discharged. The heart therefore corresponds normally to an after-loaded muscle. Frank showed by his studies that the laws which govern the contraction of skeletal muscle under these conditions apply equally to the heart. Thus, as in skeletal muscle, the isometric curve culminates before the isotonic. He found also that the maximum of the isometric curve of the ventricle increases with increasing tension up to a certain point, and then decreases. This means that the contraction of the ventricle, as is well known, increases in force with the amount of its filling up to a certain point, but after that it decreases and the ventricle dilates. Thus for the frog's heart Frank found the following figures :—

Volume in ccm. in ventricle	0	·18	·34	·47	·63	·84	·93
Tension mm. of mercury	12	60	68	66	60	59	58

During the isotonic curve the change of tension varies with the load. Increasing load defers the beginning of the contraction, shortens its duration, and diminishes the velocity of the movement of the free end of the muscle. Similarly in the ventricle, increased load—that is, increased resistance to the outflow of blood from the ventricle—defers the beginning of the period of expulsion, the opening of the semilunar valves, shortens the period until their closure, and diminishes the rate of flow of blood through the aortic orifice, and consequently lessens the systolic discharge. As an example from experiments upon the frog's ventricle, if resistance increases from 10 mm. to 40 mm. of mercury, the flow decreases from ·06 to ·02 per second, and the period of expulsion diminishes from ·56 second to ·51 second, and the systolic discharge from ·33 cc. to ·08 cc. This method of studying the ventricle under both isometric and isotonic conditions gives valuable information in working out the effects of drugs upon the heart muscle.

So far we have spoken of the similarity between cardiac

and other forms of muscle as regards its response to a single stimulus. But there is this remarkable difference to be noted, that whereas in other forms the response varies in force according to the intensity of the stimulus, cardiac muscle responds with a maximal contraction to all efficient stimuli, be they minimal or maximal. This is sometimes termed "the all or nothing law"; therefore once a heart responds to a stimulus it is of no avail to increase the intensity of that stimulus. It should be noted, however, that heart muscle may give in response to the first few stimulations gradually increasing contractions, thereby manifesting the so-called "Treppe or staircase phenomenon." This is explained on the supposition that the first few contractions render the tissue more excitable to that form of stimulation.

Another peculiarity manifested by the heart muscle is in response to rhythmic stimulation. If a ventricle preparation, giving but one contraction to one stimulation, be treated in this way by single induction shocks, it starts to pulsate in regular fashion, but the frequency of beat is always less than the stimulation frequency. The number of contractions obtained by this method can be increased either by increasing the frequency of stimulation or the intensity of current with the same rate of stimulation. The same phenomenon can be produced upon the ventricle by a constant current of appropriate intensity, the normal response being twenty to thirty regular beats, after which it ceases. The ventricle can also be made to give a similar rhythmic response by injecting blood or normal saline into it at a suitable pressure. Certain drugs, such as delphinin, are said to cause a series of rhythmic contractions.

A further peculiarity of cardiac muscle is that it cannot be tetanised. It is impossible to bring about a summation of stimuli in the normal heart. This, however, is said to be possible on the muscarine-poisoned heart, and on the heart stopped by excitation of the vagus.

Thus far we have discussed the effect of stimulation upon the heart at rest. When we come to study the effect upon the beating heart, certain other remarkable differences from skeletal muscle are revealed. For instance, if a stimulus be applied to the rhythmically beating ventricle just before or during systole it is without any visible effect. The heart muscle is therefore said to possess "a refractory period," and the possession of this

property explains the inability to tetanise it. If, however, the stimulus be applied during diastole, a contraction is produced which is known as an "extra-systole." Such extra-systoles are followed by a longer pause than normal. This is called the "compensatory pause." It is about equal in length to the pause following the normal beat plus the amount cut off from the previous pause by the induction of the extra-systole. The ventricle therefore, owing to this property, makes but the same number of systoles as usual in a given time. This is known as the "law of conservation of rhythm to physiological stimuli" (Engelmann). The length of the compensatory pause is due to the refractory period; the impulse causing the normal contraction reaches the ventricle while it is in a state of systole from the artificial stimulus, and it therefore has no effect. The ventricle is then not stimulated again until the next normal impulse arrives.

If, however, the ventricle be thrown into rhythmical contractions by a continuous stimulus, and an extra-systole produced by a strong artificial stimulus, the extra-systole so induced is not followed by a compensatory pause, for the continuous stimulus still acting produces another contraction as soon as the refractory period of the extra-systole is passed. This is adduced as proof that the normal physiological stimulus is not continuous, but discontinuous, inasmuch as there could be no compensatory pause if it were not so.

Another important point to be noted is that the compensatory pause does not follow an extra-systole induced at the venæ cavæ. It therefore follows that all extra-systoles observed to be followed by a compensatory pause are produced by a stimulus applied to some other part of the heart (*e.g.* auricle or ventricle). It also follows that the stimulus is not conducted from outside to the venæ cavæ, but actually arises there.

Like other forms of muscle, the heart muscle is said to possess the property of tonicity This is masked in part by the incomplete relaxation of the heart between the beats, since as Gaskell points out the degree of relaxation depends not only upon the tonicity of the muscle, but also upon the rate of beat, which is usually such that the heart muscle probably never completely relaxes. An alteration in tone can therefore only be manifested when the rate of beat remains the same. The little but distinct evidence that exists for this change is derived from the action of

certain solutions and drugs upon the beating ventricle. If a frog's ventricle be placed in a weak solution of caustic soda (1 in 20,000 of normal saline) it relaxes less and less between the beats and eventually stands still in systole, whereas if lactic acid (1–10,000 normal saline) be used the contractions become less and less, so that finally the ventricle stops in a state of complete relaxation. Similar results to that with alkali can be obtained by such drugs as digitalis and veratrine, and to that of acid with muscarine. Moreover, acid solutions antagonise the effect of alkaline on the same preparation, as does muscarine that of digitalis. The heart muscle, therefore, would appear to be possessed of a certain degree of tonicity which, like the other properties of cardiac muscle, probably varies in the different parts of the heart.

Another peculiar form of tonicity has been observed by Fano (quoted by Gaskell) upon the heart of Emys Europæa. If this heart be clamped in the A-V groove, the auricles exhibit a rhythmical variation of tone. A similar phenomenon has been seen by Botazzi in the frog's heart. It apparently does not occur in many cold-blooded animals. At present a satisfactory explanation is wanting.

Lastly, the heart possesses the properties of automaticity, rhythmicity, and stimulus conduction. Do these properties reside in the heart muscle itself or in the nervous tissue abounding in the heart? This is the vexed question which we discuss in the following section.

E. The Site of Origin and the Mode of Conduction of the Excitatory Wave

By the site of origin is meant the kind of tissue, muscular or nervous, in which the heart impulse arises. A long controversy has raged around this point, and much fruitful research has been the outcome. It is necessary to keep clearly in mind the difference between the site of origin of the excitatory wave and the mode of its conduction. These are frequently confused, and experiments in regard to the site of origin of the excitatory wave are quoted as evidence as to its mode of conduction. Certainly it must be granted that if the excitatory wave be found to arise in one form of tissue, it is highly probable that it will also be conducted by that tissue; but it is not necessarily the case. There are several

possibilities. The excitatory wave, for instance, may conceivably arise in nerve and be conducted by nerve. This is the neurogenic theory. Or the excitatory wave may arise in the heart muscle and be conducted by muscle. This is the myogenic theory. These certainly seem more probable than either (1) that the excitatory wave may arise in nerve and be conducted by muscle; or (2) that it may arise in muscle and be conducted by nerve. Even here the possibilities do not cease, for the co-ordination of the movements of the different chambers of the heart is essentially a complicated yet all-important process, so that it may well be that, arise the excitatory wave how it may, both muscle and nerve may be called into play as conducting agents in order that the proper sequence of contraction of the different chambers of the heart may be assured.

Taking the first possibility, that the excitatory wave may arise in nervous tissue and be conducted by that tissue, let us consider the evidence for and against it. This view gained sway in the middle of the last century chiefly perhaps because it offered a satisfactory explanation of the great discovery by the brothers Weber of the action of the vagus nerve upon the heart. At that time such an inhibitory influence could only be explained on the analogy of nervous influence of centres situated in the central nervous system, such as the respiratory centre of the medulla and the motor centres of the spinal cord. The ganglion cells, therefore, were thought to be the central apparatus of the heart, sending out a continuous stimulus to the heart muscle. Different afferent impulses to this central apparatus modified the stimulus in different ways. The very plausibility of the view immediately accorded it a place as a theory without any very substantial evidence. Its chief support is the experiment of Stannius, now known as the Stannius ligature experiment. If in the frog's heart a ligature be placed around the sino-auricular groove and tied tightly, the auricle and ventricle of the heart are reduced to a standstill; in consequence, it is asserted, of the cutting off of the influence of Remak's ganglia in this neighbourhood. The sinus, however, continues to beat. If now a ligature be placed round the A-V groove and tied, the ventricle again starts to beat, owing, it is said, to the stimulation of Bidder's ganglia in this region. Bidder's ganglia are therefore looked upon as a subsidiary centre normally under the control of Remak's at the sinus. In

further support of this view Kaiser claims to have shown that, after extirpation of Bidder's ganglia, this second ligature no longer has any effect in starting the ventricle. Now a stimulus applied is followed by only one contraction instead of by a series of contractions. We shall refer to this experiment again later on.

Kronecker and Schmey claim that when a needle is thrust into a certain spot in the dog's ventricle, the heart immediately falls into fibrillary contractions as far as the ventricles are concerned. The needle is thrust into the ventricular septum at the lower end of the upper third. The experiment frequently fails. It is adduced, however, by its authors as evidence of the neurogenic theory.

The experiments of Carlson upon the heart of a horse-shoe crab (Limulus) undoubtedly afford evidence of neurogenic origin of a heart beat. The heart in this case consists of a tube 10 to 15 cm. long, divided into segments by the origin of arteries. During systole all the parts appear to contract simultaneously, although it is probable that there is really a rapid wave of contraction. Three nervous strands (one median and two lateral) run along the heart and anastomose freely. The median contains ganglion cells, and one especially large ganglion. This strand can be easily separated from the heart without injuring the latter. Fine branches pass into the muscle substance. Carlson has shown that if the whole of this median nerve be removed, the heart immediately ceases to pulsate ; if a part only be removed, then activity ceases in the corresponding portion of the heart. The ganglionated chain therefore appears to be the site of origin of the excitatory wave in this heart.

As regards the conduction of the impulse the neurogenic theory holds that it is conducted by nerves. The delay in the passage from auricle to ventricle is said to arise in Bidder's ganglia.

The chief points in the evidence brought forward for nervous conduction are—

(1) The assertion by Kronecker that he has produced allorhythmia (inco-ordination of auricle and ventricle) by cutting a nerve running between auricle and ventricle.

(2) At first the fact that in the mammalian heart no muscular connection was known to exist between auricle and ventricle. For instance, MacWilliam, as the result of his researches, came to the conclusion that in the mammalian heart, at any rate, the mode

of conduction from auricle to ventricle must be nervous, as he could find no muscular path. Since the discovery of the A-V bundle this piece of negative evidence is of less value; but the fact that the bundle contains nerve fibres is insisted upon by the upholders of the neurogenic theory. This point we shall deal with when considering the evidence of muscular conduction by the A-V bundle.

(3) In the heart of Limulus Carlson has shown that section of the nervous strand immediately abolishes the synchronism of the different parts. The parts on either side of the cut continue to pulsate, but with a different rhythm. This points to nervous conduction of the master rhythm. Further, it is interesting to note that in this heart, so long as the nerves are intact, section of the muscle produces no inco-ordination whatever.

In estimating the value of these experiments of Carlson it must be pointed out that the muscle tissue of this invertebrate heart differs very materially in its properties from that of the mammalian heart, being in fact much more akin to mammalian smooth muscle. It possesses no refractory period, gives sub-maximal contractions, and is capable of tetanisation.

It was in 1882 that the first serious criticism of the neurogenic theory was advanced. Gaskell came to the conclusion, as the result of his experiments upon the heart of the turtle, that in cold-blooded animals the heart's excitatory wave arises in the heart muscle itself and is conducted by it. He showed that if the ventricle be warmed its beat was not quickened, whereas warming of the sinus caused a quickening of the whole rhythm of the heart. This therefore proved that the stimulus is discontinuous and not continuous, as was thought before. But were the nerve cells concerned in the origin of the excitatory wave? Gaskell found that if the Stannius ligature be applied to the turtle's heart, the effect at first is essentially the same as with the frog's heart. Soon, however, the auricle starts beating with its own rhythm, slower than that of the sinus, and the ventricle follows it. If now the second ligature be applied, the ventricle stops for a moment, but quickly resumes beating with its own rhythm, which is slower than that of the auricle. Therefore in the same heart it is possible to obtain the sinus, auricle, and ventricle beating with different rhythms. It seemed that in such a case as this it would be strange for nerves to set a different rhythm in different parts

of the same heart; and, knowing the muscle of the heart to vary in these different portions, it was more probable that the difference in power of originating the automatic rhythm lay in the heart muscle itself. This was proved to be the case. Gaskell found that small strips of muscle from the different parts of the heart, so small as to contain no ganglion cells, show the same power of developing different rhythms; a piece of ventricle, for instance, from a well-nourished animal beating for thirty hours. Gaskell, as we have said, explains the different degrees of automatism by the variation in the type of muscle. The more "embryonic"—that is, approaching the type seen in the embryo—possesses the greatest automatic power. This being the case, then stimulation of the musculature of the sinus or of the auricular ring should originate a series of contractions. Gaskell showed this to be so, proving conclusively at the same time that the experiment of Kaiser in regard to the function of Bidder's ganglia was incorrect.

Gaskell's result may be summarised as follows :—

Stimulation of auricle or ventricle . .	One contraction.
Stimulation of Bidder's ganglia . .	No contraction.
Stimulation of the auricular ring . .	Series of contractions.

Consequently the ring musculature and not the ganglia were concerned in originating the rhythm. Further support in this direction came from Munk, who also showed that a series of contractions was the normal response to the excitation of this musculature. Ewald found and confirmed by microscopic examination that in only two cases out of twenty-nine were the ganglion cells or nerves injured as the result of the excitation of the ring musculature, which, however, in all cases responded with a series of contractions.

In the twenty-five years following Gaskell's first work much has been done in endeavouring to support the myogenic contention. Engelmann and his pupils have been particularly strenuous in upholding it. During this time, however, the neurogenic school have provided but little new evidence for their somewhat slenderly-founded theory, their chief work consisting in endeavours to refute the evidence brought forward by the myogenic school. The chief points which have been offered as evidence are :—

(1) Engelmann isolated portions of the great veins said to contain no ganglion cells and showed that they beat automati-

cally; a small piece (2 cmm.) of the sinus of a frog beat for four days and recorded 17,000 contractions.

(2) In certain molluscs, arthropods, and tunicates, the heart undoubtedly contains no ganglion cells but possesses automatic rhythm.

(3) The apex of the mammalian heart, said to have no nerves whatever, shows slow rhythmic contractions.

(4) The embryonic heart beats when no ganglion cells have invaded the heart, and before the muscle and nerve have become differentiated (His). In the chick, the heart of which pulsates 36 hours after the beginning of hatching, no ganglion cells appear until the sixth day; in the human heart Pflüger saw pulsations at the beginning of the third week, whereas no ganglion cells are said to occur until the end of the fourth or the beginning of the fifth week. Fano found that if he divided the heart of a chick into three or more parts, all the parts pulsated—the frequency being greater the nearer the part was to the venous end—although, as we have seen, the ventricle at that period was the more excitable. W. His has also found differences in the behaviour of different parts of the heart towards drugs such as muscarine and digitalis, the ventricle being the most affected. The inwandering of the ganglion cells leads to no noticeable effect on this. This being the case, it is difficult to believe that later on they should take over the function of initiating the heart rhythm.

(5) Hearts can be revived many days after death—even the hearts of children dead of disease. In ten such hearts only three gave negative results. The heart of a boy dead of pneumonia revived in all parts 20 hours after death. In the case of the heart of an ape, Hering recovered the heart after 4½ hours, and then froze it. After 28 hours 32 minutes the heart was again resuscitated. If now the ganglion cells be the site of origin, then Ringer's fluid must possess the power of enabling them to recover their functions; but if Ringer's fluid have not this power, then the ganglion cells cannot have the power of automatism. Now Langendorff and others have shown that sympathetic ganglia and fibres die very quickly. Hering found in the rabbit that the pre-ganglionic cervical sympathetic was without action 15 minutes after death, the post-ganglionic 33 minutes after death, the vagus on the heart 55 minutes after death. The corresponding times for the cat were 11, 26, and 40 minutes. It was not found to be possible to restore

the functions of the cervical sympathetic by perfusing with Ringer's solution, whereas the irritability of the vagus could be restored for some time, and that of the acceletor almost indefinitely.

It is in the tissue of the sinus in the frog's heart that the automatic power resides. This is the part of the heart which can be affected by such agents as heat and cold. Destruction of the sinus or cutting it off alters the rhythm of the remaining portions of the heart. One would expect, if the results obtained upon the frog's heart be applicable to the mammalian heart, that similar results should be obtained by experimenting upon the parts representing the sinus. Such indeed is the case. At the junction of the superior vena cava with the auricle Adam has succeeded in altering the mammalian heart rhythm by the application of heat and cold. Hering has shown that the rhythm in the dog can be completely changed by a cut in this region. Langendorff has obtained somewhat similar results with the Stannius ligature experiment upon the mammal. The results were not so marked as with the frog, the period of rest being slight, and the heart resuming its beat more quickly, although with a different rhythm. As we have seen, the sino-auricular node is situated in this region, and it may well be that this is the spot acted upon in these experiments. Experimental evidence to this effect, however, is still wanting, and the true function of this node has yet to be worked out. In the meantime it has been suggested that in view of its embryonic structure it is likely to possess great automatic properties, and that seeing how carefully it is supplied with blood, and how intimately the nerves of the heart come into contact with it, this isolated node of tissue is probably the site of origin of the heart's impulse. On the other hand, also without physiological evidence, Tawara has claimed that the heart's impulse normally arises in the A-V node, which he has termed the "cardiomotor centre." No proof of this is as yet forthcoming, but the view more generally held, although as yet without definite evidence, is that the A-V node must be regarded as a subsidiary centre, and that it is only under certain circumstances that the heart rhythm is initiated there. While dealing with such hypothetical problems it may be suggested that the possible explanation of the effect of the first Stannius ligature is due to the cutting off of the automatic tissue at the sinus, *i.e.* in the case of mammalian heart possibly the sino-auricular node. Under these circumstances the

auriculo-ventricular node after a time takes up the function of initiating the heart rhythm. Examples of this "nodal rhythm" have been recorded clinically by Mackenzie.

Coming now to the evidence of muscular conduction, it will be remembered that there is no histological reason against it, since the heart muscle is now regarded as a continuous network. The earliest experiment on cold-blooded animals was the well-known zig-zag experiment of Engelmann, in which the ventricle of the frog is so cut that it is claimed that all conducting nerves must be cut and yet the impulse still passes. Gaskell also showed in the tortoise that section of the well-marked coronary nerve had no effect on the passage of the impulse, whereas the clamping of the muscular tissue induced varying degrees of allorhythmia (2A : IV, 3A : IV, 4A : IV), according to the tightness of the clamp. Gaskell also showed that section of the part of A–V grooves containing the most nerves had no effect upon the ventricular rhythm.

MacWilliam came to the conclusion that in the eel the conduction of the impulse was by muscle. He also drew attention to the sino-ventricular rhythm, whereby the ventricle can follow the rhythm of the sinus without the auricle being influenced. In this case the impulse arising in the sinus passes down the basal wall (Fig. 1) and thence to the ventricle. MacWilliam thought there was evidence of such a rhythm in the mammalian heart. We may here point out that it is indeed quite possible, for the excitatory waves arising in the great veins may conceivably, under certain conditions, pass down the interauricular septum which corresponds to the basal wall, and thence to the ventricle, without affecting the other parts of the auricle during its passage.

As regards the evidence of muscular conduction in the mammalian heart, Fredericq has brought good evidence to show that such is the case in the auricles. He found that the two auricles remained co-ordinate so long as he left a thin strip of muscle connecting them. It did not matter where this strip was, whether in neighbourhood of superior vena cava or of inferior vena cava or coronary sinus. When, however, he cut this strip, then he found that the two auricles became inco-ordinate. It is interesting to note, however, that the ventricle continued to beat with the same rhythm as the right auricle. He argued that conduction in this case was muscular and not nervous, since the bridge

of tissue might be situated in any position. Histological investigation proves this free muscular continuity (Keith and Flack). With regard to evidence of muscular conduction between auricle and ventricle in the mammalian heart, it is usually held that the A-V bundle effects this, and that the conduction by it is muscular. The evidence that the A-V bundle is the sole passage of conduction is also tolerably strong, although some investigators bring results which appear to the contrary. The chief evidence in favour is as follows :—

(1) Hering cut in the region of the A-V bundle in four dogs, and in three cases out of four obtained allorhythmia. Tawara showed by histological investigation that in three only was the bundle cut ; the fourth had escaped.

(2) Erlanger compressed the bundle in dogs by means of a specially-devised atriotome, and succeeded in obtaining varying degrees of arrhythmia and finally allorhythmia. Retzer confirmed histologically the damage done to the bundle.

(3) Humblet has successfully obtained allorhythmia in dogs on many occasions by ligaturing the A-V bundle. No allorhythmia was produced when any other part of the septum was tied.

(4) The evidence afforded by syphilitic disease of the bundle in certain cases of Stokes-Adams disease. Several very satisfactory cases with tracings and post-mortem examination of the heart have been published.

On the other hand, Kronecker states that in rabbits he is unable to obtain any allorhythmia by ligature of the A-V bundle, and in this he is confirmed by his pupil Imchanitsky. In some cases the bundle was certainly not tied, but in others it is claimed to have definitely been so. It may be that the heart of the rabbit affords an exception, since Biggs also appears to have obtained uncertain results upon the rabbit's heart. An interesting point, however, is that Kronecker always attempted to tie the bundle through the left auricle, and Humblet found in dogs that he was not successful by this method. All the observers mentioned above attack the bundle through the right auricle. It is undoubtedly the more certain method. There is great danger of getting above the bundle or only obtaining part of it from the left side, owing to the manner in which the left septal division comes off.

The main evidence is undoubtedly in favour of the A-V bundle being the sole path for the transmission of the impulse from auricle

to ventricle in the mammalian heart. But it does not necessarily prove muscular conduction, since the bundle contains nerve fibres and a few ganglion cells. Fredericq, however, states that he has destroyed all the nerves in the bundle and its neighbourhood by ammonia, but yet got no evidence of allorhythmia. He states also that histological evidence shows that the nervous elements of the bundle do not extend right through it. According to Fredericq the mode of conduction in the bundle is undoubtedly muscular. The opinion of Fredericq is weighty and all the more interesting since formerly he held the neurogenic view. Even now he holds that under certain conditions there is a nervous conduction in the heart. He bases his view upon the following experiments. As long ago as 1886 he found that with feeble indirect shocks he got these results :—

Applied to one ventricle .	{ Both ventricles stopped. { Both auricles continued beating.
Applied to one auricle .	{ Both auricles stopped. { Both ventricles continued beating.

He came to the conclusion, therefore, that there must be some abnormality in the conduction in these cases, since ordinarily he could obtain reciprocal conduction, whereas this mode of conduction affected both auricles and both ventricles, but did not connect auricles to ventricles. More recently he found that if he threw the heart into fibrillary contractions he obtained the same results. The fibrillary contractions arising in one auricle pass quickly to the other, but not to the ventricles ; similarly with the ventricles, from ventricle to ventricle but not to the auricles.

Fredericq thinks that fibrillary contractions pass quickly by nervous means, and adduces the above experiments as evidence that the A-V bundle contains no nerve fibres passing throughout its course, since fibrillary contractions never pass from auricle to ventricle. On the other hand, the rhythm of the ventricle is normally that of the auricle, and is influenced whenever that of the auricle is altered. Therefore the heart impulse passes by muscular tissue and traverses the A-V bundle in its passage from auricle to ventricle. The rate of conduction of the impulse along the bundle is explained by the character of the muscle tissue of which it is composed, since Fano has shown that the rate of conduction in cardiac muscle varies according to the stage of development. It would therefore seem that the difference in structure

of the bundle in different hearts has, in a measure at least, to do with the rate of conduction required for that particular heart. In the dog's heart Stassen finds the time taken is ·08 to ·10 of a second.

To summarise, the chief points usually adduced in favour of muscular conduction in the vertebrate and especially in the mammalian heart are :—

(1) The zig-zag experiment of Engelmann and the bridge experiment of Fredericq.

(2) There is muscular connection between auricle and ventricle. Disturbance of conduction follows cutting or compression of this connection.

(3) There is no effect upon stimulating or cutting the nerves from auricle to ventricle.

(4) The conduction of the excitatory wave may occur after the nerves have degenerated.

(5) The rate of conduction is more in accordance with muscular conduction.

(6) Conduction takes place from the point of stimulation in all directions.

(7) Reverse conduction occurs from ventricle to auricle.

The balance of evidence lies in favour of the myogenic theory. Certain objections, however, may be urged against it. For example, the evidence brought from the invertebrate kingdom in its favour is no more applicable than that obtained upon the heart of Limulus. Against the zig-zag experiment may be brought the histological evidence of certain observers. If every fibre is surrounded by a nervous network, then that network may manifestly be the conducting medium. As to the rate of conduction, it has been shown by Nikolai and Garten that non-medullated nerves conduct at a rate compatible with that of the excitatory wave of the heart. On the other hand, Bökelmann has found that the non-medullated terminals in the cornea of a dog are not appreciably slower in conduction than ordinary nerve. More recently Bethe has made experiments on the warm-blooded heart, and concludes that the rate of conduction of nerve in the dog is 130 to 225 cm. per second—a result quite in accordance with that required for this heart. Bethe also states that it is difficult to induce degeneration of nerve in the manner usually employed, namely, by placing a ligature round the heart. He himself has been surprised to find

how difficult it is to induce degeneration in an isolated nerve by a tight ligature. Anatomical evidence of such degeneration in the heart must be brought, and at present this has not been furnished.

In regard to the proofs offered for the automaticity of the heart residing in its muscle, considerable importance rests upon the evidence obtained from the embryonic heart. Here one may object that this embryonic tissue is probably neither muscular nor nervous. Bethe claims that recent methods show that from it both muscle and nerve cells develop. The action of muscarine upon the heart before the inwandering of the ganglion cells is also brought as evidence on this point. If this be the case, it leads on to the idea that the automaticity of the adult heart may possibly reside in a similar tissue neither muscular nor nervous. This tissue, akin to nerve-muscular cells from which the heart is developed, may be shut off at any early stage of development for this special purpose of leading the automatic rhythm of the heart. May it not also in some ways correspond to the form of tissue in the myoneural junctions, in being easily affected by nervous influences and manifesting the effect upon the adjacent muscle. Why, moreover, may it not be acted upon by certain internal secretions, thus providing the heart with a further reflex mechanism for preserving the well-being of the body as a whole ?

Again in regard to the conduction of the impulse, it is possible that the conducting mechanism of the heart is developed from such a tissue, becoming nervous in one form of heart, muscular in another, according to the requirements of the organ in that special genus. This would explain the discrepancies in the evidence from the invertebrate kingdom. Then again the Purkinje fibres of the sheep's heart are not seen in the human. This is probably something to do with the requirements of co-ordination. The Purkinje fibres are totally different from the surrounding musculature—it is difficult to call them muscle ; but it is easy to understand how such a fibre can be differentiated from a tissue capable of giving rise to both muscle and nerve. From such a tissue, moreover, a conducting mechanism can be evolved presenting different histological appearances, but having the requisite rate of conduction for the co-ordination of that heart.

The above are the chief facts in regard to both the neurogenic and myogenic theories. Neither theory is a dogma—one may

survive, both may pass away; but that only further anatomical and physiological research can show.

F. The Movements of the Heart in situ

By virtue of the properties enumerated above the heart co-ordinates itself to meet the circulatory needs of the body. More research is needed before one can speak with certainty upon the exact movements made by the heart in the unopened thorax, although a considerable amount of work has been done on the subject (Ludwig, Haycraft, Keith). As emphasised by Keith, the heart has certain fixed fulcra from which it executes its normal movements, and the moment the thorax is opened these are taken away, and the true movements made by the heart are in part obscured. These fulcra are as follows :—

(1) The venous mesocardium, or the part of the pericardium attached around the great veins (Fig. 4, over *a*, *i*, *i*, and *b*).

(2) The arterial mesocardium, or the part of the pericardium attached around the great arteries (Fig. 4, over *g* and *f*).

Except at these two points the heart lies absolutely free within the pericardium. But these mesocardia are attached to the surrounding structures, and it is by this means that steadiness is obtained. For instance, the part attached to the venous end is bound to three structures :—

(1) To the root of the lungs, and by the lungs to the wall of the thorax.

(2) To the diaphragm, especially to the crura.

(3) To the structures in the root of the neck through the fibrous tissue surrounding the superior vena cava.

Now to this fulcrum the longitudinal muscle of the auricle is attached, and it is obvious that when the thorax is opened the auricle can no longer perform its normal movement.

As we have seen, the heart's excitatory wave arises in the great veins, especially in the neighbourhood of the sino-auricular groove between the superior vena cava and auricle. Of this there is physiological proof, since, as stated above, it is only in this region that the rhythm of the heart can be modified. The wave passes from here to all parts of the heart, and they respond to it in orderly sequence. We should expect, perhaps, that since it arises in closer proximity to the right auricle, this auricle would contract

slightly before the left, since the wave presumably has less ground to cover to fire off the right auricle. It is usually stated, however, that the auricles beat simultaneously (cf. Tigerstedt and other authorities). According to Arloing and Doyon, however, Chauveau appears to have stated that in the horse the right auricle beats before the left. Fredericq also noticed this in his records on more than one occasion, especially when the heart was beating feebly and slowly. Recently further proof has been forthcoming under his direction. Schmidt-Neelsen finds that normally the right auricle precedes the left. If, however, an extra systole be induced by stimulation of the left auricle, then that auricle precedes the right. Another interesting observation made by him is that when the auricles are induced to beat by stimulation of the ventricle, the right more often precedes the left, but the results are variable. When the heart beats during excitation of the vagus, the normal order of beat is preserved. Stassen finds that in the dog the right auricle precedes the left by ·02 to ·03 second. He also finds that the ventricles do not beat simultaneously, but that the left normally beats in the dog ·03 to ·04 second before the right. But when it is stimulated electrically the right precedes the left by a greater time than the left normally precedes the right. From this Stassen infers that there is a form of " antidromic " conduction in the A-V bundle, since if the left be similarly excited, the interval before the right is the same as normal.

When the auricle beats in the lower vertebrate heart, regurgitation is prevented by the action of the venous valves. In the mammal these valves have disappeared, and the prevention of regurgitation into the great veins is not altogether effectual. It is on this account that the jugular pulse can be recorded over the jugular bulb even in health. There is undoubtedly a guillotine action by the tænia terminalis tending to prevent regurgitation, but this is insufficient especially with high pressures; and according to the degree of its insufficiency, so will the jugular tracing vary. Regurgitation through the inferior vena cava cannot be prevented by muscle, since there is none. The most important factor here is undoubtedly the high abdominal pressure, and indirectly therefore the tone of the belly wall. The whole system of abdominal and thoracic veins may be looked upon as a large venous cistern, having a capacity in man of about 430 c.c. The abdominal portion has by far the greater capacity (Keith). The blood is

kept in this cistern by valves, *e.g.* femoral and jugular, and the pressure caused by the body movements must therefore send the blood on to the right heart.

The chief function of the right auricle, however, is to expel the blood into the right ventricle at the end of joint diastole, and thereby place its walls on a certain tension. According to this degree of tension the heart muscle will contract. Within certain limits, the greater the tension, the more powerful the contraction. It is by this means in part, that the amount of blood passing to and from the heart is regulated to meet the needs of the body in general.

It is necessary, therefore, to inquire into the movements accompanying auricular systole. The key to them lies in the study of the auricular and ventricular musculature. The function of the musculi pectinati of the auricle has been neglected. In the human heart they are fifteen to eighteen in number, and from 1 to 2 mm. in diameter. They take origin from the right tænia terminalis, and end in the musculature of the auricular canal in the A-V groove. The tænia terminalis is a fixed point through the venous mesocardium; therefore when the musculi pectinati contract, they are drawn towards the fulcrum, the ventricle being also drawn up at the same time. It will therefore be seen that this movement which empties the auricle at the same time draws the ventricle over its load. There is therefore in auricular systole a movement of the A-V groove towards the venous base of the heart. This function of the musculi pectinati has been well demonstrated by injecting warm wax into the auricle, the casts so obtained showing that the musculi pectinati shorten to quite half their diastolic length during systole (Keith). In hearts from cases of back pressure there is great prolongation and hypertrophy of these muscles. Now an anatomical axiom is that every muscle in the body has its opponent, the opponent in this case being part of the inner longitudinal layer of muscle of the right ventricle. Inspection of the ventricle will show two layers of muscle—an inner longitudinal and an outer spiral layer. The longitudinal layer can be divided into two systems—(1) That to the auricle or venous base; (2) that to the aortic exit or arterial base. The significance of the system to the arterial base is perhaps at first not quite apparent. According to Keith, its function is to act with the spiral fibres in rendering the apex a fixed point. The spiral fibres will tend by

their contraction to lengthen out the ventricle; the longitudinal layer from the arterial base will tend by their contraction to shorten it. Between them, therefore, they render the apex a fixed point. The apex thus being fixed, the force of their combined contraction is to empty the ventricle of its contents. The significance of the longitudinal layer of trabeculæ to the auricle is quite clear. This layer is the opponent of the musculi pectinati of the auricle. The apex being a fixed point, its contraction in ventricular systole draws down the A-V groove towards the apex. By the action, therefore, of these opponent sets of muscles in the auricle and in the ventricle, the well-known to-and-fro movement of the heart at the A-V groove is executed (A, B, Fig. 4). It should be noted that this movement of the A-V groove towards the apex in ventricular systole expands the auricle and at the same time produces therein not only more room but also a negative pressure facilitating the flow of blood thereto.

During joint diastole two things happen—(1) The base of heart replaces itself owing to the relaxation of the ventricular fibres; (2) the ventricle opens out to fill with blood. A glance at the tracing of the jugular pulse given on page 88 will reveal these movements of the auricle and ventricle during the cardiac cycle. The positive wave *a* takes place during auricular systole; the fall *v* is due to the contraction of the ventricle inducing the negative pressure in the auricle; lastly, during diastole there is, first, a rise due to the reposition of the A-V groove, and secondly, a fall owing to the relaxation of the ventricle.

Thus far the right side of the heart has occupied our attention. The manner in which the left auricle acts is more obscure, and has had far less attention paid to it. It is situated between the roots of the lungs, being firmly attached to each. By this means it is bound down in the unopened thorax to the chest wall. Behind it are the unyielding structures of the posterior mediastinum. Above, too, are unyielding structures, the pulmonary arteries and bronchi; to the latter and to the trachea the upper border of the left auricle is firmly bound.. There is left, therefore, only (*a*) the anterior surface in contact with the ascending aorta, and (*b*) the floor in contact with the left ventricle. Anatomical evidence, therefore, points to the fact that in systole of the left auricle the anterior wall moves backwards and the ventricle upwards. The former movement would involve a backward movement of the

aorta also, and it seems probable that in auricular systole the beginning of the aorta swings back and to the right, while in systole of the ventricles it moves forwards and to the left. Absolute physiological evidence of this movement is wanting, but Keith has pointed out :—

(1) That with the heart in situ, if the auricle be filled with injection of wax, the aorta is pushed forwards and recedes when it is emptied.

(2) In mitral stenosis and cases where the left auricle is dilated the aorta is pushed forward.

(3) No other movements are available on anatomical considerations.

(4) There is a portion of the pericardium so arranged as to act as a bursa for this movement.

(5) The attachment of the musculature of the interauricular septum is such that its only action can be to serve in this movement.

Considering the musculature of the left auricle in more detail, we find that, unlike the right auricle, there are no pectinate muscles. This is due to its being developed as mentioned above, mainly from the auricular canal. The place of the pectinate musculature is taken by a series of muscular bands (Fig. 5) which are inserted into the inferior vena cava, and through it into the pericaridum and diaphragm. Chief of these bands is the left tænia terminalis (*h*, Fig. 5) which, arising in front at the superior vena cava, sweeps round to the left in the anterior wall of the left auricle, and turns down between the auricular appendix and left pulmonary veins, to end in the inferior vena cava. Above and laterally the left auricle is attached to the roots of the lungs by the pulmonary veins and the fibrous venous mesocardium (xx, Fig. 5). The musculature of the left ventricle is essentially the same as the right. The outer spiral fibres (Fig. 5) and the inner longitudinal system again render the apex a fixed point. The opponent to the auricular musculature is the longitudinal system passing to the auricular part of the A-V groove. There is therefore the same to-and-fro movement here—the auricular musculature in auricular systole draws the ventricle up (from A—A′ Fig. 5), while by ventricular systole the A-V groove is drawn from A′—A, thereby expanding the left auricle and causing a negative pressure. There should therefore be a rapid flow of blood from the lungs to the left auricle during ventricular systole, but

there is no very positive evidence of this point, although the tracings of the cardio-pneumatic movements appear to indicate its presence.

From anatomical considerations, therefore, we come to the conclusion that the excitatory wave in its passage through the heart travels from the parts representing the venous end of the primitive cardiac tube to those developed from the arterial end. If this be the case, evidence of this passage should be forthcoming from the records obtained by different observers in regard to the electromotive phenomenon of the beating heart. Considerable discrepancy, however, appears in such records. Waller and Reid found in several mammalian hearts that the excitatory wave normally passed from apex to base. Bayliss and Starling, on the other hand, observed the wave to pass normally from base to apex, and only in the injured heart to pass in the reverse direction. Schlüter's experiments on the cat's heart appear to support Waller and Reid.

In view of this divergence of opinion the recent valuable work of Gotch upon the frog's heart is of great interest. His records distinctly show that it quite depends upon which part of the base of the heart the electrodes are placed as to what form of curve is obtained. Normally, however, he is convinced that the excitatory wave passes from the venous base of the ventricle to the apex and thence to the aortic base in connection with the great arterial trunks. Gotch's results also show that a high intracardiac pressure brings into prominence the action of that part of the ventricle leading up to the aorta. This is therefore important confirmatory evidence of Keith's view of the action of the different sets of muscles in the ventricle.

When, too, we realise how small an area the A-V bundle in the mammalian offers to the electrode, it is easy to understand that contradictory results should be obtained for the mammalian heart. There is every reason to suppose, therefore, that in the mammalian heart also the excitatory wave follows the direction of the primitive cardiac tube, and passes from the venous base to the apex, and thence back to the aortic base, ensuring thereby an orderly sequence of movements. More work is wanted to elucidate these movements and also many other points, the importance of which lies in the fact that "the heart . . . is the beginning of life; the sun of the microcosm; . . . it is the house-

hold divinity which, discharging its function, nourishes, cherishes, and quickens the whole body, and is indeed the foundation of life, the source of all action" (Harvey).

BIBLIOGRAPHY

General Reviews with Extensive Literature—

Burdon Sanderson, J., Schäfer's Text-book of Physiology (1900), vol. ii. p. 439.

Gaskell, W. H., Schäfer's Text-book of Physiology (1900), vol. ii. p. 169.

Heinz, R., Handbuch der exp. Path. v. Pharmakol., vol. i. p. 638. Gustav Fischer, Jena, 1905.

Hoffmann, F. B., Nagel's Handbuch der Physiol. des Menschen, vol. i. p. 222. Braunschweig, 1905.

Langendorff, Ergebnisse der Physiol., Abth. II. (1905), p. 764.

Papers—

Carlson, American Journ. of Physiol., xii. p. 67.

Erlanger, Journ. Exp. Med., viii. p. 8.

Fredericq, Archives Intern. de Physiol., iv. p. 57.

Gotch, Proceedings of the Royal Society, B, Vol. 79 (1907), p. 323.

Heidenhain, M., Anat. Anzeiger, xx. (1901).

Hering, Pflüger's Archiv., cviii. p. 267.

Humblet, Archives Intern. de Physiol., i. 278; ibid., iii. p. 330.

Imchanitsky, Archives Intern. de Physiol., iv. p. 1.

Keith, Journal Anat. and Physiol. xlii. p. 1.

Keith and *Flack*, Lancet, August 11, 1906; Journal Anat. and Physiol., xli. p. 172.

Stassen, Archives Intern. de Physiologie, iii. p. 338; v. p. 61.

Schmidt-Neelsen, Archives Intern. de Physiol., iv.

Tawara, Das Reizleitungssystem das Säugetierherzens. Gustav Fischer, Jena, 1906.

PULSE RECORDS IN THEIR RELATION TO THE EVENTS OF THE HUMAN CARDIAC CYCLE

By THOMAS LEWIS

THE study of the arterial pulse in man has occupied the attention of physiologists and physicians for centuries. With the advent of the graphic method, it yielded, at the hands of such investigators as Marey ([33a]), Landois ([31]), Mosso ([38]), and a host of other workers, results which have greatly enhanced our knowledge of the human cardiovascular system. Not infrequently it has served to stimulate research on problems of general and far-reaching physiological significance, and in some instances has contributed facts to our knowledge of the heart and arteries which it would have been difficult to obtain from experiments on the lower animals. The study of the human pulse carries with it a natural advantage, which can hardly be overestimated; the subject of experiment may be observed under normal conditions, and is amenable to reason and more perfect control.

The examination of the individual curves of arterial sphygmograms, upon which an incalculable amount of labour has been expended, is, with the exception of a few instances, abortive in yielding such information to the clinician as can bring him a profitable return for the time he expends. Empirical diagnosis from pulse tracings is a method fraught with abundant and dangerous pitfalls. It is for the evidence which the curves give of the events of the cardiac cycle that they are to be chiefly valued, and it is in this direction that the researches of modern, nay recent, years have yielded such fruitful results. *Above all, graphic curves taken simultaneously from different pulsating points are invaluable, for they accord information of the time relations and nature of the contraction of the separate chambers of the heart.* The observations of the past ten years, while supplying important physiological know-

ledge, bid fair to revolutionise the technique of cardiovascular diagnosis.

Records can be obtained of the contraction of both auricles and both ventricles in a large percentage of subjects. In certain conditions the information so derived is of great service, for a particular chamber may fail to contract, its contraction may be imperfect, or it may enter upon its systole too early or too late. Many irregularities of the heart have already received careful analysis along these lines, and knowledge of much clinical importance has been gathered in respect of them. In regard to one affection of the heart, the pathological state now known as "heart block," in which the path of conduction from auricle to ventricle is disturbed or broken, and in which a slow pulse and its concomitant symptoms constitute the chief features of the disease, a flood of light has been shed upon a condition of which our ignorance was formerly profound. As to the therapeutic action of cardiac drugs, much work has been accomplished, and more remains to be done. A wide field for study has been opened up which awaits careful and painstaking investigations; and the day, it is hoped, is not far distant when the functions of the heart, and the disturbances of the same, will be profitably referred to at the bedside, in the terms employed by Gaskell in his well-known researches.

But the study of pulsations in man can never reach that pitch of mechanical perfection to which modern physiological experiment has attained, and the conclusions drawn from the more indirect observations on man must ever remain in a measure subservient to, and controlled by, the more direct readings acquired from animals. That emphasis should be laid upon this aspect of the question is imperative, for there is a tendency to-day, frequently noticeable in the consideration of human pulsations, to fly in the face of physiological knowledge, which, as it is unquestionably of less fallacious origin, should guide, and form the basis of, all conclusions.

In the following pages the methods recently introduced for the study of the cardiac cycle in the normal subject will be examined; a critical account will be given of the records obtained in man; and the information so obtained will be compared and brought so far as possible into line with the correlated knowledge

derived from the lower animals. In bringing together physiological facts which may serve as an introduction to their clinical application, pathological observations may be quoted only in so far as they have a direct bearing on the several problems involved. At the same time it must be noted that the boundary between the physiological and pathological states has ever been broad, and that so far as cardiovascular studies are concerned, recent observations have tended to its extension rather than to its limitation. For the older conception of pulse irregularities as evidence of the pathological state is no longer justified. Apart from the irregularity, chiefly in the length of diastole, which, occurring as an accompaniment of the respiratory movements, and dependent upon vagal influences, is so familiar to physiologists, a closely allied irregularity, termed by Mackenzie ([32b]) the "youthful irregularity" (p. 84),[1] has been described as a normal event which occurs at or about that epoch when the pulse diminishes in rate and the heart takes up the rhythm which it will maintain within narrow limits during adult life.[2] Further it must be recognised that spontaneous ventricular contractions[3] are of common occurrence from time to time in individuals in whom no further evidence of ill-health is available. These "extrasystoles," though incompatible with our view of a heart functionating in an ideal fashion, may be regarded with justification as consistent with the indefinite borderland which lies 'twixt health and disease. The frequency of their occurrence, in the otherwise

[1] References to pages and figures allude to the bibliography, except where otherwise stated.

[2] Some of these irregularities are undoubtedly anomalous responses to respiration (cp. Hering [23b]); but it is equally beyond dispute that others have no connection with breathing.

[3] It is now generally acknowledged that the ventricular systole results from a conducted stimulus proceeding from the auricle. But it is also recognised that the ventricle may beat when this source of stimulus is removed. If at any time this chamber contracts independently of the auricle, such a contraction may be termed spontaneous. The origin of the stimulus giving rise to a contraction of this nature is as yet imperfectly understood. There is reason to believe that it arises in embryonic remains to which the function of rhythmicity is particularly attributed. But for a further and fuller account of these autochthonous ventricular beats, or extrasystoles as they are frequently designated, the reader is referred to the works of Mackenzie ([32b, d]) and Wenchebach ([49]). (The term "extrasystole" is here employed in its broadest sense.)

normal subject, over long periods, and more especially in association with pregnancy, hard toil, or advancing years, brings them into a domain, closely approaching, if not included within that of physiology.

Marey and his associates; Chauveau ([6, 7]) and François-Franck ([11]), were amongst the chief pioneers of graphic records. The collected observations of Marey, published in his books of 1863 ([33a]) and 1881 ([33b]), are comprehensive. In *La circulation du sang*, &c., are found records of almost all visible pulsations of the normal human body. Numbers of tracings taken from the healthy or diseased, experimental observations, and records of apparatus combine to form a rich storehouse of facts, never equalled before or since, for the study of hæmodynamic problems. The apparatus figured, and employed in the experiments, show an almost unrivalled wealth of ingenuity, and many of the instruments in their original or slightly modified forms are still in general use.

The methods of sphygmography are too well known to need description. Sphygmographs fitted with additional levers are numerous, and serve in the procuration of simultaneous tracings from apex beat, arteries, jugular vein, liver, fontanelle, or chest wall. The mechanism used in clinical work upon the jugular pulse, the apparatus with which we are chiefly concerned, is described later. The best receiver for cardiographic records is perhaps Marey's, consisting essentially of a cup, covered by a rubber membrane to which a button is attached. But a hollow uncovered receiver answers well for general purposes, and may be employed over a less restricted field.

In animals the earliest work on intra-auricular and intra-ventricular pressures was carried out by Marey's school. Small rubber balloons tied over the extremities of narrow metal sounds were passed through jugular vein or aorta into the corresponding chambers of the heart, and records of the pressures within these cavities were obtained by connecting the metal tubing to tambours supplied with levers and writing styles. It might be supposed that the introduction of such sounds into the auricle or ventricles would seriously interfere with their normal functions. This, however, is not the case. Chauveau relates that he passed a double cannula of the sort, fitted with balloons for auricle and ventricle, into the right heart of a horse, without disturbing the pulse rate, or the meal of which the animal was at the time partaking (*Assoc. franç. p. l'avanc. d. Sciences*, 1887).

The apparatus used by the earlier workers for the actual records

has undergone improvement. Many instruments have been introduced, amongst which those of Hürthle require special mention. The inertia of the levers and membranes is reduced in Hürthle's instruments ([26c]) to an almost negligible quantity. Air is replaced by fluid transmission, for the compressibility of air renders it less reliable in obtaining records free from extraneous movements. The delicacy and reliability of Hürthle's instruments have been demonstrated by Bayliss and Starling by a photographic method ([3]). Hürthle's differential manometer is so constructed that two columns of fluid, each conveying the changing pressures of a pulsating cavity, are opposed to each other. Any difference in pressure in the two cavities is thus registered, and the instrument is of particular value in ascertaining the instant at which the pressures in two adjoining and communicating cavities, such as auricle and ventricle, or ventricle and aorta, become equal. It is with this instrument that information has been obtained in respect of two "standard movements" of the heart, namely, the opening of the auriculo-ventricular valves and the closure of the semilunar segments. The standard movements, to which further reference will frequently be made, are of importance; they may be regarded as fixed points of time, and it is convenient to describe and figure all other cardiac movements, and oscillations to which these cardiac movements give rise, in relation to them. The third standard in common use is the commencement of ventricular systole, or perhaps more accurately, the moment at which the pressure in the ventricle commences to rise in systole. The onset of systole is an instant which it is not difficult to fix in animal experiments; but in man, as will subsequently be seen, it is by no means so easy. It is possible that with the further elaboration of Einthoven's recently introduced electrical method [1] more accurate indications may be obtained. Einthoven uses a sensitive "string galvanometer" to estimate the change of potential in the limbs, which occurs with the heart beat. The observations, however, which have as yet been made, have little bearing upon the subjects of this article.

In conclusion, the attempts instituted to obtain graphic records of the heart sounds may be briefly referred to. Einthoven and Geluk ([9]) employed a microphone and capillary electrometer. Hürthle ([26b]) also used the microphone for a similar purpose. Observations which are referred to in the text have thus been carried out on the instants of onset of the first and second sound; but given more

[1] *Archives Internat. de Physiologie*, vol. iv., 1906–7, pp. 132–164; *Archiv. f. d. ges. Physiol.*, Bd. 122, 1908, s. 517–584.

convenient and reliable instruments, many problems of no inconsiderable clinical significance would receive elucidation. There is no question that by assiduous training a clinician with keen perceptive faculties may acquire great skill in timing and interpreting abnormal heart sounds. Yet the dogmatism of the present day upon the subject of heart murmurs is entirely unjustified, a conclusion which is completely borne out by the inconsistent yet equally peremptory opinions of independent observers of the same subject. Franck [1] in a preliminary communication has recently described a new instrument, based on the principle of the middle ear, with which graphic records may be taken. Einthoven [2] has successfully used his galvanometer for the same purpose. Further results are awaited with expectancy, for there is every possibility that the apparatus may supply a long-felt want.

I. The Ventricular Cycle and the Standard Movements

The interpretation of the time relations of the human ventricular movements at present [3] depends on cardiographic tracings, complex curves involving changes of pressure, volume and diameter in the left ventricle, and the errors emanating from this method must constantly be borne in mind. It is probable that the shock of the apex beat gives in thin-walled chests a fair approximation of the onset of systole, with an error which, though difficult to state accurately, probably does not exceed ·02 sec.[4]

[1] Otto Franck, *Münchener mediz. Wochensch.*, Bd. 51, 1904, s. 953. Weiss and Joachim (Pflüger's Archiv., Bd. 123, 1908, s. 341) have more recently succeeded in obtaining numerous records of heart sounds and murmurs which appear to be of considerable value.

[2] Pflüger's Archiv., Bd. 117, 1907, s. 461.

[3] Eventually it will probably be controlled by electric curves.

[4] In one of Hürthle's tracings ([26b]) (Fig. 7) there is an exceptional difference of ·06 sec. between the upstroke of the cardiogram and the registration of the first sound. In animals the tracings of Chauveau and Marey ([7]), Roy and Adami ([43]), Hürthle ([26a]), and most other writers show the upstroke of ventricular pressure and cardiogram to be synchronous; but such tracings are taken under exceptionally favourable circumstances.

TABLE I

Author	Auricular Systole.	Auricular Systole to Ventricular Systole. The $A_R V_S$ Interval.	Presphygmic Interval.	Period of Rising Arterial Pressure.	Plateau.	Postsphygmic Interval.	The Pause.	Pulse Rate.	Remarks.
Landois [31], 1872	...	·17	·085	·088	·085	...	·400	55–65	
Mosso [38], 1879	...	...	·06	...	...	...	...	...	
Edgren [8], 1885	...	...	·093*	·099	·135	·05	·484	70	* Probably includes transmission from aorta to carotid.
Keyt [29], 1887	...	...	·055	·268		·540		70	From tracing on p. 60.
Martius [34], 1888	...	...	·08	...	...	...	...	...	
Hürthle [26b], 1895	...	...	·02	...	...	...	...	...	
Erlanger [10], 1907	·1	·14	·16		·24	·06	·32	66	From defective chest wall.
Rautenberg [42b], 1907	...	·1 to ·18	...	...	...	...	...	...	From Minkowski's œsophageal tracings.
Young and Hewlett [50], 1907	...	approx. ·1	...	...	...	...	...	...	Œsophageal tracings.
Tigerstedt [47], 1908	...	+ ·1	·051	·254		·445		80	From defective chest wall.
Hürthle [26a] (for dogs)	...	...	·027	·03	·18	·06	·38	90	From Taf. III., Fig. 12.

TABLE II

Author.	Delay from Aorta to Carotid.	Delay from Carotid to Radial.	Velocity, Carotid to Radial.	Velocity, Aorta to Radial.	Velocity, Aorta to Carotid.
Landois . . .	...	...	...	5·7 m.p.s.	...
Mosso . . .	·02	...	...	...	...
Keyt	·0279	·0797	7–9 m.p.s.	...	...
Edgren . . .	·026–7	·0792	...	8 m.p.s.	...
Grünmach [20] . .	·03	·06	...	9 m.p.s.	6·6 m.p.s.
Martius . . .	·03	...	...	...	...
Hürthle [26b] . .	·03	...	...	...	6 m.p.s.

The terms employed in Table I. require brief definition. It must not be forgotten that the curves of intra-ventricular pressure cannot be taken as indicative of the changes in the volume of the ventricular blood content. When the ventricles contract and the pressures in them augment, their blood content remains unchanged, for no blood leaves them until the pressures rise to aortic and pulmonary pressure. The interval which elapses in this way, prior to the raising of the arterial valves, constitutes what is termed the "presphygmic" interval. But the pressures in the arteries begin, and those of the ventricles continue, to rise subsequent to this interval; this continued rise in the ventricles is consequently spoken of as the "period of rising arterial pressure." Following upon it is the plateau, indicated in the pressure curve by a wavy line, which runs horizontally, or slopes slightly upwards or downwards. During the whole of this plateau the volume of the ventricles is decreasing and blood is leaving them; but as it leaves them at a lessened rate, it does not, necessarily, further raise the arterial pressures.

At the end of the plateau, the pressures in the ventricles fall, and when they are reduced below the arterial pressures, the pulmonary and aortic valves close. It is, however, a little while before the pressures fall sufficiently to allow the auriculo-ventricular valves to open, and this interval is often spoken of as the "postsphygmic" interval. Following upon it there is a pause, during the whole of which the

ventricles are expanding and receiving blood from the veins and auricles. The term ventricular diastole is usually loosely applied, and has been avoided in the table; we have not sufficient knowledge of the period over which the ventricles are expanding actively, if they ever do so, to define the time limits of diastole with precision.

In referring to the accompanying tables mention must be made of observations recently carried out by Erlanger ([10]) and Tigerstedt ([47]), the results of which are included. The estimates were made from subjects in whom there were partial defects of the chest wall and in whom the heart was readily accessible. The figures are probably as accurate as any we possess; Keyt's numbers ([29]), dependent on numerous and elaborate measurements, compare well with them. The figures given in the first table are taken as far as possible from young adult subjects, and the delays and velocities exampled in the second table are illustrative of normal pulse rates. Some figures from a tracing after Hürthle ([26a]) (Taf. III., Fig. 12) are also given for the comparison of man and the dog. No such estimates are absolute; there is a wide variation with numerous factors, such as pulse rate and blood pressure.

But though eventually the cardiographic upstroke is the standard movement on which the chief measurements are based, in clinical practice the frequent absence or inversion of the apex beat renders it unreliable, and it becomes necessary to fix further standards. For this purpose the carotid pulse is chosen as the safest and most useful guide. Its utilisation involves under many circumstances a calculation of the presphygmic interval, and the normal transmission delay of the pulse wave from the semilunar valves to the carotid. In the normal subject the presphygmic interval may show variations of at least ·03 sec., with age, pulse, rate, &c. In disease it may amount to as much as ·06 sec. *In clinical application*, in which relatively slow travelling recording surfaces are used, an error of less than ·05 sec. is as a rule negligible, *and the figure ·05 sec. may be taken as a comparatively secure working estimate of the presphygmic interval.* The error entailed in calculating the transmission delay from aorta to carotid is probably not greater than ·01 sec. in health and ·03 sec. in disease; the interval may be taken for clinical purposes at ·03 sec.[1]

[1] Weiss and Joachim have recently measured the interval between the first heart sound and carotid pulsation in man (Pflüger's Archiv., 1908), and find it as a rule ·08 to ·09 sec.

When jugular tracings are taken simultaneously with a standard movement, the radial pulse is usually employed on account of its convenience. This method involves a third error, the variation in transmission delay from the aorta to radial vessel. The variation in this delay is so great, and the accumulated error becomes so magnified, that it is unsafe to fix the radial pulse as the standard movement if the carotid to radial delay is not first estimated and allowed for in the particular case.[1]

The determination of the position of closure of the semilunar valves (S.C.) and of the opening of the auriculo-ventricular valves (A.O.) upon human cardiographic and carotid curves presents considerable difficulties.

In animals it is now held that the S.C. point occurs a short distance along the downstroke of intra-ventricular pressure (Hürthle ([26a]), Porter ([39]), Bayliss and Starling ([3]), &c.). This point is found in simultaneous tracings to correspond on the aortic curve to the bottom of the dicrotic depression (aortic notch); [2] on the carotid tracing, which is slightly delayed, it falls at or about the beginning of the same depression. On the cardiographic curve it corresponds in animals to a point near the end of the ventricular plateau; thus Marey ([33b]) (Fig. 40) places it before the end of the plateau, Hürthle's tracings ([26a]) show it before or slightly after the end of the plateau. To sum up, there is no constant relationship between cardiographic and intra-ventricular curves at this phase.

In man the S.C. point is placed by Edgren ([8]) at the bottom of the cardiographic downstroke, at a point indicated by a small wave. According to Hürthle ([26b]) it is situated in the first third of the downstroke, and it is placed at the same instant by Einthoven and Geluk ([9]), despite the fact that they were guided by the record of the second sound, which occurs later than the closure. The method in which the second sound is marked on the tracing by a signal worked with the hand, allowance being made for reaction time, is obviously unreliable and gives varying results (cp. Edgren's

[1] The figures given and statements made are the result of a critical examination of a large number of statements and tracings. The space at our disposal prohibits a full examination of the facts. There is a good deal of divergence between the figures given by different authors, and further work giving more detailed analysis would be of much value, for at present general statements are of necessity very approximate.

[2] Porter and Hurthle.

tracings). As the cardiographic curve in its relationship to the second sound in man shows no constancy, and as it shows a similar divergence when compared at this phase to the carotid curve,[1] it cannot be regarded as a safe criterion in fixing the S.C. point. The constancy of the relationship of the S.C. point to the aortic curve in animals shows the necessity of taking the carotid curve as the standard in man. The nearest approach to accuracy is obtainable by allowing for the transmission time from aorta to carotid. The S.C. point in man is thus fixed at a point ·03 sec. in advance (to the left in Fig. 1 of this article) of the bottom of the dicrotic depression.

The actual determination of the A.O. point in man is impossible. In animals most writers are agreed in placing it at the bottom of the intra-ventricular downstroke.[2] On the aortic curve it is marked at the summit of the dicrotic (Porter, Hürthle, Bayliss and Starling). Cardiographic curves show no constant relationships at this phase. In man the A.O. point is best fixed on the carotid tracing, ·03 sec. in advance of the summit of the dicrotic wave. It is to be noted, however, that this introduces a possible source of fallacy. Galabin[3] states (15) that the dicrotic summit recedes from the apex of the primary wave as the pulse travels along the vessels. The error from this alteration is probably so small as to be quite negligible in the carotid tracing, but it constitutes an important element in radial tracings, which should therefore never be employed in estimating this point, in exact work. *It must not be forgotten that the A.O. point in man is the most difficult of all the standard movements to ascertain; conclusions drawn from it must always be received with due caution.*

II. The Relationship of the Auricular and Ventricular Cycles

(*a*) **The Evidence obtained from Intra-auricular Curves in Animals.**—The events of the auricular cycle have received

[1] Thus in Keyt's tracings the bottom of the cardiographic downstroke corresponds on the carotid to the bottom of the dicrotic depression, or to a point on the upstroke of the dicrotic itself. In Edgren's tracings, as in Hürthle's, it is placed as a rule at the bottom of the depression; but there is very considerable divergence in the individual curves of these authors.

[2] Estimated by differential tracings.

[3] The statement of Galabin is supported by many of the tracings which Keyt gives. The question is discussed by Frey (*Untersuch. d. Pulses*, 1892).

careful investigation at the hands of Chauveau and Marey, D'Espine,[1] Fredericq ([12a]), Frey and Krehl ([13]), and Porter. Recently Hering ([23a]) has studied the same subject, using the perfused heart; and further observations have been made by Rautenberg ([42c]). For the most part the experiments have been on dogs; those of Chauveau and Marey were carried out on the horse.

The curves given by Porter are perhaps as much in accord with the general evidence as any, and it will be found convenient to take these as typifying the changes in intra-auricular pressure, eventually examining the results of experimental work in relation to such a type. In common with all other observers Porter found that auricular contraction is accompanied by a positive wave of pressure. At or a little before the termination of auricular systole this "first positive wave"[2] gives place to a "first negative wave," a wave which, but for the interposition of the "second positive wave," forms with the "second negative wave" the main depression of auricular pressure during the cycle. (A curve illustrating the waves and their relation to the curve of intra-ventricular pressure is given in the accompanying figure, Fig. 1). The second positive wave, which breaks this otherwise steady fall, is said by most writers on the subject to occur at the onset of ventricular systole, and is usually figured as lasting until the point which marks the opening of the semilunar valves.[3] The wave is well shown on the tracings of Chauveau and Marey, D'Espine, Fredericq, Porter, and Rautenberg, but it is absent from those of Frey and Krehl. Porter (p. 526) noted its absence on occasion. Fuller details of its significance will be discussed later. Relaxation of the auricular wall is stated by Porter to last to the beginning or end of this wave. The point at which the second negative and "third positive waves" meet is at present the subject of considerable discussion. Chauveau and Marey placed it at the end of ventricular systole,[4] but otherwise there appears a consensus of opinion,

[1] Cited by Fredericq ([12a], p. 524 and Fig. 19).

[2] In the auricular tracings given by Porter there are in all three main elevations and three main depressions. The terminology of the curves is at present so confused that the employment of Porter's original designations is impossible. In the following pages the rises and falls will be spoken of as the first, second, and third positive, and the first, second, and third negative, wave respectively.

[3] A point estimated by means of differential manometer tracings (Hürthle and others).

[4] In the tracing given in the *Gaz. méd. d. Paris*, 1861, p. 673, the second positive wave is not shown, and the third positive wave commences during the systolic

amongst those who have taken auricular pressure curves, that it occurs earlier (Frey and Krehl, Fredericq, Porter, Hering, and Rautenberg). While it may probably be placed with a fair degree of certainty in the middle or last third of the systolic plateau, there is every possibility that it is subject to variation. The third positive wave ends in the "third negative wave" during ventricular relaxation. Generally the point is given at the bottom of the falling ventricular curve, the instant at which is placed the opening of the auriculo-ventricular valves.[1] Porter himself figures it at a slightly earlier time interval,[2] at a position in the cycle recognised as representing the closure of the semilunar valves, namely, a short distance after the end of the systolic plateau.

(*b*) **The Venous Pulse in Animals and Man.**—Pulsation of the veins of the neck in pathological conditions is often such an obvious phenomenon that it must have been recognised for many centuries. References to venous pulsation can be traced in the writings of Lancisi ([30], p. 182) and Morgagni ([36]) in the early and middle years of the eighteenth century. In 1794 Hunter described pulsation in the veins of a dog; but it is questionable if these writers appreciated the extent of the movement; their observations appear to have been confined to the veins in the immediate neighbourhood of the heart. Later, similar movements were described by Weldemeyer ([48]) in the veins of a horse.[3] Friedreich ([14]) took venous curves from the neck of pathological subjects in 1865; and two years later Potain ([40]) obtained simultaneous tracings of the apex beat, carotid, radial and jugular pulses in the normal human subject, and his description of the events and his interpretation of them are, in the light of our present knowledge, wonderfully accurate. From the time of Potain's contribution, observations have been published by many writers, amongst whom may be mentioned, Mosso, Gottwalt ([19]),

plateau; the tracings repeated in Marey's book show the second positive wave, and the third positive wave occurs at the close of systole. The collected curves given by Chauveau in 1887 (*Assoc. franç. p. l'avanc. d. Sciences*) are very various, but as a rule show the three chief waves distinctly.

[1] The point is estimated by differential pressure tracings.

[2] Porter's curves were from the left auricle, and show, like most others, some variation in their last phases.

[3] For full historical accounts the reader is referred to Mackenzie's earlier papers, and the recent publication of Baum ([2]).

Riegel ([41]), and François-Franck ([11]). In 1893–4 Mackenzie ([32a]) published his first papers, which, with his collected observations on "The Study of the Pulse," appearing in 1902, have given the impetus to a careful investigation of the whole subject.

Pulsation in the veins of animals is not confined to the larger vessels feeding the auricles; it is a constant phenomenon in dogs, cats, and rabbits, and may be seen extending in many of them into the smaller veins of the neck and limbs. Gottwalt was of opinion that the jugular veins of all normal persons pulsate, and this conception is receiving constant confirmation. *It is possible at the present time to obtain venous records from the neck of a large percentage of normal individuals;* Wenchebach states that it is feasible in most subjects, healthy or diseased. Pulsation is frequently so well marked as to be visible, and in thin or anæmic subjects often constitutes an obvious movement. It is highly probable that with improved apparatus curves will be invariably obtainable.[1] Any agency which tends to promote a heightened venous pressure, such as raised intra-thoracic or abdominal pressure, or gravitation, increases the force and visibility of venous pulsation. It is for this reason that tracings are best taken in the reclining posture, and that in those cases, where pulsation is feeble, expiratory suspension of respiration increases its prominence.

In man, the venous pulse is seen and recorded with the greatest facility in those veins which have but a short distance to travel before reaching the heart. A special and valuable anatomical description of the veins of the neck in relation to this subject has recently been given by Keith ([28]). Tracings may be taken direct from the external jugular vein when this is engorged, but more often the receiving instrument must be applied to the jugular bulb, which lies a little above and 25 mm. external to the sternal end of the clavicle.[2] A needle passed back into the neck at this point strikes the internal jugular vein at a point where it is guarded by a pair of valves, which, when the path to the auricle is obstructed, or when blood is regurgitated, produces a bulging in the vessel from which the "bulb" derives its name. Passed further on the needle transfixes the subclavian artery. Tracings

[1] If they are not already.

[2] The receiver should be as a rule applied between the two heads of origin of the sterno-mastoid muscle.

are obtained from the neck, in which the sterno-mastoid is relaxed, by applying to it with light pressure a small receiver, whose width is about 4 cm., and depth 1 cm.[1] The interior of the shallow cup communicates with a delicate tambour carrying a writing style. This simple apparatus is perhaps the most satisfactory as yet employed. The accuracy of its records has been checked by Mackenzie, its originator, and by Gerhardt, by comparisons with the tracings given by light levers directly attached to the skin overlying a superficial vein; and the movements of the recording tambour and lever, so far as the main waves are concerned, have had their reliability checked by comparison with the tracings yielded by a Hürthle manometer (Gerhardt). Air transmission is employed, and the curves obtained from the jugular bulb are frequently complicated by the primary wave of the carotid pulse, which in clinical work is not without its advantages, and by the respiratory movements when these are present. Curves are best obtained from the right side of the neck, for here the course of the innominate is shorter and more direct from neck to heart (Friedreich, p. 282); clinically they may also be taken from the pulsating liver.

With regard to the rest of the mechanism little comment is necessary; when the apparatus described is adjusted to a modified Dudgeon sphygmograph, as in Mackenzie's original instrument, the fitting of a reliable time-marker renders it cumbersome. Another convenient instrument for clinical work is "Mackenzie's ink polygraph,"[2] with which tracings of any length and at various speeds may be taken. It allows a simultaneous record of any two given pulsations, and carries a reliable time-marker. The curves from the jugular vein give, considering the indirect methods of determining them, surprisingly constant results, and in this lies their chief justification.

[1] There is a tendency, not without its advantages, towards the use of smaller receivers.

[2] The apparatus, an account of which is published in the *British Medical Journal* for June 13, 1908, p. 1411, is open to improvement; more particularly the writing styles, and that portion of the mechanism used for the record of the radial pulse. The momentum of the levers and membranes is considerable, and extraneous movements cannot be entirely excluded. For the interpretation of the main waves it answers its purpose admirably, but for the investigation of the minor waves more delicate apparatus would be requisite.

It is necessary to insist on the disuse of time markers whose movement depends on the clockwork which drives the paper.

In animals curves have been secured from the vein wall or blood stream, by Gottwalt, François-Franck, Morrow ([37]), Fredericq ([12c]), Rautenberg ([42c]), and others. The results in man and animals are in such general agreement that one description of them will suffice.

Speaking broadly, the venous pulse, like the auricular curve, shows three main elevations and three main depressions;[1] the general outlines of venous and auricular curves are such as to leave no reasonable doubt that the factors ultimately concerned in the production of their waves are identical for each, a relation on which many writers have laid emphasis. The final evidence depends on the detailed analysis of each wave of the curves and will be undertaken subsequently. For the time being it will be convenient to recognise the three main elevations of the venous curve (the "a," "c," and "v" waves of Mackenzie) as corresponding to the three positive waves of the auricular pressure curve, and the three main dips of the venous tracing (the "x," "x′," and "y" depressions of Mackenzie) as corresponding to the three chief negative waves of the auricle. These events are represented in the accompanying figure (Fig. 1), and their relations may be tabulated as follows:—

"a"	First positive wave.
"x"	First negative wave.
"c"	Second positive wave.
"x′"	Second negative wave.
"v"	Third positive wave.
"y"	Third negative wave.

The waves of the jugular pulse have not received such an accurate comparison to standard movements as have the auricular pressures in animals. This is but natural, for with the indirect methods available the sources of error are comparatively large, and little advantage is to be gained by the use of more rapidly travelling recording surfaces. But writers are in the habit of expressing themselves dogmatically as to the time instants at which certain events are taking place, while at the same time they appear to lack a due appreciation of the comparatively rough methods by which the standard movements of the cardiac cycle are fixed in man. Cardiographic curves are notoriously uncertain,

[1] A record of the venous pulse is shown in Fig. 3, at the end of this article.

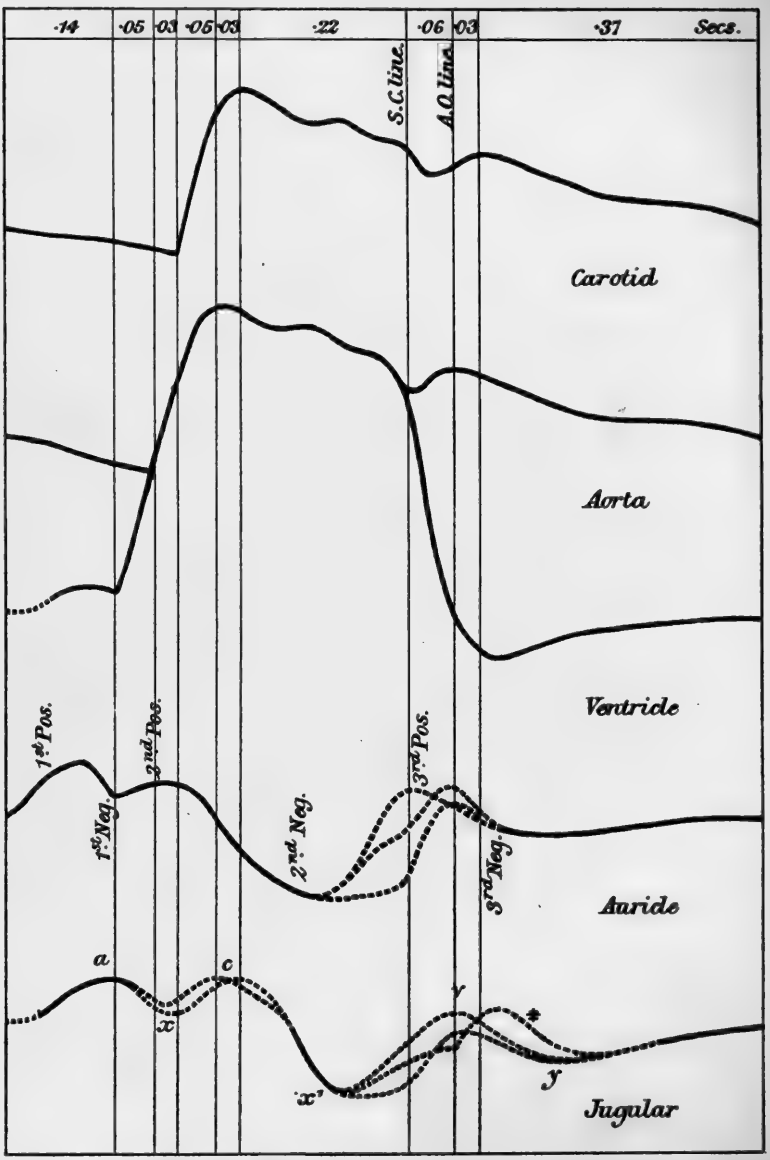


FIG. 1.—Diagrammatic representation of the events of the cardiac cycle and of the carotid and jugular pulses in relation to standard movements. The scale of abscissæ is 1 mm. to $\frac{1}{100}$ sec. S.C. = semilunar valve closure; A.O. = auriculo-ventricular valves open. The broken lines indicate those portions of the respective curves over which there is doubt or controversy.

and carotid tracings must be judged on their merits. The discrepancies in the findings are greater in the case of jugular curves than they are in the case of the auricular. Considerable confusion appears to exist as to the events occurring in that portion of the heart's cycle which lies between the closure of the semilunar valves and the opening of the tricuspids. Further work is needed, and the first appeal must obviously be to experiments upon the time relations of the venous curve in animals. But though there are differences of opinion, it must be understood that they are in the main of a minor character, and their complete elucidation is chiefly necessary that the origin of the waves may be accurately determined. The differences which have so far arisen are, in other words, of such a nature as to in no way invalidate the information which can be obtained at the bedside.

The majority of writers are agreed in timing the commencement of the "c" wave in man as synchronous or almost synchronous with the primary wave of the carotid at the same level of the neck. Fredericq ([12c]), moreover, has recently shown them to be simultaneous in the carotid and jugular of the dog. For practical purposes the two waves may be taken as starting together, but the actual evidence for their absolute synchronicity is perhaps not convincing. In certain instances Fredericq found a slight deviation, and Bard ([1b]) has obtained similar results in man.[1]

The "a" wave and "x" depression have together a duration of $\frac{1}{6}$ to $\frac{1}{5}$ sec. (Mackenzie, Gibson ([18]), and many other writers), and constitute the *a–c* interval. This *a–c* interval, the time distance between the beginnings of the waves representing the commencement of auricular and ventricular systole, is taken as a measure of the function of the heart in respect of the conduction of impulses from auricle to ventricle, and is of great clinical importance.

Over the relations of the "v" wave there is some difference of opinion, and this apparently for several reasons. In the first place, it shows considerable variation in form; it may show a division into two; it assumes an entirely new outline and new

[1] Bard's tracings ([1b]) are not beyond criticism. It is not expressly stated that the jugular and carotid curves were taken at the same level in the neck, and the deviation might be attributable to transmission delay. Professor Bard has recently published further notes ([1c]) on this subject. Bachmann has confirmed his results (*Amer. Journ. Med. Sci.*, vol. 136, 1908, p. 674).

time relations in conditions where there is engorgement of the right side of the heart. Secondly, different writers refer it to different standard events, which constitutes a wide source of error, and but rarely indicate the evidence from which the standards are derived. Thirdly, it is frequently impossible to be certain whether writers are referring to the actual time relations of the events, or whether a phase of the "v" wave is attributed to a particular ventricular movement. It so happens that a definite statement of the relationship of the "v" wave to a standard movement is not of common occurrence. The collected evidence as to the time relations in the normal subject is so involved that it is impossible to consider it in detail. It is held by the majority that the wave commences during the systolic plateau. Gerhardt [16] and Wenchebach consider that it is a purely diastolic event. Gerhardt times its occurrence with the commencement of the dicrotic wave; and Wenchebach finds it synchronous with a notch on the downstroke of the cardiogram. The evidence of the tracings of individual writers is nevertheless in favour of the view that the point of commencement is subject to variation, and that it may commence during the plateau or near its termination. Its termination in the "y" depression is universally stated to be synchronous with the opening of the auriculo-ventricular valves. The evidence for this last relationship does not appear to be so conclusive as one might expect from the statements made on the subject. Thus in Mackenzie's tracings the point as a rule corresponds to the bottom of the cardiographic downstroke,[1] while in certain of those of Wenchebach (as in Figs. 6 and 7 of his paper), it starts at a point distinctly later. A critical examination of the subject reveals many sources of fallacy, and the majority of tracings are taken on comparatively slow-moving surfaces, so that the error in marking the points is large. Later when œsophageal tracings are discussed it will be seen that the fixation of the "y" depression at the A.O. line involves an obvious discrepancy.

Other waves have been described on the venous tracing; a positive wave preceding the "a" wave (Gibson and Ritchie's sinous wave [18]); a positive wave between "a" and "c" (Bard's *accident inter-systolique* [1b]); a fourth positive wave following "v" (Morrow's second outflow wave [36b]). There is no unanimity of opinion on the subject, and these waves cannot be regarded as

[1] Or to the bottom of the dicrotic notch. Potain and Gottwalt agree.

fundamental and constant, or at present of any great practical significance. It would be premature and unprofitable to discuss them.

(*c*) **The Evidence obtained from Intra-œsophageal Tracings.**—By means of an œsophageal bougie, fitted with a small elastic balloon, tracings have been obtained from the heart, which are not without value. The auricular curves are from the left auricle, which lies in contact with the gullet. They are to be used with caution, for they suffer in a measure from the same defect as do cardiographic curves; it is not possible to say to what extent they are volume and to what extent pressure curves. Moreover they show considerable variation according to the level at which the balloon is placed (Young and Hewlett [50]). In dogs such tracings were obtained as early as 1888 by Fredericq, and recently Minkowski ([35]), Rautenberg ([42a-c]), Joachim ([27]), Young and Hewlett, and others have secured them in man. The tracings are in the main in fair agreement, and show curves similar to those of intra-auricular pressure in animals. Disagreement, however, has arisen over that portion of the curve representing auricular contraction.

According to the earlier observations, auricular contraction is indicated by a depression in the tracing, whereas Rautenberg ([42a]), in all tracings but one (Fig. 5), attributes a convexity to the same event.

Now cardiographic curves from the ventricles, when taken from any other point than the apex of the left ventricle, show a curve which is roughly an inverted picture of the intra-ventricular pressure. In one respect the picture shows no inversion, the auricular wave when present retains its intra-ventricular form. Briefly, those portions of the curve are inverted which are dependent on active movements of the ventricular wall. In the same way it would be expected that when intra-auricular and œsophageal curves were compared, those portions of the œsophageal curve would show inversion, which were independent of ventricular movements. The curves as interpreted by Fredericq, Joachim, and Minkowski fulfil this expectation; Rautenberg, on the other hand, finds as a rule no inversion of any part of the curve. As Hering states, it is difficult to understand how a contracting left auricle can raise the œsophageal pressure, at a point at which

this chamber is alone in contact with the gullet. Rautenberg has attempted to defend his position by taking tracings in animals from the œsophagus, simultaneously with others from the right auricle, the apex beat or jugular vein. But his tracings do not offer convincing evidence, and necessitate the assumption that the apex beat is long delayed, an assumption which is not borne out by the simultaneous tracings from apex beat and œsophagus. It must be admitted that the auricular contraction *may* give a negative curve, and if at the same time it is to be recognised that a positive curve may result, the possibility of intermediate types, half negative and half positive, introduces serious difficulties into the interpretation of the tracings. The same problem arises in the case of those curves obtained from the auricle through the chest wall. Erlanger's curves taken from the auricle, and already referred to, show the auricular waves inverted, while Rautenberg's curves ([42d]) recorded in a similar manner are interpreted as showing a convex wave. Here again there is the necessary assumption of delay in the appearance of the apex beat, sometimes amounting to ·1 sec. An illustration (Fig. 2 of this article), based on one of Rautenberg's curves ([42d]) (No. 2), will make this point clearer. The upper curve is from a point on the chest wall overlying the right auricle; the lower curve is from the apex beat. Four corresponding points have been marked on the curves, the upper of which is open to two interpretations. According to Rautenberg, auricular contraction is represented by *a*–*c*, and there is a delay, *c*–*d*, between the commencement of systole and the upstroke of the cardiogram. On the other hand, it may justly be argued that the contraction of the auricle is represented by *b*–*d*, and that the curve is inverted; and this view receives confirmation from two sources. In the first place, other observers do not find delays in the upstroke of the cardiogram of a nature comparable to those given by Rautenberg; and secondly, Rautenberg's cardiographic curve itself shows a rise which can only be attributed to the auricular wave, namely, at *b*. In view of the argument which might be raised, that the auricular wave is delayed, it would perhaps be safer to await further work

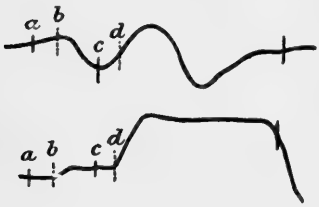


FIG. 2.

before pronouncing a definite opinion as to the time relations of the auricular contraction as represented in œsophageal curves; and this the more as the example given is one of the most simple.

It is requisite that the delay in onset of the "a" wave in the neck should be definitely ascertained, but at present the data are insufficient.[1]

Œsophageal curves show the second positive wave with great constancy (Fredericq, Joachim, Minkowski, Rautenberg, and Young and Hewlett), and its onset is said to coincide with ventricular systole. Young and Hewlett, and Rautenberg agree in showing that it occurs on these curves earlier than the "c" wave upon the jugular tracings. According to the former, the delay[2] is ·1 sec.; according to the last named, ·079 sec.[3] (average of six observations). The necessity of fixing the time difference between the second positive and the "c" wave will be obvious when the following facts are taken into consideration. As we have seen the *a–c* interval is of great clinical importance, and is usually of ·2 sec. duration as recorded with the polygraph from the jugular vein in the neck. Such evidence as we possess tends to show that the time difference between the onset of auricular and ventricular contraction, as registered by œsophageal and direct auricular curves in man and animals, is less, and amounts to little more than ·1 sec.[4] The difference in the two figures can only be accounted for, assuming them to be correct, by the quicker appearance of the "a" wave in the neck.

In œsophageal tracings a third positive wave is present. Here, as in the case of the "v" wave, opinion is divided as to its moment of onset. Minkowski finds that it commences with the second sound; Young and Hewlett represent it as commencing in the middle of the ventricular plateau, and ending at or a little before

[1] The electrocardiogram taken simultaneously with the jugular curve should give a speedy answer to this question. A few such curves obtained by the author show a delay of approximately ·08 sec. (For which see appended note and Fig. 3.)

[2] It is necessary to anticipate the discussion of the identity of the two waves. The full evidence will be considered later.

[3] The figures are in agreement with other values, for allowing ·05 sec. for the presphygmic interval and ·03 sec. for transmission from aorta to carotid or subclavian, we obtain a delay in the arterial shock of ·08 sec

[4] Einthoven's electrocardiograms show an interval varying from ·1 to ·2 sec. between onset of auricular and ventricular potential change. The average is about ·14 sec. in man.

the opening of the auriculo-ventricular valves.[1] In these particulars as to the positive wave the curves of Rautenberg agree in that the third *negative* wave starts at the end of the plateau. According to Young and Hewlett the wave occurs ·1 sec. earlier than the "v" wave in the neck, and they attribute much of the confusion which has arisen in its interpretation to a neglected consideration of this delay. Rautenberg finds a delay both in man and animals; the average of observations on six human subjects gives the figure at ·081 sec.

If the diagram (Fig. 1) is again referred to, the discrepancy mentioned at the end of the last section will be understood. The majority of the intra-auricular pressure diagrams show the third negative wave as commencing at the A.O. line. If the "y" depression is fixed at the same point, no delay is allowed for. For this reason a curve more nearly corresponding to those given by Porter of intra-auricular pressure is also introduced. If the third negative wave is regarded as terminating on the A.O. line, it becomes necessary to move the "y" depression to a position indicated in the figure by the broken line, marked ♯.

In connection with the delays, it is important to note that transmission of *pressure* waves in the venous channels is slower than in the arterial, for the tension is less in them, and the waves travel against and not with the stream. Young and Hewlett estimated the rate of transmission in a case of tricuspid failure at 1·2 m. per sec. Rautenberg's figures indicate a transmission velocity of 1·5 m. per sec. Morrow found in animals a variation in velocity from 1 to 3 m. per sec.[2]

The main conclusions to be drawn from œsophageal curves are, first, the similarity of intra-auricular curves in man and animals; and secondly, the fact that the separate waves of the jugular pulse show an appreciable delay in transmission from auricle to neck.[3] They are also of importance in providing a

[1] A point estimated apparently as half way down the downstroke of the cardiogram. It frequently happens, as in this instance, that the evidence upon which this standard instant is timed is not fully stated.

[2] The rate of transmission of the several waves is not of necessity the same. As will subsequently be seen, it is improbable that they are all of the same nature.

[3] Of further conclusions which have been drawn, there is one which deserves notice. Joachim and Rautenberg have shown in certain cases of heart block that right and left auricles beat in unison. The statement is only approximately true and applies to clinical work. Some recent observations may be quoted in this connection. Stassen ([46]) finds that the right auricle in dogs contracts ·02 sec.

means of recording the movements of the left auricle. As a routine practice the method is naturally impossible, and contraction of the left auricle is also frequently represented on the cardiographic curve. In this connection it is of interest to notice that the auricular wave in the cardiogram often shows a shortened duration, as does that in the œsophageal, when compared to that in the jugular.

The evidence so far considered has led to certain conclusions as to the time relations of the events of the cardiac cycle in the normal human subject, and these conclusions have been incorporated as carefully as possible in the figure given on page 88. The subsequent discussion will be based to a large extent on the assumption that the events are correctly represented. That they are approximately correct is beyond doubt, but that they are rigidly correct is perhaps improbable. The diagram represents the conclusions which the evidence we possess to-day appears to warrant.

III. The Interpretation of the Auricular Pressure Curve and the Jugular Pulse Tracing

In passing to a consideration of the events involved in the production of the three main waves and three main depressions of the tracings, it will first be convenient to examine the ultimate factors to which each in its turn is due, whether it occurs on the jugular, œsophageal, cardiographic, or auricular curve, and then to briefly notice, where necessary, the modifications which occur in the jugular tracing by the interposition of interfering factors.

(*a*) **The First Positive or "a" Wave.**—The presystolic onset of this wave leaves little doubt that it is due to the contraction of the auricle, and it is universally attributed to this cause. According to Fredericq ([12a, c]) it disappears from the tracing, when as a result of tetanisation of the auricle, this chamber ceases to beat.[1] In cases of partial heart block, in which the auricles maintain a rhythm which is a multiple of the

before the left; that on the other hand the left ventricle contracts ·03 to ·04 sec. before the right; and that the delay between the onset of auricular and ventricular systole is ·08 to ·10 sec. Schmidt-Nielsen's figures ([45]) for the delay from right to left auricle agree with those of Stassen. Compare Fredericq's remarks ([12b]).

[1] Hering ([23c]) has confirmed this result by the use of vagal inhibition.

ventricular rhythm, the wave occurs more frequently upon the jugular tracing and at equal time intervals. Experimentally it has also been shown that cessation of ventricular contraction does not affect it. The wave is consequently established as due to auricular contraction and auricular contraction only.

The question arises as to how it is propagated in the neck. It may be supposed to result from regurgitation of blood into the veins at the auricular systole. Such a view could apply only to its production in the veins in the immediate neighbourhood of the heart. But whether such regurgitation actually takes place is by no means easy to settle. For even assuming that the right auricle is supplied at the entrance of the *superior vena cava* with a specialised band of muscular tissue, the *tænia terminalis* (Keith), which effectually closes the orifice by its guillotine action, yet it might be supposed that a slight degree of regurgitation occurred prior to the complete closure. The most direct evidence which we possess is that given by François-Franck, and this applies solely to the veins of the neck. He found on fitting a Chauveau's instrument into these veins (in the donkey and horse) that there was no sign of reflux, as indicated by a retrograde movement of the blood column, at any period of the cardiac cycle.[1]

Secondly, it may be attributed to a positive and centrifugal wave of pressure originating in the auricle, or at the mouth of the superior vena cava, and ascending the vein. Thirdly, the wave may be regarded as due to the filling of the veins when the outlet is obstructed; namely, as consequent upon stasis. So far as the second and third views are concerned there is little or no evidence on which to base a discussion. The former tends to recognise the wave as one mainly of pressure, the latter as one mainly of volume. The curves obtained from the neck by means of the tambour and pelotte are chiefly pressure curves, while the receiving capsule, usually used, yields curves for the most part

[1] The instrument used was Chauveau's hæmodromograph. Both François-Franck and Chauveau and Faivre state that they have observed regurgitation from the auricle into the roots of the great veins. But François-Franck says he is convinced that there is no reflux into the *neck* veins by experiments too long to report.

The evidence for the tributaries of the inferior vena cava is even less complete. There is of course every reason to suppose that it occurs in pathological conditions. Experimental work on the subject is rendered very difficult, as the opening of the chest which is usually necessary, produces serious alterations in the pressures of the veins and right heart.

representative of volumes (Bard [1a]); it is possible that a careful comparison of curves obtained by the two methods might throw some light on the subject.

But whatever its method of propagation, the main fact rests on an assured basis; *the wave may be taken as an indication of auricular contraction.*[1]

(*b*) **The Second Positive or "c" Wave.**—The discussion which centres around this wave involves many questions of considerable intricacy.

It is sometimes held that no such wave occurs in the curve of intra-auricular pressure, but the tracings of Porter and Fredericq demonstrate it too clearly and constantly to allow of doubt. While the weight of evidence is in favour of its presence, yet Frey and Krehl fail to show its presence in their tracings, and recently Hering ([23a]) has published a similar curve. Hering's experiments were performed under perfusion; the chest wall was removed; and the conditions generally were of an extremely artificial character.[2]

In man its presence is attested not by the jugular curves so much as by the œsophageal, and the results of such observations warrant the statement that it is a normal event of the human intra-auricular pressure curve.

It is timed by all those who admit its occurrence as commencing in the auricle with ventricular systole. According to Fredericq the wave persists when by faradisation the auricle is caused to fibrillate, and when the chest is opened. It disappears when the ventricle ceases to beat. The wave must consequently have its origin in ventricular systole.[3]

It is often held to originate in the bulging of the auriculo-ventricular valves, at the onset of the systole (Chauveau, Fredericq, and Porter). Chauveau in examining the heart of a living horse (Chauveau and Faivre [6]) inserted his finger into the beating

[1] Porter estimated the auricular pressure in the dog during auricular contraction at 9 mm. Hg. This and other auricular pressures are given by Porter at page 533, and will be subsequently quoted. They are the pressures from one curve.

[2] Moreover it must be stated that Hering ([23c]) firmly believes in the presence of this wave in the auricular pressure curve. He has recently commented upon the reference to his own curve and also that of Cushny and Grosh, published by Mackenzie ([23c]).

[3] Similar experiments have been performed by Fredericq with the chest wall intact, either by vagal stimulation, or by stimulating through the chest wall.

auricle, and reported that the ring is not completely closed in ventricular systole, for the multiple dome of the tricuspid valves is palpable at this phase.[1] It must be remembered that such an experiment is conducted with the thorax open, and also that the palpating finger is frequently misled in attempting to gauge changes of volume where there are also changes of pressure. In a consideration of the possibility of this bulging the experiments of Roy and Adami are of importance. These observers recorded the contractions of the papillary muscles by means of a hook passed through the wall of the auricle and around a *chorda;* they registered, simultaneously, the movements of the heart wall itself. The conclusion arrived at was that there is an appreciable delay between the onset of ventricular wall and papillary muscle contraction. Now this conclusion has been called in question by Haycraft and Paterson. In the freshly excised heart they found the contraction of the papillary muscles and adjoining part of the ventricular wall to be synchronous. The subject has recently received further attention from Saltzman (44), who experimented on the perfused heart. His findings, though they lack complete uniformity, on the whole favour the view that the musculature of the heart contracts according to the length of the branches of the Purkinje system which supply the particular part considered. The order of contraction in his typical experiments is as follows: First, the base of the heart; secondly, the papillary muscles and adjoining wall; and thirdly, the apex. Previous results, which were conflicting, are thus brought nearer into line, though they do not show complete conformity.[2] In four experiments the base contracted on the average ·031 sec. before the papillary muscles, and the papillary muscles ·036 sec. before the apex. There is a variation on either side of these figures of ·02 sec. Hering, however, in a preliminary note (23d), states that he finds the papillary muscles contract before either base or apex. Whatever the actual events, the delayed pull of the papillary muscles and chordæ observed by Roy and Adami requires explanation, and it appears rational to assume that it is due to delayed contraction, stretching of the chordæ, or to a relatively greater shortening of the ventricular muscle, and it constitutes evidence that under the conditions of the experiment the valves bulge back into the auricle.

[1] Fredericq (12a) makes the same statement.

[2] In some cases Saltzman found the order of contraction reversed or irregular.

At the moment when the valves may be supposed to balloon into the auricle, that chamber is rapidly enlarging, and it may be held that any decrease in the capacity of the auricles from the former source will be fully compensated by the dilatation of the organ. But granted that a positive wave of pressure is started by the tricuspid valves,[1] its appearance in a recognisable form upon the curve of intra-auricular pressure will depend on the relationship of the pressures represented in this wave and the pressures produced by other influences tending to expand the auricle; thus there is no reason to deny the possibility of the appearance of the wave on the auricular pressure curve. Again its conduction into the veins of the neck will depend on the relationship of the rate at which the wave is propagated and the rate at which the blood enters the auricle, and, assuming its origin in the auricle, there is every reason to believe that this relationship is such as to allow of conduction.

From the collected evidence *we may conclude that the second positive wave is a real auricular event in man and that it may appear in the neck as a component part of the jugular pulse.*

In considering the causal factors of the "c" wave in the neck further complications arise. The shock of arterial pulsation may be transmitted to the receiver, for it occurs at or about the instant when the "c" wave has its onset. There is also the possibility of a direct conduction of the arterial pulsation, either aortic, innominate, or carotid to the accompanying veins with which these vessels are in contact. Each of these factors has been advocated in turn as the chief element in the production of the "c" wave (cp. Friedreich [14], p. 289, Belski [4]). The leading points and arguments alone require consideration.

It is held by Mackenzie, Gerhardt and Wenchebach that the "c" wave is due to the impact of the neighbouring artery [2] alone. Given in the main by Mackenzie, the chief evidence in favour of

[1] The origin of the second positive wave in the bulging of the auriculo-ventricular valves cannot be regarded as proven, though it appears to be the most rational view to hold of its production. Hering has convinced himself that it is independent of the shock of the root of the aorta, and auricular branches of the same, by numerous experimental researches, but he does not detail the evidence ([23c]).

[2] While the actual statement is frequently made that the impact is from the carotid, yet it is understood that an arterial impact is intended, and that the particular artery involved is that which lies in the neighbourhood of the receiver by means of which the tracing is obtained. In the light of Keith's anatomical description it would appear that the artery is usually the subclavian.

this view is as follows: The proof of the occurrence of the second positive wave in the auricle is not considered as final [1]; tracings of an obviously arterial nature are obtained with the greatest ease from many points of the neck; as the receiver is moved higher in the neck the tracing gradually acquires the arterial character and eventually loses all trace of jugular waves; the wave is said to be synchronous with the primary wave of the carotid pulse; it is occasionally absent from the jugular tracing when the latter has a large amplitude; [2] it is said to be absent from a type of liver pulse known as the auricular liver pulse.

There are many observations in opposition to this evidence. Morrow ([37b]) finds that clamping the carotid near its origin does not affect the wave.[3] Fredericq ([12c]) states that in animals the wave persists when the artery is completely separated from the vein from which the record is taken. Bard ([1b]) has also noted the "c" wave in a subclavicular vein, isolated from all arteries, and Rautenberg has recorded it in its full dimensions in the superior vena cava of a dog. Hering states that in heart bigeminus where the second pulse beat has a longer presphygmic interval than the first, there is no corresponding delay in the appearance of the "c" wave in the neck.

There can be no doubt that in many tracings of the jugular pulse the arterial shock contributes to the "c" wave; the difficulty is frequently in avoiding the arterial pulsation. The main question is as to whether it is the only factor, or as to whether on occasion it may contribute but slightly or even take no part in its production. The character of the wave is of importance. In many tracings it is very prominent and peaked, and shows

[1] This question has already been dealt with as fully as space will permit. It is questioned if the apparatus used in recording auricular pressures may not tend to the production of the wave. The apparatus has varied very greatly, as has also its position in the process of recording; yet the majority of the curves show the same characters. Porter has registered the wave in the pulmonary veins, and Rautenberg in the superior vena cava; more recently Delchef has recorded the wave in the inferior vena cava (*Archiv. Internat. d. Physiol.*, vii. 1908, p. 96).

[2] Hering ([2c]) explains this by the magnitude of the "a" wave in the tracings given, and states that the "carotid shock" may also disappear.

[3] Morrow holds that the essential part of the "c" wave is conducted from the auricle where it may be produced by—

1. A force exerted during ventricular systole, through the auriculo-ventricular valves.
2. Contraction of the ring of muscle in the auriculo-ventricular junction.
3. Pressure exerted upon the auricles by the systolic twist of the heart.

no outward resemblance to the waves of the pure carotid pulse. Briefly, in such cases it must be assumed that the primary wave is alone transmitted, an assumption which it is difficult to make. It may be asked why, if the primary wave is recorded, the dicrotic should not also leave its impression on the tracing. Again, it requires as a rule a firmer pressure to bring out a maximum arterial tracing than it requires for the venous. Venous tracings of the greatest amplitude are often to be obtained by the lightest application compatible with closure of the mouth of the receiver. We have further seen that the synchronicity of the "c" wave and the carotid shock has not been fully established (Bard and Bachmann). The tracings given to show simultaneous onset often show a slight deviation, which may of course be explained by a difference in level at which they were obtained and to a slight transmission delay. The argument that the "c" wave is absent from the liver pulse is the strongest of those brought in favour of its arterial origin, and has not yet met with a satisfactory explanation. The liver tracings are of a very complex nature, combining expansile pulsation with up and down movements of the whole organ. Rautenberg ([42c]) has given a tracing in which the "c" wave appears to be present, but it is possible that in this instance insufficient care was employed to avoid the transmitted shock from the aorta. The author is of opinion that the "c" wave is occasionally visible in the veins of the neck.

Finally, it cannot be affirmed at present that the "c" wave is purely arterial or purely venous in origin, and while it cannot be denied that both factors may be contributory under certain conditions, it is highly probable that in one case the arterial and in another the venous element will predominate.

As to whether there is a transmitted shock from the aorta or its branches direct to the veins, there is little evidence beyond that already examined. Fredericq points out that, as the rate of transmission is dissimilar in artery and vein, the view is incompatible with the opinion that the waves appear together in the neck. Morrow uses, as an argument against such transmission, the fact that the "c" wave is frequently absent from the femoral venous curve, though the venous channel which connects the femoral vein to the heart is throughout in close contact with pulsating arteries.[1]

[1] The question has been recently discussed more fully by the author (*Brit. Med. Journ.*, Nov. 1905).

Whatever the ultimate factors involved, the practical outcome remains unaffected. *The "c" wave in the jugular may be safely taken for clinical purposes as synchronous with the primary wave of the arterial pulse in the neck at the same point, and it thus forms a valuable standard in the interpretation of tracings.*[1]

(*c*) **The Third Positive or "v" Wave.**—The chief difficulty in interpreting the third positive or "v" wave lies in the difference of opinion in regard to its instant of onset. The explanation of its occurrence, as given by any particular author, depends upon the time relations which he accepts for its various phases. Thus, those who believe in its onset during systole of the ventricle, consider that the venous flow which fills the auricle during this phase is an important contributory cause (Potain, Porter, Gottwalt, Mackenzie, Morrow, Hering). Those who regard it as arising with the commencement of ventricular diastole, attribute it to an elevation of the auriculo-ventricular ring (Porter,[2] Gerhardt). A similar view is held by Wenchebach. It has also been attributed in part to dicrotic rebound at aorta and pulmonary orifices (Riegel [3]); and to tricuspid regurgitation [4] (Mackenzie).

For our present purposes it will be convenient to regard the onset of the "v" wave as inconstant in position, and to briefly discuss those factors held to take part in the production of the wave, either in that portion of it which is said to occur before,

[1] The second positive wave was estimated by Porter as representing an auricular pressure of 5 mm. Hg.

[2] Porter recognised it as a contributory cause.

[3] Cp. criticisms of Gerhardt and remarks by Hering ([23c]).

[4] The difficulties of this question are very great. That the wave is enhanced when there are evidences of tricuspid regurgitation is generally admitted. The opinion rests chiefly on the proposition that tricuspid reflux may be a normal event. Such a reflux is not admitted by physiologists, but is strongly held by the northern schools of clinical medicine. The evidence cited is the presence of a systolic murmur, regarded as an indication of tricuspid insufficiency. Whether those presenting such a murmur, a sound which is said to be of common occurrence, are to be recognised as falling within the category of normal subjects, is a question outside the bounds of this article. Full references and many interesting observations may be found in the writings of Gibson ([17]) and in the first articles of Mackenzie. Our ignorance of the conditions under which tricuspid leakage may occur in its earlier stages appears to be very great, and little or no experimental work has been done on the subject. Statements attributing to Gibson the view that regurgitation is a factor in the production of the "v" wave are without foundation.

or in that which it is claimed occurs subsequent to the S.C. closure.

During the systole of the ventricle, the auricular pressure falls and the blood pours into that chamber. There is no exit for the stream and the reservoir must gradually fill. If the systolic plateau is prolonged or the filling is rapid, it is reasonable to expect that the pressure in the auricle will rise, for any influences, other than the passive one, which tend to dilate the auricle, must of necessity be diminishing during the last phases of ventricular systole. When in a venous or auricular curve, there is a rise which can but be attributed to events occurring before the termination of systole, it is rational to attribute it to this auricular filling and to a stasis wave passing back into the veins. As yet no curves indicative of the changing velocities in the large veins have been obtained.

The second possible factor in the production of the "v" wave, namely, the upward spring of the auriculo-ventricular junction at the beginning of diastole, must be dealt with at greater length.

The direction of movement of the different parts of the heart wall has been for many years the subject of contention, and there is accumulated evidence that the earlier observations, in which the heart was exposed, were fallacious. The experiments which chiefly concern us are those of Brücke ([5]) and Haycraft ([21]). The method employed was the same in each case, and is in all probability a very accurate one. Needles were used, and the chest wall and heart muscle was transfixed. The needles carried light straw levers from the movements of which the excursion of the heart wall could be observed. As a result it was shown that in systole the apex is the only fixed point of the musculature, and that all other parts tend to move towards the mid-line and apex. The auriculo-ventricular line is considered by most authorities to have a decided downward movement in systole, and a corresponding upward fling in diastole. Keith, who regards the mouths of the great vessels as other fixed points, has recently laid much stress on this movement of the A-V line. According to this author, whose researches are in the main anatomical, the systole of the ventricle causes expansion of the auricle, and diastole of the ventricle its collapse. The auricle is opened like a concertina, and the upward movement of the A-V line in diastole is said to pro-

pagate a positive wave in the uppermost chamber.[1] Now the movements of the A-V line are also offered as an explanation of an earlier negative wave (second negative or "x′" depression), and the view, as we shall subsequently see, has much to support it. If the descent of the A-V line is sufficient to produce a negative wave, its ascent must assuredly be adequate to determine a second wave of equal intensity but of opposite sign. The explanation is a feasible one, and there remains but one serious difficulty. A positive wave of the sort, if propagated, may be entirely swamped by other events occurring at or about the same time. And the event which has to be considered is the effect of the lowering of ventricular upon auricular pressure. It must be noted that the factor can only be of avail between the S.C. and A.O. points; and until there is more unanimity as to the timing of these events opinion must necessarily vary as to the part played by the A-V line in the production of the "v" wave.[2]

The interpretation of the "v" wave which has just been discussed attributes it to a movement of the ventricle, and makes it independent of auricular contraction or relaxation. Fredericq has found that when the ventricle is thrown into a state of fibrillation, the wave is abolished. François-Franck and Morrow, on the other hand, give curves in which some portion of it at least remains when the ventricle is no longer beating. It is for this reason that Morrow is more inclined to attribute it to inflow and stasis. In cases of heart block there is as a rule no "v" wave corresponding to the purely auricular beats, but in a tracing of Wenckebach's a small wave is seen. *It is probable that both factors play a part in the production of the wave under certain circumstances; that with quick filling of the auricle or sustained plateau the first will be prominent, and that with slower filling and quicker heart beat the pressure in the auricle will be low when the ventricle passes into diastole, and that as a consequence the tricuspid valves will open later. Under these circumstances the second factor may be the more pronounced.*

[1] This movement of the auriculo-ventricular junction was described by Chauveau in 1887 (*Assoc. franç. p. l'avanc. d. Sc.*), in a paper in which he gives a figure (No. 12), illustrating views very similar to those recently published by Keith. The movement is fully discussed by Fredericq ([12a]), and many other writers.

[2] Allowing the S.C. to A.O. instant at ·04 to ·06 sec., there is time for the production of an appreciable wave. But this time interval is very difficult to measure with any degree of accuracy, and it cannot be held that our estimates of it are at present anything more than approximate.

If the view is accepted that both are contributory causes, not only do many of the apparently discordant observations assume an aspect of greater harmony, but the occasional division of the wave at or about the time of S.C. closure is no longer difficult to appreciate.[1]

(*d*) **The First and Second Negative Waves, or "x" and "x′" Depressions.**—The two first depressions of auricular and jugular tracings may be considered together, for the line of descent is usually continuous, and is but broken by the second positive or "c" wave. The complete depression commences with the relaxation of the auricle,[2] and is continued well into the systolic plateau. The fall in pressure is a marked one, and attracted much attention from earlier writers, for it causes a collapse of the veins of the neck. Hunter (25) regarded systole of the ventricle as a valuable aid to the filling of the auricle, by the creation of a partial vacuum in the chest. This view was readvanced by Brücke and Mosso. François-Franck performed some experiments with a schematic apparatus to demonstrate its possibility. But François-Franck himself, and also Gottwalt and Riegel, clearly showed that it is a factor of little importance, for the fall remains after the chest is opened. Nevertheless it cannot be denied that it contributes, for the systole of the ventricle produces a fall of intra-pleural pressure, which may be recorded by a manometer in connection with that cavity. It is certain that it is not the main cause of the fall.

Active relaxation of the auricle has never been demonstrated, and its enlargement in the normal chest is attributable at its onset to the low pressure in the chamber surrounding it (François-Franck). But the auricular relaxation is in itself insufficient to account for the complete fall,[3] though it suffices to explain that portion of it which occurs before the commencement of ventricular

[1] Bard finds this notch so constantly that he considers, and perhaps with justification, that the origin of the separate portions of the wave should be separately discussed. It must be noted that Hering and Rautenberg strenuously deny the intervention of the second factor.

Porter gives the third positive wave a pressure value of 5 mm. Hg.

[2] Porter found that it occurred, as a rule, a little before relaxation of the auricular appendix. This writer estimates the value of the complete fall at −10 mm. Hg.

[3] Fredericq's tracings, with intact chest wall, in which auricle and ventricle were dissociated.

systole (first negative wave or "x" depression). Porter states that relaxation of the auricular appendix proceeds for a variable time, terminating at the beginning or end of the second positive wave; but the observation is of little value, for under the conditions of his experiment the relaxation would depend in the main on passive filling. When the ventricle is inhibited by vagal inhibition in the dog, or if clamped off from the auricle in the tortoise, a negative wave is still present (François-Franck); it also occurs in the jugular pulse in certain cases of heart block when the ventricle fails to respond to the auricular contraction (Wenckebach). Morrow's tracing (Fig. 12) shows similar characteristics; but while the ventricle is inactive, the depression, though still present, is reduced in size. While François-Franck found it abolished by irritation of the auricle, Fredericq ([12c]) has shown that this is not the case, and states ([12a]) that when the auricles have passed into delirium, at each ventricular contraction the auricular appendices diminish in volume, *and are, as it were, aspirated towards the cavity of the auricle*, and the negative wave persists.[1]

From these observations it is clear that the systole of the ventricle plays a considerable part in causing the depression, and it has been attributed by many writers to an event occurring at this time, namely, descent of the A-V line (Fredericq, Porter, Wenckebach, &c.).

In concluding this section it may be said that *the two negative waves which together form the most prominent depression of the*

[1] François-Franck's observations were carried out with the chest open. Fredericq has controlled his own observations by repeating the experiments with the chest intact, the advantages of which are obvious.

There is a fact which is often insufficiently appreciated, namely, that the circulation is completely obstructed at two points during approximately half the cardiac cycle. The obstructions are situated at the auriculo-ventricular valves. Nevertheless it is only during a small fraction of the cardiac cycle, during systole of the auricles, that blood is not pouring into the heart. The main function of the auricles is not to load the ventricles; the ventricles fill well when the auricles are paralysed, and by comparison the auricles are small chambers. They serve mainly as reservoirs, and during their brief contraction the large veins in their vicinity adopt this function. In contracting the auricles return to the state of potential reservoirs.

So the over-engorgement of the veins, which would otherwise occur, is prevented; and so it happens that in spite of the fact that the circulation of man is never an open path, the flow of blood through peripheral vessels is constant and uninterrmitting. While in heart block venous stagnation is rare, clinical observations of to-day point to its frequent origin in inefficient, ill-timed, or obstructed systole of the upper chambers.

auricular and venous curves are due to three causes: the increased negative pressure in the chest, consequent on ventricular systole; the auricular relaxation dependent on the original intra-pleural pressure; and the stretching of the auricular walls as a result of ventricular systole. Of these causes, the first is insignificant; the second is most active during the early phases, and the third most prominent in the later phases of the depression.

(*e*) **The Third Negative or "y" Depression.**—With the diastole of the ventricle, the pressure within it falls rapidly and may become markedly negative. The fall of pressure is accompanied by the opening of the auriculo-ventricular valves, and the blood contained in the auricle passes into the ventricle. As a consequence, the pressure in the auricle falls, and the depression in the auricular tracing timed to occur with the opening of the valves [1] is universally attributed to this cause. The depression may be due not only to a relief of the previous stasis, but to a transmitted pressure wave of negative sign. To what extent the negative pressure is thus transmitted to the auricle is uncertain. Porter estimated the auricular pressure corresponding to this event at ·5 mm. Hg, and as a consequence concluded that the negative pressure in the ventricle has little direct effect upon the pressure in the auricle. Porter's experiments were carried out on dogs and

[1] The timing of this instant in man and the dangers which the methods involve have been repeatedly referred to; to emphasise them now entails tiresome but necessary reiteration. The interpretation of the "y" depression may be correct, but it has not been arrived at by scrupulously accurate methods. It cannot be said that the intra-auricular curve falls at the A.O. instant, while the curves of Porter and those of Young and Hewlett and Rautenberg show it otherwise. Moreover the drop in the jugular curve must be placed later, to allow for the delay in transmission which undoubtedly occurs. So that if the drop in the jugular curve is to be placed at the A.O. instant, the drop in the human intra-auricular curve must be placed approximately ·1 sec. earlier, at a point at or near the closure of the semilunar valves.

Almost all writers, early and late, express the opinion that the drop occurs both on auricular and jugular curves at the A.O. instant, or refer to unanimous statements to that effect. And it is attributed by similar processes of reasoning to a definite cause. In the above synoptic account the same line is taken, but for that very reason this proviso is essential. For if the auriculo-ventricular valves are bulged into the auricle during early systole, they must remain bulged during the plateau, and when the ventricular pressure begins to fall the tension in the valves must decrease. The fall in auricular pressure should therefore commence slightly earlier than the A.O. point, namely, at or near the S.C. point. Porter, who took differential curves of the pressures in the two cavities, actually found that the fall in auricular pressure commenced at this instant.

the chest was open. In this connection it must be remembered that although lower pressures have been recorded in the ventricle with the chest wall uninjured, yet pressures as low as −28 and −38 mm. Hg have been found in dogs by Goltz and Gaule, de Jager and others,[1] with the thorax open.

The jugular and œsophageal curves *in man* often show the third negative wave or "y" depression to be of considerable extent, and a relief of stasis is certainly insufficient to account for it.

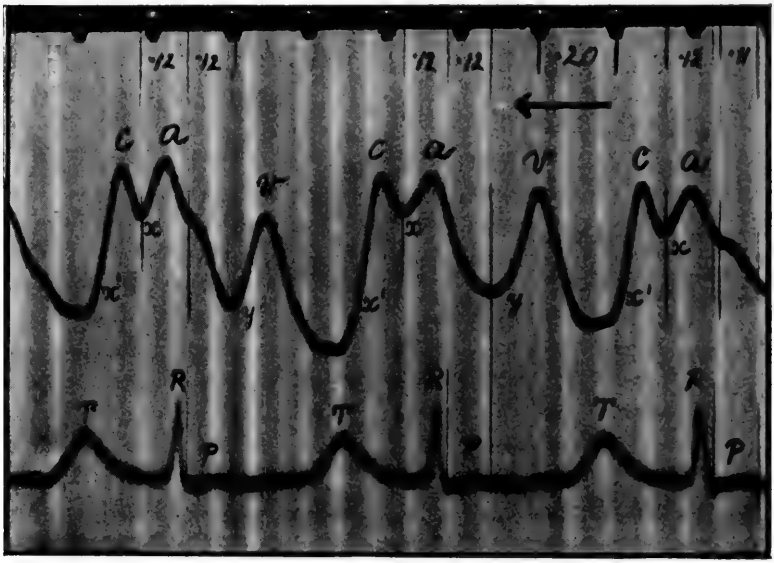


FIG. 3.

The evidence of the jugular pulse in this respect is occasionally such as to indicate that the inflow from the veins is as great during ventricular diastole as during ventricular systole. It is probable that the larger the ventricle the greater is its power as a suction pump.

APPENDED NOTE

In sending off the proofs, the author is able to include a simultaneous jugular curve and electrocardiogram (Fig. 3). The figure shows:—time in $\frac{1}{5}$ sec.; the jugular curve, taken photographically

[1] Full references to these observations will be found in Porter's article.

with the polygraph, in which a delicate lever replaced the usual pen, which is heavy for the purpose; and an electrocardiogram taken in Professor Waller's laboratory with an Einthoven "string galvanometer." The jugular curve has been marked with the letters used by Mackenzie and employed in the text. The electrocardiogram has been marked with the letters used by Einthoven; P represents auricular contraction, R and T are the result of ventricular contraction. The curves were obtained from a lad with a prominent jugular pulse.

The a-c interval, as measured in the jugular tracing, in the first and last curves is ·14 and ·12 sec. respectively. The time interval between auricular and ventricular contraction, as measured in the electrocardiogram, is ·11, ·12, and ·12 respectively. It will be seen that the delay in the appearance of "a" and "c" waves in the neck is practically identical, namely ·12 sec., and that the a-c interval is, as taken by this method, less than $\frac{1}{5}$ sec. The delay of ·12 sec. in the appearance of the waves in the neck is the uncorrected value. A deduction of ·04 sec. must be made for instrumental delay in the jugular curve. The true value is consequently ·08 sec.

The figures given are in agreement with others obtained from the same subject, and accord very closely with the estimated values quoted in the text.

BIBLIOGRAPHY

[1] *Bard*, (*a*) Jour. d. physiol. e. d. pathol. gén., mai 1906, pp. 454–459. (*b*) Ibid., pp. 466–479. (*c*) Archiv. d. Maladies du Coeur, &c., juin 1908, No. 6.

[2] *Baum*, Verhandl. d. phys.-med. Gesell. z. Würzburg, N. F., Bd. 38, 1906, s. 61–102.

[3] *Bayliss* and *Starling*, Internat. Monatssch. f. Anat. U. Phys., Bd. 11, Hft. 9, 1894, pp. 426–435.

[4] *Belski*, Zeitsch. f. klin. Med., Bd. 57, Hft. 5 u. 6, 1905, s. 565.

[5] *Brücke*, Vorlesungen über Physiologie, Wien, 1885, Bd. 1, Aufl. 4, s. 178–179.

[6] *Chauveau* and *Faivre*, Gaz. méd. de Paris, T. xi., 1856, p. 406.

[7] *Chauveau* and *Marey*, ibid., 1861, p. 675.

[8] *Edgren*, Skand. Archiv. f. Physiol., Bd. 1, 1889, s. 67–151.

[9] *Einthoven* and *Geluk*, Archiv. f. d. ges. Physiol., Bd. 57, 1894, s. 617–639.

[10] *Erlanger*, Johns Hopkins Bulletin, No. 177, vol. 16, 1905, pp. 394–397.

[11] *François-Franck*, Gaz. hebdo. d. méd. e. d. chir., fév., mars, av. 1882, pp. 92, 225, and 255.

[12] *Fredericq*, (*a*) Archiv. d. Biol. (Paris), T. 8, 1888, pp. 497–622. (*b*) Archiv. Internat. Physiol., iv. 1906–7, pp. 57–75. (*c*) Ibid., v. 1907, pp. 1–25.

[13] *Frey* and *Krehl*, Archiv. f. Anat. u. Phys., 1890, s. 31–88.

[14] *Friedreich*, Deutsch. Archiv. f. klin. Med., Bd. 1, 1866, s. 241–291.

[15] *Galabin*, Journ. Anat. and Physiol., vol. 10, 1876, pp. 297–319.

[16] *Gerhardt*, Archiv. f. exper. Path. u. Pharmak., Bd. 34, 1894, s. 402–445, and Bd. 47, 1902, s. 250–266.

[17] *Gibson*, Edinb. Med. Journ., 1880, vol. 25, pp. 979–991.

[18] *Gibson* and *Ritchie*, Practitioner, vol. 78, No. 5, 1907, p. 602.

[19] *Gottwalt*, Archiv. f. d. ges. Physiol., Bd. 25, 1881, s. 1–30.

[20] *Grünmach*, Archiv. f. path. Anat., Bd. 102, 1885, s. 569–577.

[21] *Haycraft*, Journ. of Physiol., vol. 12, 1891, pp. 452 and 473.

[22] *Haycraft* and *Paterson*, Journ. of Physiol., vol. 19, 1896, p. 262.

[23] *Hering*, (*a*) Archiv. f. d. ges. Physiol., Bd. 106, 1904, s. 1–16. (*b*) Verhandl. d. Kongress f. in. Med., 23. Kongress, München, 1906, s. 138. (*c*) Deutsch. med. Woch., 1907, No. 46. (*d*) Zentralb. f. Physiol., Bd. 21, No. 22.

[24] *Hewlett*, Journ. Med. Research, O.S., vol. 17, 1907-8, pp. 119–136.

[25] *Hunter*, A Treatise on the Blood, Inflammation, &c., London, 1794, pp. 185 and 187.

[26] *Hürthle*, (*a*) Archiv. f. d. ges. Physiol., Bd. 49, 1891, s. 29–104. (*b*) Ibid., Bd. 60, 1895, s. 263–290. (*c*) Ibid., Bd. 43, 1888, s. 399–437.

[27] *Joachim*, Berl. klin. Woch., Feb. 1907, s. 215–216.

[28] *Keith*, Journ. of Anat. and Physiol., vol. 42, Oct. 1907, pp. 1–25.

[29] *Keyt*, Sphygmography and Cardiography, London, 1887.

[30] *Lancisi*, De motu cordis et aneurysmatibus, 1740 (earlier ed., Romae, 1728, is cited by Baum, *loc. cit.*).

[31] *Landois*, Die Lehre vom Arterienpuls, Berlin, 1872, s. 307.

[32] *Mackenzie*, (*a*) Journ. of Path. and Bact., O.S., vol. 1, 1893, p. 53; ibid., vol. 2, 1894, pp. 84–154. (*b*) The Study of the Pulse, &c., London, 1902. (*c*) Amer. Journ. Med. Scien., July 1907, pp. 1–23. (*d*) Diseases of the Heart, London, 1908.

[33] *Marey*, (*a*) Physiologie médicale de la circulation du Sang, Paris, 1863. (*b*) La circulation du Sang, &c., Paris, 1881.

[34] *Martius*, Zeitsch. f. klin. Med., Bd. 13, 1888, s. 344 and 346.

[35] *Minkowski*, Zeitsch. f. klin. Med., Bd. 62, 1907, s. 371–384; and Deutsch. med. Woch., 1906, No. 31, s. 1248–1250.

[36] *Morgagni*, De selibus et caus. morbor., Napoli, 1762 (cited by Baum, *loc. cit.*).

[37] *Morrow*, (*a*) Archiv. f. d. ges. Physiol., Bd. 79, 1900, s. 442–449. (*b*) B.M.J., Dec. 22, 1906, p. 1807.

[38] *Mosso*, Die Diagnostik des Pulses, u.s.w., Leipzig, 1879, s. 60–63.

[39] *Porter*, Journ. of Physiol., vol. 13, 1892, pp. 513–553.

[40] *Potain*, Mém. d. l. soc. méd. d. h. d. Paris, mai 1867, pp. 3–27.

[41] *Riegel*, Deutsch. Archiv. f. klin. Med., Bd. 31, 1882, s. 1–62.

[42] *Rautenberg*, (*a*) Deutsch. Archiv. f. klin. Med., Bd. 91, 1907, s. 251–290.

(*b*) Berl. klin. Woch., iv. 1907, No. 21, s. 657. (*c*) Zeitsch. f. klin. Med., Bd. 65, Sept. 18, 1908. (*d*) Berl. klin. Woch., iv. 1907, No. 46, s. 1478.

[43] *Roy* and *Adami*, Practitioner, Bd. 44, 1890.

[44] *Saltzman*, Skand. Archiv. f. Physiol., Bd. 20, 1908, s. 232–248.

[45] *Schmidt-Nielsen*, Archiv. Internat. Physiol., iv. 1906–7, pp. 417–433.

[46] *Stassen*, ibid., v. 1907, pp. 60–75.

[47] *Tigerstedt*, Skand. Archiv. f. Physiol., Bd. 20, 1908, s. 249.

[48] *Weldemeyer*, Untersuch. ü. d. Kreislauf. d. Blutes, Hannover, 1828 (cited by Baum, *loc. cit.*).

[49] *Wenckebach*, Archiv. f. Anat. ü. Physiol. (Physiol. Abth.), 1906, s. 297–354.

[50] *Young* and *Hewlett*, Journ. Med. Research, O.S., vol. 16, 1907, p. 427–434.

THE VASCULAR SYSTEM AND BLOOD PRESSURE

By LEONARD HILL

Experimental Operations on the Vascular System

Carrel has opened up a new field of experimental work by showing that it is possible to join together the divided ends of arteries or veins, or a vein with an artery. Having inserted thread through each end of the divided vessel, at three points in the circumference apart from one another, he brings the ends of the vessel together by these threads and stitches intima to intima with a very fine needle and a running thread.[1] The outer coats are finally stitched together. Then the blood flow being re-established, he watches for the slightest sign of oozing, and if any, stops it by further stitches.

He has succeeded not only in stitching an artery to a vein, but in inserting a length of transplanted artery or vein between the ends of a divided artery. More wonderful than all, he has succeeded in transplanting whole organs from one animal to another. In one experiment he dissected a length of the carotid of a young dog, kept it in physiological salt solution for twenty days at 32° F., and finally inserted the piece in the course of the abdominal aorta of a cat.[2] On the forty-eighth day after he opened the abdomen and found the artery of normal appearance and serving its function well. On the seventy-seventh day the cat was in perfect condition.[3]

"Seven months ago," he writes, "one of the animals had the

[1] The needles are sixteen cambrics, the threads single strands of Chinese twist silk sterilised in paraffin oil.

[2] John Hunter stated that the arteries have considerable surviving power. On transplanting them he obtained union thirty-six hours after their removal from the body. Palmer's Edit., vol. iii. p. 157.

[3] Guthrie not only has repeated this experiment, but has inserted a length of artery hardened in formol; at the end of twenty-two days it was serving its function perfectly. The dead artery is the scaffold on which repair of the living vessel takes place. (*Journ. Amer. Med. Assoc.*, 1908, l. p. 1035.)

peripheral end of the external jugular vein united to the central end of the carotid artery. Now the circulation through the vein is apparently as active as it was on the day of the operation. In another case, where the jugular has numerous collaterals, there appears to be some dilatation of the main portion of the vessel, and feeble pulsations can be detected in the jugular of the other side. In three cases of reversal of the circulation through the thyroid gland the results seem to be permanent, even after

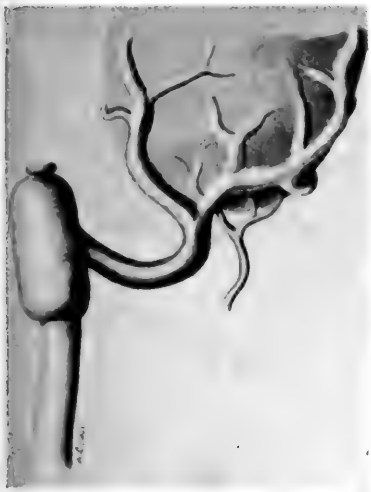


FIG. 1.—External jugular united to carotid artery. Reversal of circulation through the thyroid gland. A method of modifying the function of the gland by producing hyperæmia.

FIG. 2.—Preparation of host for receipt of kidney graft. The viscera are covered with pads wet with warm saline during the operation. Clips on divided aorta of vena cava.

several months. On no dog kept in the laboratory has obliteration of the vessels occurred, even after several months.

"At the present time we can only state that seven months after the operation the veins have performed the main arterial functions and that occlusion has not occurred."

Carrel and Guthrie amputated and replanted a dog's thigh. "The circulation was easily and entirely re-established. The pulsations of the femoral, popliteal, and posterior tibial arteries were as strong as the pulsations of the corresponding arteries of the other side. The arterial circulation was seemingly normal. The capillary circulation was exaggerated, the temperature of the

limb being higher and its hue redder, owing doubtless to the fact that the vaso-motor nerves were cut. The venous circulation was observed to be good immediately after the operation." The collodion dressing, however, contracted and impeded the circulation in the limb which became swollen, so that after fifty hours the animal was killed.[1] The most striking of these remarkable experiments is that of transplanting the kidneys from one cat to another. Secretion of urine may begin immediately after the arterial circulation is re-established. In the best cases the func-

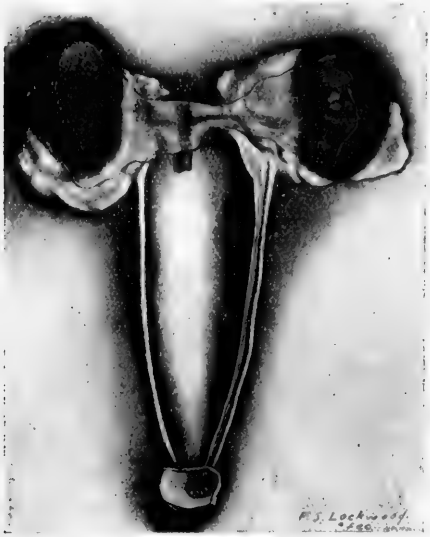


FIG. 3.—The graft ready for insertion.

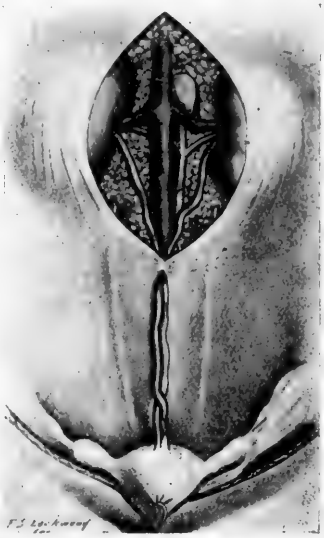


FIG. 4.—The operation completed.

tion of the kidney was for some twenty days almost normal. 120 to 160 c.c. of urine a day were secreted, and urea in proportion to the proteid eaten. When fed on raw meat 2·7 to 5·1 grms. of urea were passed per diem. The cats were fat and in good health, with glossy skin and good appetites, playing, running, and jumping about the room. Nevertheless there was some albumen in the urine, and œdema of the kidneys leading to their slow and progressive enlargement. Upon the twenty-ninth day one cat was well, and then gastro-intestinal symptoms set in and the animal died on the thirty-first day.

[1] Guthrie reports "a transplanted fore-limb without any serious derangement of metabolism, six days after the operation." (*Journ. Amer. Med. Assoc.*, 1908, li. p. 1658.)

In one case the kidneys of a middle-aged cat were successfully grafted on to a young adult. The animal lived as a normal cat for fifteen days, but then became emaciated and died on the thirty-sixth day. The arteries of the young cat, the costal and bronchial cartilages and all the scar tissue where it had been incised were calcified as hard as glass. The transplanted kidneys and renal vessels, on the other hand, showed no sign of calcification. The kidneys were somewhat œdematous but showed no very serious pathological change. This result—the calcification of the host

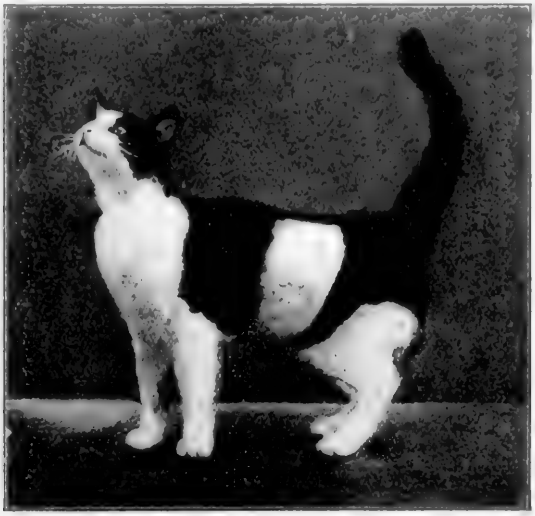


FIG. 5.—The cat three weeks after the operation.

but not of the graft—was only obtained once, but it is one which opens up a wide vista of new ideas and research.

In carrying out the operations the kidneys are deprived of circulation for more than an hour, and are washed out with Ringer's solution. The vaso-motor nerves are cut—it has been proved that kidneys can functionate normally after this operation—and the anæmia probably destroys the local renal ganglia, for nerve cells in the central nervous system do not recover function after at most twenty minutes [1] total deprivation of blood flow. It is very important in such operations that the veins be given their normal situation and direction. The writer's explanation of this is that every departure from the normal course by preventing the

[1] In one case twenty-nine minutes (Guthrie).

full action of the respiratory movements on the renal circulation leads to diminished flow and œdema of the transplanted organ. The capillaries and veins are naturally so arranged to run that each muscular action of the body promotes the flow in them towards the heart. It is important also that no bleeding take place into the connective tissues during or after the operation, as blood has an irritative effect and produces sclerosis. Bier has utilised this property, and injected blood to excite callous formation in cases of pseudo-arthrosis.

The experiments of Carrel bring just within the limits of the

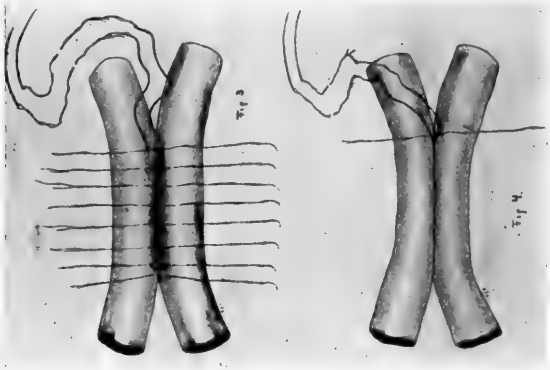


FIG. 6.—Operation method of J. E. Sweet (*Journ. Exp. Med.* vii. 163, 1905) for joining the portal vein and vena cava (Eck's operation). The double thread is the wire of an electric cautery, and cuts the opening between the two vessels.

possible the operation of transplanting from a man killed by an accident such an organ as the thyroid into the neck or other part, where it may carry on its function and compensate for thyroid inadequacy in the recipient. Guthrie has succeeded in exchanging the ovaries of black and white Leghorn hens, and finds the foster-mother modifies the colour of the chicks hatched from the eggs laid afterwards. The controls gave pure white or black chicks.

THE ELASTICITY AND CONTRACTILITY OF ARTERIES

When the carotid artery of the ox or horse is exposed immediately after death, it is found to be soft and flaccid, more or less flattened in section, with a large bore usually 5 or 6 mm. in diameter. On exposure to the air, cooling, and especially on manipulation

the artery quickly becomes rigid and contracted, and circular in section, with a calibre greatly lessened, the diameter being reduced to 2 or 3 mm. or less. The artery becomes often so stiff that a piece 7 or 8 mm. long may be held by one end in an almost horizontal position. Arteries left undisturbed *in situ* for a day or two after death and then exposed may show little sign of contrac-

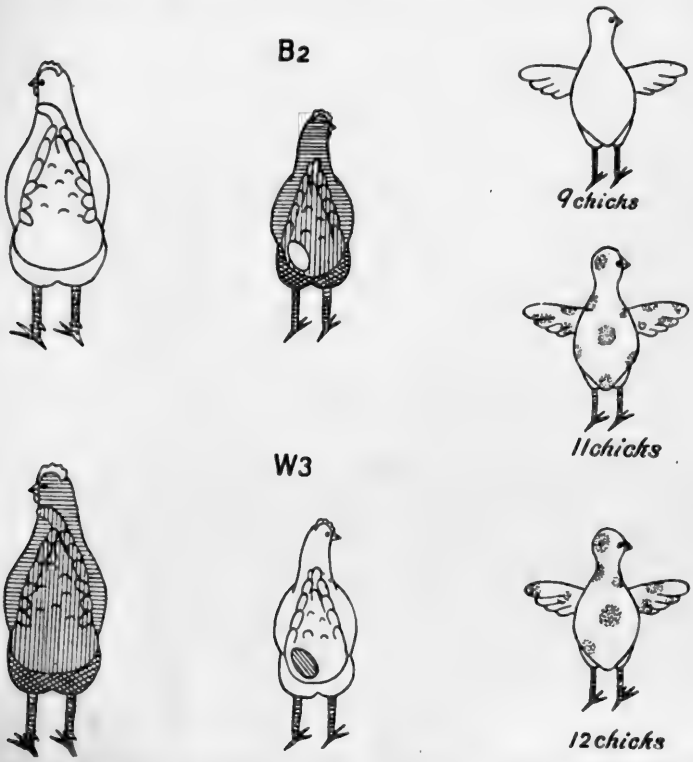


FIG. 7.—B_2, white ovary grafted on black; fertilisation by white cock. W_3, black ovary grafted on white; fertilisation by black cock (Guthrie).

tion at first, but under the influence of manipulation may soon contract strongly and persistently, the contracted state lasting for days. John Hunter noticed that the arteries of the umbilical cord contracted up to the third day, and not on the fourth. Freezing relaxes permanently the arteries, so that if the "pluck" of a freshly killed ox be bought, and one piece of carotid be taken and frozen on a freezing microtome, and another be manipulated, a striking contrast between the two becomes demonstrable.

Heating to 50° C. also causes a permanent loss of contractility. The carotid behaves to moderate changes of temperature like other unstriped muscle—retractor penis of dog, iris and bladder

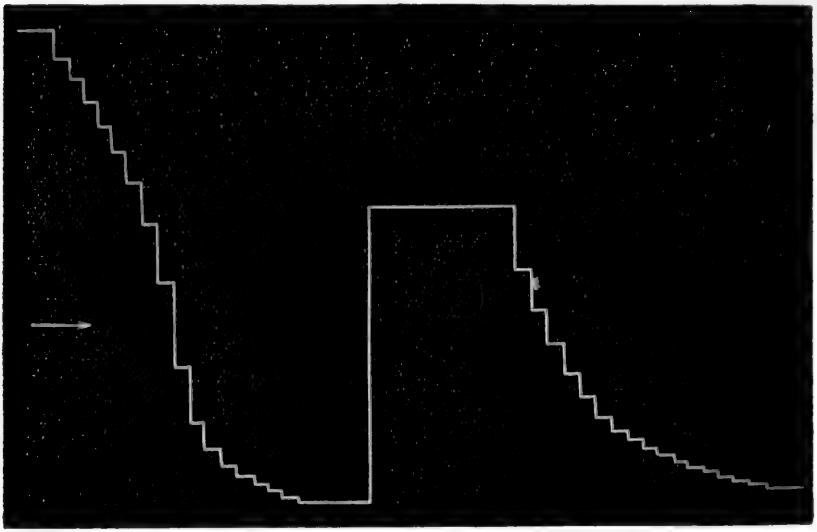


FIG. 8.—Carotid (ox), contracted. Transverse strip; 8 hours *p.m.* Second loading after $1\frac{3}{4}$ hours.

strips of cat, strips of lower portion of gullet—contracting on cooling and relaxing on warming. The relaxing effect of warmth is taken advantage of by the surgeon in passing catheters, &c.

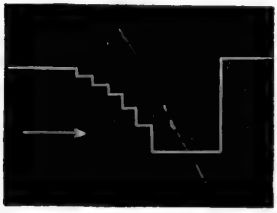


FIG. 9.—Elongation of contracted artery with rise of internal pressure, 0–300 mm. Hg. Length 16 mm.

The aorta and pulmonary artery contract much less than the carotid, for in them there is less muscle and more elastic tissue.

In the case of a relaxed artery MacWilliam — to whom we owe these observations—finds the greatest amount of extension is produced by the first addition of weight. Successive additions cause diminishing increments in length per unit increase of weight. In the early part of the process of stretching a contracted artery, the resistance is solely muscular; later, when the muscular resistance

has been so far overcome that the strip is stretched to what would be the normal length of a passive or relaxed artery, further stretching brings into play the resistance of the elastic elements and the extension curve then becomes like that of a relaxed artery. On repeating the stretching the curve is like that of a relaxed artery throughout. As the difference between contracted and relaxed arteries depends on the muscular element, it is much more evident when transverse rather than longitudinal strips are used. The increments of cubic capacity of relaxed arteries, just as of veins, when subjected to equal increments of internal pressure, is greatest at first, and successively diminishes as the pressure is raised. On repeating the distension a second time the relaxed artery is found to yield much more.

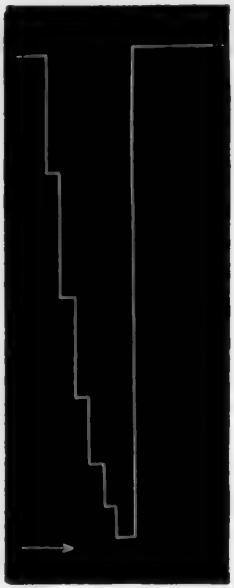


FIG. 10.—Elongation of relaxed artery with rise of internal pressure. Length 21 mm.

Contracted arteries, on the other hand, yield relatively little at first, and go on yielding with each increase up to very high pressure, but only very gradually. The distension of an artery whose muscular coat is thin augments up to a certain point, and then becomes less as the muscular resistance is wholly overcome, and the elastic elements come into play. Second distensions of contracted arteries cause much greater expansions. MacWilliam says that Roy's conclusion which has been generally given in the text-books—that maximum distensibility

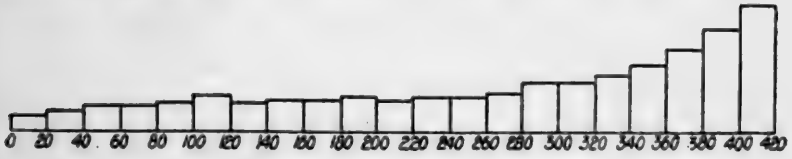


FIG. 11.—Carotid (ox), strongly contracted (48 hours *p.m.*). Increase in capacity on rise of pressure.

of arteries corresponds to normal blood pressure—was based on experiments with arteries more or less in a post-mortem state of contraction. Fully contracted muscular arteries and relaxed

arteries both give results wholly different to those of Roy. MacWilliam finds that there is a great tendency to elongation, in the case of relaxed arteries, when submitted to even low or moderate internal pressures. Prolonged and frequently recurring periods of relaxation tend, he says, to produce tortuous arteries; hence the tortuosity of the anastomotic arteries which dilate after the ligation of a main trunk, and of the arteries of the uterus and mammæ which develop so in size during pregnancy, and the extensive pulsation of arteries in inflamed parts. The pulsatile expansion of a contracted artery is very small at any pressure, and there is no evident difference in its amount at different pressures. Hence the assertion of the surgeon is explained, that there is no evidence of the transverse expansion of an artery when exposed and measured with callipers (Lister). On the other hand, the pulsatile expansion of a relaxed artery for a given pulse at 0 mm. Hg, 50 mm. Hg, and 100 mm. Hg is in the proportion 3 : 2 : 1. The measurements taken by Roy and others, which show the extensibility of arteries to be increased in pathological states, such as marasmus and phosphorus poisoning, in the light of MacWilliam's work, must be interpreted by showing that the muscular rather than the elastic elements are at fault, and that the power of post-mortem contraction is lacking. The extreme degree of contraction produced by exposure and manipu-

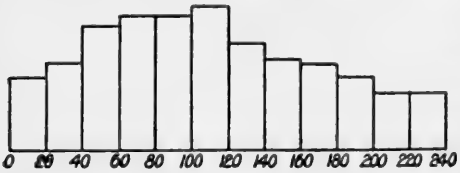


FIG. 12.—Carotid (ox), weak contraction (5 days *p.m.*). Increase of capacity.

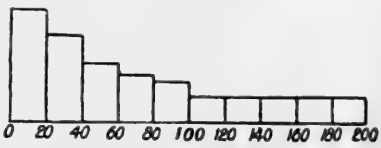


FIG. 13. — Carotid (ox), relaxed, having been kept in defibrinated blood for several days. Length (between ligatures) 14 mm. Increase of capacity.

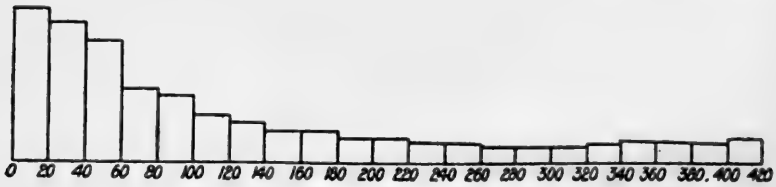


FIG. 14.—Second elevation of pressure in same portion of artery as in Fig. 12.

lation is of the greatest importance in stopping hæmorrhage from wounded arteries; the abolition of contractility produced by freezing explains the extra hæmorrhage which results after freezing has been used as a local anæsthetic for minor operations. The contraction of excised arteries, says MacWilliam, is excited by chloroform vapour and adrenalin, and abolished by sodium fluoride. It is a vexed question how far the extreme degrees of contraction, such as may be excited post mortem, may occur in living arteries in continuity under the influence of drugs, or in disordered states of metabolism. The view has been put forward that such contraction does occur, and that the arteries become so rigid in consequence of it, that serious errors arise in the reading of blood pressure by the accepted methods. It has been asserted that in cases where high readings of blood pressure have been recorded much of the pressure has gone in compressing the stiff walled artery.

The Arterial Pressure in Man

There are two methods at our choice for measuring the arterial pressure in man. The one, the method of obtaining the maximal oscillation and reading the pressure at which this occurs. The other, the method of finding the pressure at which obliteration of the artery occur and the pulse ceases to be felt. The instrument hitherto generally used is the armlet, independently invented by Riva Rocci and by Hill and Barnard, which consists of a rubber bag encased in soft leather. The rubber bag is connected by tubing and T piece to a syringe bulb and a manometer; the latter may be either a Hg manometer or some form of spring gauge.

Several forms of sphygmometers have been invented by v. Basch and others for application to the radial artery. Small rubber bags are used and connected with metal spring gauges. The graduation of such spring gauges alters with time, and the writer finds small bags cannot be applied so that the pressure always wholly reaches the artery. Some of it may go to distending the elastic wall of the bag or to distorting the surrounding tissues, and thus large and unavoidable errors arise with the use of these instruments. The rubber bag must be large enough to transmit pressure equally to all parts of the tissues in which the artery lies; then the tissues—protoplasm contains 80 per cent. of water—transmit the pressure equally to the artery. The bag must be

flaccid, and so closely confined by a rigid covering that *the pressure cannot be spent in distending its wall rather than in compressing the tissues.* The armlet satisfies all the requirements if it be large enough (20 cm. broad), and be bound round so as to *closely* fit the arm.

The writer has introduced a sphygmometer which gives the same readings as the armlet, and can be carried conveniently in the pocket. It consists of a flaccid rubber ball enclosed in a silk cover, and a gauge which can be carried in a case like that of a clinical thermometer. The gauge is formed of a glass tube closed at one end and having a hole in the side near the open end. If the open end be placed in water, the water meniscus rises as far as the hole in the side.[1] The rubber tube of the bag is then slipped over the gauge until this hole is covered. On now pressing the bag the meniscus rises up the gauge and compresses the air before it. The air acts as a spring, and the stem of the gauge is calibrated in mm. Hg by testing it against a Hg manometer. To use the instrument properly the bag must be only partially full of air, and must be entirely covered with the fingers and palm of the hand, and then pressed upon the radial artery, the thumb of the hand exerting a counter pressure against the back of the wrist.[2] The arm must be held at the same level as the patient's heart apex to eliminate the influence of gravity, and the radial artery must be felt with the fingers of the other hand, the second finger being employed to prevent the pulse regurgitating from the ulnar, while the first finger determines when the radial pulse disappears. The operator, when setting the index, holds the gauge by the solid glass end, so that his fingers may not heat the air within. The gauge when taken out of the pocket must be cooled to room temperature before it is used.

The instrument may be used, but not very easily, to obtain the maximal pulsation. To effect this as little air as possible must be used in the bag, and the bag must be closely confined to the hand. There is some debate as to when maximal pulsation occurs. According to Roy and Adami, and to Howell and Brush, it occurs when the pressure just exceeds the minimal or diastolic pressure as recorded by a Hürthle manometer connected directly with the artery. Hill and Barnard, however, found when the armlet

[1] If water gets into the side hole it must be blown out, or else the meniscus will not rise.

[2] The fingers grip the junction of tube and gauge and support the latter.

was placed round the neck of a dog, the maximal pulsation corresponded to about the mean pressure as indicated by a mercurial manometer connected with the femoral artery, and C. J. Martin supported this finding. If the pressure just exceeds diastolic pressure the artery should fill in systole and be emptied in diastole. It takes time to do this, and when the pulse is frequent and the pressure oscillations are large, not only is a very rapidly acting instrument required to follow accurately the pulses, but there may not be time for the full swing of the artery to be carried out. Thus in aortic regurgitation the maximal pulsation extends over a wide area of pressure. It is owing to this that divergence of opinion arises as to what the maximal pulsation indicates. The obliteration pressure, on the other hand, unquestionably indicates the maximal or systolic pressure, and the only error which can arise is that due to rigidity of arterial wall, if the instrument be properly used. v. Basch and C. J. Martin found that a sclerosed radial artery is collapsed by a few millimetres of mercury. The writer found the carotid of a child collapsed by 2 mm. Hg.

FIG. 15.—The Leonard Hill sphygmometer.

Herringham and Womack, investigating a number of arteries taken from the post-mortem room, found 4 to 18 mm. and in two cases 30 to 34 mm. The pressure required bore no relation to the age of the men from whom the arteries were taken; the varying amounts were probably due to post-mortem contraction, a conclusion which is confirmed by the fact that the two brachials in one case differed as much as 10 mm. Hg.

W. Russell and G. Oliver disbelieve the readings of the armlet method in the case of contracted and sclerosed arteries. Russell says he has felt arteries in life almost as brittle as glass, in other cases rigidly contracted. He thinks it impossible that the high

blood pressure, *e.g.* 250 mm. Hg, obtained, should be endured by the circulatory mechanism. As to the question of brittle arteries, in order that the obliteration method should fail, the artery must be rigid in the whole of its course enclosed by the sphygmometer. Rigid atheromatous patches with soft parts between would not disturb the readings. On inquiry among clinicians and pathologists the writer has not obtained from them evidence of the existence during life of such rigid contracted arteries as W. Russell describes. The post-mortem carotid of the ox, contracted maximally by mechanical irritation, feels as if it would require some pressure to obliterate it. What pressure is required the writer has not succeeded in ascertaining owing to the difficulty of putting the whole length of the artery which is enclosed in the gauge in a state of such contraction. G. Oliver finds in states of sclerosis considerable differences between the armlet readings and those obtained with his hæmodynamometer,—a metal spring gauge used with a small fluid pad on the radial artery,—and believes that the maximal pulsation index thus obtained is the safer guide because it necessitates, not the obliteration of the artery, but only the balancing of the pressure wave. Now the maximal pulsation method shows two maxima, one corresponding it is said to the diastolic pressure and the other to the pressure which obliterates the artery, *i.e.* the systolic pressure. The second maximum is produced by the pulse wave striking against the upper edge of the pad or bag, and diminishes when, as the pressure is lowered, the systolic wave just slips through the artery (Erlanger).

Oliver prefers this index to that of pulse obliteration. He gives readings taken from the arm and forearm, on the two arms of the aged, by the obliteration method, and adduces the variation of these as evidence that the method of obliteration is liable to error. Thus—

Woman Recumbent, 90 *Years old.*

Radial Hæmodynamometer Max. Pulsation Method.	Armlet Obliteration Method.	
Right side, $\frac{110\ S}{95\ D}$	Forearm, $\frac{130\ S}{95\ D}$	Arm, $\frac{140\ S}{95\ D}$
Left side, $\frac{110\ S}{95\ D}$	" $\frac{145\ S}{95\ D}$	" $\frac{180\ S}{95\ D}$

Woman Recumbent, 93 Years old.

Radial Hæmodynamometer Max. Pulsation Method.	Armlet Obliteration Method.	
Right side, $\frac{135\ S}{105\ D}$	Forearm, $\frac{175\ S}{125\ D}$	Arm, $\frac{190\ S}{130\ D}$
Left side, $\frac{135\ S}{105\ D}$	" $\frac{155\ S}{115\ D}$	" $\frac{180\ S}{127\ D}$

The writer, however, investigating the accuracy of small unenclosed sphygmometer bags, has come to the conclusion that they introduce grave errors. The pressure may not be transmitted by them to the artery, but go to displacing surrounding tissues, or to stretching the rubber bag. The bag must be big, must be flaccid, and must be entirely enclosed by a rigid casing, *e.g.* the hand, or leather cuff of the armlet. Oliver's hæmodynamometer appears to him not free from the errors which pertain to small unenclosed bags.

In seventeen out of the eighteen "diastolic" readings taken with the armlet cited by Oliver, the readings are almost the same (within 5 mm. Hg) on forearm and arm, or right or left arm. On the other hand they exceed by 15 mm. Hg, in all except one case, those taken by the hæmodynamometer. This suggests the inaccuracy of the latter instrument, for the maximal pulsation index of the armlet method has been tested against the blood pressure of dogs. The writer has found the systolic pressure of old people may vary with the different strokes of the heart, and in the young with emotional excitement, and as the obliteration method gives us the maximal stroke in any period, it is necessary to test the armlet method by having two instruments at once on the opposite arms, with two observers reading at the same time. Doing this Martin Flack and the writer have found the readings taken by the obliteration method to be the same, not only in normal people but in several cases of high pressure (180 to 230 mm. Hg) and of thickened arteries. They have also taken the pressure with one arm up and the other down, and found that the difference corresponds to the pressure of the column of blood separating the top of one armlet from the top of the other—top meaning the part next the shoulder. If the rigidity of the arterial wall came

seriously into play we should not expect this correspondence, for it is unlikely that the arteries on the two sides would be equally degenerated and rigid. It is also unlikely that they would be equally contracted, because an artery exposed to lessened blood pressure dilates, while to increased blood pressure it contracts. We should expect, therefore, the artery in the upraised arm to be less contracted than the other. In one case of aneurism they were quite unable to make these tests owing to the greatly varying inequality of the heart strokes. Tested on the thigh of dogs both the armlet and the writer's pocket sphygmometer gives the same readings as the opposite femoral artery taken directly with cannula and manometer.

The conclusion the writer has come to, then, is that the method is exact, when carried out with either the armlet or the large enclosed bag of his pocket sphygmometer, and that these are the simplest and best methods of testing the systolic arterial pressure in man. The first act of obliteration must relax the artery and make subsequent readings exact.

It has been suggested that during obliteration of such a large artery as the brachial, the general arterial pressure may rise, but no error arises thus, if two or three consecutive readings be taken. The readings should be taken when the excitement and novelty of the operation has passed off, as emotional excitement raises the pressure considerably. Thus the writer's pressure in the morning is 110 to 115 in the holidays, and 140 when teaching and working in the laboratory. He has observed the pressure to rise 10 mm. Hg on addressing a question to the subject. There is no advantage gained by reading the pressures nearer than within 5 mm. Hg, or in the use of complicated instruments for recording the maximal oscillations, such as that of Erlanger.

The average systolic pressure of the resting man according to a number of observations taken by H. J. Starling is—

15 to 40 years	119
41 to 60 „	142
61 and over	155

but some robust old men, he says, have pressures no higher than those of the young.

The writer has found the pressure to be as low as 80 mm. Hg in children; to be 80 to 110 in young adults; and to be no higher

in several active men, eminent in their walk of life and carrying some 60 years. Oliver gives armlet systolic readings of 135 in a man of 100 years, and 185 to 190 in a woman of 96 years, and says: "In women the pressures are generally 5 to 10 per cent. less than in men."

M'Cay of Calcutta says the pressure there varied between 83 and 118, and the average of a large number of observations was slightly over 100 mm. Hg (sitting position, arm level with heart). The low pressure there he attributes to the hot climate relaxing the cutaneous vessels. In the standing posture the arterial pressure is no lower, and may be higher, than in the horizontal posture, and this without more than 5 to 10 extra pulse beats a minute. In exhausted states the frequency of the heart may be 30 or 40 more in the standing posture, and yet the pressure be lower than in the horizontal position. The change of pulse frequency with posture is an excellent test of the vaso-motor tone.

The diastolic pressure in the small arteries, such as the phalangeal, has been measured by G. Oliver by applying a small bag (2·5 cm. × 9 cm.) round the third phalanx of the middle or ring finger or the second phalanx of the thumb, and raising the pressure till the maximal pulsation is obtained and felt by the patient. To obtain the systolic pressure the finger is rendered bloodless by squeezing a stout rubber ring over it as far as the lower edge of the bag; the pressure in the bag is then raised to over 100 mm. Hg, the ring removed, and the pressure lowered till the bloodless finger suddenly flushes (Gärtner). The lower range of readings so obtained by Oliver are $\frac{65-70\ \text{S}}{45-50\ \text{D}}$, the higher $\frac{80-90\ \text{S}}{60-70\ \text{D}}$. On the arm, he says, there is no difference in pressure between the brachial and radial arteries, but the pressure in the phalangeal artery at the level of the first phalanx is 10 to 25 mm. less, and at the level of the third phalanx the pressure is a little less than half that in the big arteries. Thus the fall is unnoticeable in the big, and rapid in the small arteries. In the latter too the systolic and diastolic pressure approximate more and more. The ingestion of food, according to Oliver, raises the arterial pressure in the distal area; the pressure in the last phalanx rises 15 to 20 mm. Hg within an hour of taking food, and then slowly sinks down again. Exercise raises the arterial pressure. In athletes immediately after races the writer found systolic pressures of 140 to 220 mm. Hg. The pressure falls markedly with over exhaustion. Thus after four

exhausting bouts of boxing the pressure fell from 160 at the end of the first bout to below 100, and rose to 130 after three minutes rest. Inhalation of oxygen, then, lowers the pulse-rate and raises the blood pressure, changes the respiration from the thoracic pressure to the abdominal type, and restores the vigour of the athlete. The heart seems to be poisoned by unoxidised products such as lactic acid during extreme efforts, and therefore the compressive action of the diaphragm is held in check (L. Hill and M. Flack). After exercise the brachial pressure falls, while the phalangeal pressure remains higher owing to vaso-dilatation and for some time particularly if the subject is heated by exercise (Oliver).

The Venous Pressure

Oliver presses the pad of his hæmodynamometer on a selected vein of the back of the hand placed at heart's apex level; next empties the blood by stroking it on past the next valve; then relaxing the pressure, notes the point when the vein just refills. The writer and M. Flack have tested the method by applying the armlet to the upper arm, and raising the pressure within it to say 60 mm. Hg. The pressure in the veins below the armlet must then rise to 60 mm. Hg. Employing small bags in accordance with Oliver's method to test the pressure in the superficial veins, they have found that they cannot be used accurately. A second armlet, however, can be so used. This is placed round the forearm, and the pressure raised above that in the veins, say to 70. The pressure in this is then relaxed till some selected vein above this armlet, which has been stroked empty up to the next valve, just refills; thus an accurate reading of the venous pressure is obtained. Employing the two armlets, they found the venous refilling pressure exactly corresponded to that in the upper armlet which was obstructing the venous return. A convincing proof of the general accuracy of the armlet method can be gained by this method thus—find the obliteration pressure for the brachial artery—say it is 150—lower the pressure to 145 so that blood can get through, and then find whether there is the same pressure, viz. 145, in the superficial veins. If so, it is clear the arterial reading is correct within 5 mm. They have done this in several cases, and in one where the arterial wall felt full of stiff sclerosed patches, and have found no evidence that the arterial wall influences the readings.

Another method of Oliver's is to place the hand, with the fingers extended, in the upright position and at the level of the heart's apex, taking care that the veins are not compressed by clothes or the posture of the arm. He then observes the veins on the back of the hand, and raising the hand until the veins just collapse, measures the vertical height of the veins above the apex of the heart. This measurement gives him the venous pressure in millimetres of blood. The method demands that the veins should be visibly distended, which may not be the case in a cool atmosphere. The venous pressure varies with warm or cold atmosphere, with posture and muscular effort, pressure of the arm against the body, pressure of clothes, &c., on the arm, and taking of food. When the veins of the hand are contracted down with cold, we cannot tell what positive pressure there is in the veins at the heart's apex level by either of the above methods. The veins contract down to the thread of blood which they receive when the atmosphere is cold, and dilate to hold a large volume of blood when brought into play as a part of the heat-losing mechanism of the body. The best demonstration of this is the network of superficial veins which become visible in a child in a hot bath, or a horse heated with work.

If the hand be held at such a level that the veins are just collapsed, and then deep and prolonged expiratory efforts or a succession of coughs be made (Oliver), they will be seen to swell, and this is owing to raised arterial pressure and little if at all to obstructed venous outlet (T. Lewis). Prolonged inspirations, on the other hand, cause the visibly swollen veins to vanish. The influence of posture is seen on holding the hand and arm still in the dependent position, particularly in a warm atmosphere, or after exercise, or food. The veins fill under the hydrostatic pressure, and the colour of the hand becomes bluish owing to the lessened velocity of blood flow. A dull feeling of pressure arises which is uncomfortable and causes one to move the part. Contraction of the muscles of the hand empties the blood in the capillaries and veins on past the valves, and so long as the hand is at work no distension or discomfort arises. If the hand be kept quite still at the level of the heart's apex little congestion arises. How much bodily movements further the circulation of the blood can be seen by alternately placing the hand dependent, and elevating it above the head, and observing how the hand

changes from the flushed to the blanched state. The vaso-constrictor control of the hand (for changes of posture) seems to be much less than that of the foot. If in a warm atmosphere foot and hand be lowered together from the heart's apex level and be kept still in the dependent posture, it will be seen that congestion arises much less quickly in foot than in hand, and the pressure in the veins on the back of the hand reaches the full gravity effect much sooner than in the veins on the dorsum of the foot. It is the same with the face. The parts always exposed to the atmosphere congest quickest. The control of course varies with the effect of external temperature on vaso-dilatation, as may be seen by plunging the hand and foot in iced or in hot water and then repeating the observation. The pumping action of the movements of walking may be observed very well on the veins of the back of the foot. Let the reader stand still with the feet bare, and observe the veins of his feet becoming prominent. If he bend to feel them he can estimate the high pressure within. Now let him take a few steps and observe the veins again. They are emptied by the movements, squeezed between skin and muscle, and feel soft for some little time until they fill again on standing still. Similarly the contractions of the muscles which occur with slight changes of posture empty the veins and prevent congestion when we sit working at a desk. It is the deficient flow or quality, not the pressure, of blood which leads to œdema, degeneration, distension of the venous wall, and varicose veins in those whose occupation requires them to stand for long periods of time. Some attention has been drawn to a curious hereditary œdema of the legs which commences about the seventeenth year. It occurs in members of certain families on standing, and is prevented by bandaging. The venous pressure is raised, owing to vaso-dilatation, by warmth, rest, sleep or food, together with the pressure in the arterioles as measured in the distal phalanx, while the pressure in the large arteries falls. The arterial and venous pressures in the arm are both raised during muscular effort, owing to increased ventricular output, splanchnic constriction, and local dilatation.

The Capillary Pressure

As much light can be thrown upon the principles which govern the circulation of the blood, from the comparative structure of

the vascular systems, the writer cites the following suggestive passages from the admirable Principles of Animal Histology of Dahlgren and Kepner, in which he underlines certain sentences which bear in particular on the arguments that follow.

"The main blood channel system itself has many differentiated regions. The region of thin-walled capillaries and lacunæ, the strong-walled conducting vessels, the blood-forming organs, and the muscular pumping stations or hearts . . . most specific of these portions are the capillaries and *lacunæ*, for it is here that the real work of the blood is accomplished, the exchange of material with the tissues. Here the walls of the vessels are thinnest or *even apparently wanting. In this case the connective tissue cells that surround the channel, while not differentiated into definite channel walls, act in that capacity, so that we cannot say that retaining walls are altogether absent.* The vessels of the periphery have in all cases a larger total cross section than any other total cross section in the circuit. This results in the surface of contact between blood and tissue being large enough to effect necessary exchanges of materials as well as making the circuit slower to give requisite time for such exchanges. The smaller but more numerous branches of the periphery unite to form large channels that serve to conduct the blood to other portions of the periphery, or to and from the central pumping stations, or to the blood glands. These vessels and the veins, together with the vessels carrying blood back to the periphery, the arteries, act as the long-distance carriers of the circulatory system, and their walls are usually very strongly constructed.

"The pumping region comprises one or more parts of the larger channel or channels that have acquired the power of rhythmic contraction. Sometimes this region occupies a considerable extent of the larger vessels. At other times it is found in a more specialised form, occupying only a short section of the tube, but very intensely developed. Such an organ is known as a heart. Both of the preceding conditions may be found together, as they are in the squid and other cephalopod molluscs where there are three or five separate hearts, and *in addition the larger parts of the arteries are also constantly engaged in driving the blood on its course by wave-like pulsations.* Other regions of the blood-channel system are found in which the walls are differentiated and in which the blood moves but slowly and *sometimes almost comes to rest.*

These form the so-called blood glands, and in them the blood is renovated by the removal of some of its old parts and the addition of other new ones or both."

"*The internal tissue of a Turbellarian worm is a loose aggregate of several kinds of weakly differentiated cells, known as parenchyme. These cells do not touch each other at all points, but are connected by strands, and in consequence there may be easily seen between them a great many spaces, known as the intracellular spaces, which are united into a large connecting system that extends throughout the body. This system of spaces is filled with a fluid, and this fluid carries the digested food materials, the oxygen supply for internal cells, the combustion products, and in every other way acts as a simple blood. This is the undifferentiated and unorganised form of blood-vessel system, and a sort of circulation must inevitably take place as a result of the ordinary movements of the animal's body. This grade of structure is to be seen in a number of the lower and simpler animal forms and sometimes as an accessory apparatus to several grades of complete blood-channel systems.*" In the several typical forms studied by Dahlgren and Kepner, the walls of the blood channels show a strong analogy based on the physiological (which are here mechanical) needs of the vessels. The blood fluid must be confined to the channels, and this is usually done by the single inner layer of cells, the intima. In some forms the intima is formed not by the cells themselves but by a cuticle which is the product of these cells (lobster, &c.). "The intima may alone confine the blood stream, or if the pressure is too great, it may be reinforced by the connective tissue cells that immediately surround it. *These cells develop their connective tissue as fibrils or plates or webs with which they bind and hold the vessel intact when the blood presses on its walls.* Again, these primitive mesoderm cells may develop into muscle cells that surround the channel and by their contractile strength cause it to pulsate and drive the blood on its course. The arrangement of these three classes of tissues to form the wall of the vessel falls, naturally, into layers, the so-called coats of the blood vessels. *Each kind of coat usually has a particular position with reference to the lumen. This position, however, is sometimes changed in the several groups for no apparent reason.* All these cells and the tissues that they form were probably not cells that were bound in the course of their development to become so specialised, but as far as can be told, they were such of the connective tissue cells as happened

to be in the course of the developing blood channel as it pushed its way among them, *and were developed in response to the needs of the vessel.*"

The first capillaries in the area vascular of the developing chick have their origin in the secretory activity of the cells which first form vacuoles and finally networks of capillary spaces. It is the functional activity of the cells which determines the rate of flow and pressure within, and finally the structure of the vessels and of the power of the heart. The increase in size of the lumen of a vessel, says Thoma, depends upon the rate of blood flow. Hence the dilatation of collateral pathways and establishment of efficient anastomoses which follows the ligation of a main artery. The growth in thickness of the vessel wall is dependent upon the diameter of the lumen of the vessels and the blood pressure. The tension in the circular direction of a tube is equal to the product of the pressure by the radius. The longitudinal tension is equal to half this product. The wider channels first formed in the area vasculosa thus develop into arteries; collateral capillaries develop into arteries when a main artery is tied; and the thyroid vein develops the structure of an artery when the central end of the carotid is joined end to end on to it.

Thoma states that at all points where the transverse sectional areas of the lumina of the arterial trunks has been investigated the sum of the sectional areas of the main trunks is equal to that of their branches. Thus the sectional area of the ascending aorta equals the sum of that of the two carotids, and subclavians and the descending aorta, together with such smaller branches as were given off above the place of measurement. Similarly the sectional area of the abdominal aorta taken 2 cm. above its bifurcation is equal to that of the two common iliacs and the smaller branches. The same law holds good, Thoma says, in the case of the arterioles of the tongue or web of the frog. As, he says, the transverse section of the main artery is equal to the transverse section of all its branches, the average rate of flow is the same in all arteries, and the quantity flowing through the transverse section of any artery in a given time is proportional to the section of the artery. This law only holds good so long as disturbing influences due to vaso-dilatation and functional activity are in abeyance.

That the ramification of the small arteries is homonomous

is proved, says Thoma, by the microscopic observation of the axial stream. The stream of corpuscles moves so fast that it appears either completely homogeneous or faintly striated, both in the artery and its branches (excluding the capillaries), and thus must be flowing at the same rate, for the slightest diminution alters the homogeneity. When the tongue of a frog is drawn forward from the mouth of a curarised frog and pinned out for examination, there follows at first considerable deviation from homonomous ramification, owing to injury and local dilatation. Half-an-hour later the tongue is hyperæmic, but the flow is again of the same rate in all the arterial ramification.

The generalisation follows on these observations of Thoma that the total cross sectional area of the arterial ramification measured at any place is the same,[1] and that the sudden increase occurs in the ramification of the capillaries, so that the rate of flow is lessened therein from 500 mm. to ½ mm. or less a second. This important generalisation, so opposed to accepted teaching, requires confirmation or refutation.

The capillary system in the tissues of man is like the blood channel system of the Turbellarian worm, a vast system of tissue spaces lined by cells which confine the corpuscles, and by shrinking or swelling and by varying osmotic state regulate in part the outflow and inflow of lymph. These cells are capable of phagocytic action and of dividing and producing the primary type of leucocyte. The arteries deliver the blood to these spaces, and many or few of them are filled at any moment and in any tissue according as the arteries dilate and increase the supply, or the venous flow is impeded by gravity or external pressure. It is absurd, therefore, to calculate the size of the capillary bed from the relative velocity in the aorta and in the capillaries of a transparent membrane.

The cells both of the tissues and the capillaries swell or shrink under the influence of the solutions which bathe them, and thus alter both the volume of the organ and the capacity of the vascular system which is included in it. The tissue cells adapt themselves slowly to altered osmotic conditions of the tissue fluids, and do not by any means come into equilibrium with them. With the return to normal physiological relations the recovery of the normal concentrations of the cellular contents is rapid and complete. The influence on the capillary circulation of osmotic and surface

[1] Supposing the state of constriction to be the same.

energy can be no less than that effected by the heart and vasomotor system, and is, probably, as important in controlling the flow of blood. In the active conditions of life the contents of the capillaries are continually being emptied onwards by the contractions of the skeletal muscles, pressure against external bodies, and the influence of gravity in changes of posture. The capillary system is as a sponge squeezed and filled continually by the active motions of the body. The attempts which have been made to estimate capillary pressure have all been made on transparent membranes in the motionless animal fixed in the horizontal position, or on man's skin with the part fixed, immobile during the observation. In the animal microscopic observations have been made by Roy and Brown on the frog's mesentery, the capillaries being compressed by a sheet of transparent peritoneal membrane which formed the base of a glass capsule, in which the fluid pressure could be made greater or less. A pressure of 100 to 250 mm. H_2O sufficed to stop the circulation in the capillaries under these conditions, while a pressure of 200 to 350 mm. H_2O expelled the blood from the arterioles. When the heart was inhibited the pressure sank to 0, rising again to 70 to 100 mm. H_2O as the veins filled. The anæmia so produced was followed by hyperæmia and increased pressure.

Measurements of capillary pressure have been made on man by v. Kries, v. Recklinghausen, and others, the method being the finding of that pressure which just blanches the skin. V. Kries weighted a glass plate 4 sq. mm. big placed behind the finger nail. He found 0·25 grm. was the smallest difference which produced a visible effect. Now as 1 grm. equals the weight of 1 c.c. of H_2O, and $\frac{1 \text{ c.c.}}{4 \text{ sq. mm.}} = \frac{1000}{4} = 250$ mm., the error of observation would be $\frac{250}{4 \text{ sq. mm.}} = 62{\cdot}5$ mm. H_2O, a very large one considering the smallness of the pressure measured. H. W. Recklinghausen places a small flaccid rubber bag on the skin, through the centre of which he has punched a hole. He moistens skin and bag with glycerine, and covers the hole with a glass slide, holding it so as to make an air-tight junction between bag skin and glass, and then through a side tube blows air into the bag until the skin blanches. A manometer connected with the side tube gives the pressure. *These methods necessitating the fixation and immobility of the part, cannot be applied rapidly, and therefore do not give the capillary pressure*

under ordinary conditions. Moreover the pressure so applied is spent largely in deforming the horny convex plate of the epidermis, and in the case of v. Kries' method the size of the horny layer which is depressed is much larger than the square glass plate. This can easily be seen by taking a set of broom bristles and fastening them to matches in lengths of about an inch, and then finding the bristle which will just blanch the skin when pressed on it till it bends. It can be seen that the bristle depresses a horny plate selected, say, on the back of the hand, much larger than its own sectional area. If some of the horny layer be carefully removed with a razor (without producing hyperæmia) a weaker bristle will effect the blanching. Observations of this kind show that these methods are too inaccurate to use as a measure of capillary pressure ; nor can they be used to give exact comparative differences of pressure under varying conditions, for the error cannot be taken the same all through. V. Kries found that the blanching pressure at the root of the nail did not give the full gravity effect on change of posture. Here the time of fixation in any posture is an important and undetermined factor.

Difference of Level of Finger from Top of Head in mm.	Pressure in mm. H_2O.
0	328
205	397
490	513
840	738

Lewy has calculated the pressure required to overcome the resistance in the capillaries from the known facts concerning pressure, velocity, and the viscosity of the blood. The average length of the capillaries is 0·4 to 0·7 mm., their radius 0·0045 mm., and velocity 0·5 to 0·9 mm. per second. There flows per second through a capillary a quantity varying from $\pi \times 0{\cdot}5 \times 0{\cdot}0045^2$ up to $\pi \times 0{\cdot}9 \times 0{\cdot}0045^2$ c.c. From the Poiseuille formula—determined for flow in capillary glass tubes—$Q = K \times \frac{d^4 h}{l}$, where Q = the quantity per second, h the pressure difference between beginning and end of tube, d the diameter and l the length of the tube, and K a constant representing the coefficient of viscosity, from this formula Lewy calculates h to be equal to 10 to 150 mm. of blood. The mean arterial pressure being taken as 115 mm. Hg or 1500 mm. of blood the fall of pressure in the capillaries is $\frac{1}{150}$ of this

at the least or $\frac{1}{10}$ at the greatest estimate. So wide a difference makes the calculation of little value except as an indication of the fact that there is little resistance in the capillaries. In making such estimates the velocity of flow in the capillaries is observed in their membranes with the animal motionless and in the horizontal posture. We have, moreover, no reason to think that the same laws hold good for glass tubes and the living capillaries. The cross section of a capillary 10 μ in diameter is some $\frac{1}{12500}$ sq. mm., the outflow per second will be $\frac{1}{12500} \times \frac{1}{2}$ if the velocity is 0·5 mm. per second, or 1 c.mm. in about six hours, or 1 c.c. in 250 days (Stewart).

The writer has measured the capillary-venous pressure in the brain by finding the pressure which just overcomes the pressure with which the brain bulges into a trephine hole. The "brain pressure" is due to the blood pressure in the capillaries and veins which is left over after the resistance in the arteries has been overcome, and distends the brain substance. When the circulation ceases the brain collapses away from the trephine hole and no longer exerts any pressure. The intra-cranial pressure cannot be greater than that in the pial veins, for otherwise these would be obliterated, and the pressure within them must then rise to the intra-cranial pressure. Observation can be made by screwing a glass tube into the trephine hole, the tube being filled with water and closed by a flaccid thin rubber membrane at the brain end, and connected to pressure bottle and manometer at the other end. An air bubble is introduced into the glass tube to mark the zero pressure. When the tube is put in place, the air bubble is pushed outwards, and on raising the pressure bottle and pushing it back to zero the "brain pressure" is balanced and the manometer indicates its amount.

In the horizontal anæsthetised animal the "brain pressure" is about 100 mm. H_2O, sinking even to 0 in the vertical head up position, and rising considerably in the vertical head down posture. The capillary pressure in the brain varies proportionately with the rise and fall of vena cava pressure—time being granted for the capillaries to follow the alteration of venous pressure. The brain pressure does not follow in exact proportion alterations of aortic pressure, because between the capillaries and the aorta is placed the varying resistance of the arterioles. The cerebral venous pressure can be measured by inserting a tube into the torcular Herophili, and the pressure of the cerebro-spinal fluid (the lymph

of the brain) by inserting a tube through the lamina of the axis. The brain pressure, the cerebral venous pressure, and the cerebro-spinal fluid pressure are one and the same.

The writer has also measured the capillary-venous pressure in the eyeball by the same method, inserting a hollow needle into the aqueous. The globe formed by the corneo-sclera is analogous to the rigid case formed by the skull because its internal capacity is strictly limited, and cannot be increased. The intra-ocular pressure, like the intra-cranial, is purely circulatory in origin and represents the capillary-venous pressure within the eye. The venous sinus of the canal of Schlemm, according to Thomson Henderson, is formed of tributaries from the whole anterior portion of the uveal tract, and it thus offers the lowest pressure with which the aqueous humour comes into direct contact, just as the pial veins, where they pass into the sinuses, offer the lowest pressure to the cerebro-spinal fluid. The intra-ocular fluid, just like the intra-cranial, transmits pressure equally in all directions, and therefore when its exit is diminished the tension rises, and the whole of the elastic intra-vascular system tends to be converted into a rigid one.

Koster has proved experimentally the unyielding nature and rigidity of the globe under conditions of increased intra-ocular tension. If the internal pressure were raised from 19 to 70 mm. Hg, the increase in volume of the globe was only $\frac{7}{1000}$ of the original volume.

In the globe of the eye the capillary-venous pressure is the intra-ocular pressure. The intra-ocular pressure in fact equals that in the venous sinus of Schlemm's canal, just as in the skull the pressure of the cerebro-spinal fluid is equal to that in the pial veins.

Supposing the intra-ocular tension, owing to the increased secretion of the ciliary process, rise above the pressure within Schlemm's canal, then the pressure of the aqueous will obliterate the wall of the sinus until the venous pressure rises within it to that in the aqueous. Similarly, supposing by increased secretion of the choroidal fringes in the brain the pressure of the cerebro-spinal fluid rise above that in the pial veins, then these would be obliterated until the pressure of the blood within them rise to that of the cerebro-spinal fluid. Actual measurements show that the pressure of the cerebro-spinal fluid and of the cerebral venous pressure are the same.

If the arteries dilate in the brain or eyeball, room must be made by increased outflow of cerebro-spinal fluid—or aqueous—or by narrowing of the veins, or by both means. Probably each pulsatile expansion of the arteries helps to drive a little of the cerebro-spinal fluid or aqueous into the veins, and thus the effective circulation of these tissue lymphs is maintained. Each pulsatile expansion of the arteries also causes a pulsatile expulsion of venous blood into the venous sinuses and thus helps the circulation. A rise of arterial pressure accompanied by expansion of the arteries of the brain or eye, cannot compress the veins so as to produce venous congestion or stasis, for the pressure transmitted through the walls of the arteries must always be less than the pressure transmitted directly through the blood within the vessels. The veins are narrowed to compensate for the expansion of the arteries until the whole system becomes more like a rigid system, and the velocity of flow is increased, less of the head of pressure being spent in overcoming the resistance in the arterioles, more going to the kinetic energy of flow. Experimental observations show that the outflow is always increased by a rise of arterial pressure.

In pathological states the intra-ocular or intra-cranial pressures are often increased. Such increase is entirely circulatory in origin. In inflammatory states the toxins produced by bacteria on the one hand dilate the blood-vessels, and on the other hand alter the metabolism of the tissues, and increasing those cell products which are crystalloidal in character, thus raise the osmotic pressure. The tissues swell, and the blood pressure rises, keeping pace with the pressures of the tissue lymph. The swelling must be at the expense of the blood supply of other surrounding parts, where there is no toxin to excite and no vaso-dilatation or œdema. The anæmia so produced may in its turn damage the tissue metabolism of these parts, and set up congestion and œdema therein, and thus a vicious circle may be established. Relief is obtained by opening or softening the confining capsule, and so allowing free flow of blood and free exudation of lymph through the inflamed part. The lymph brings with it neutralisers of the toxins, the phagocytes and their opsonins, the chemical repairers of disordered cell metabolism. If the products of tissue damage are successfully removed by the increased flow in the surrounding dilated vessels the whole mischief subsides, and the killed tissues are removed and replaced by growth of scar tissue. During inflammation of such an organ as

FIG. 16.—Transverse section of marrow of femur of normal rabbit and of one infected with pneumococcus (Carnegie Dickson). Note in the latter the greatly congested vein and its tributary capillaries. The author has borrowed these figures to show how large a transference of substance from tissue into blood-vessels may take place.

the brain or bone marrow the amount of blood can be enormously increased by the transference of tissue fluid and tissue substance from the tissue cells into the blood channels.

The way in which increased tension may arise can be illustrated by a consideration of the cause of glaucoma of the eye.

In glaucoma the cribriform ligament is sclerosed, and by walling in Schlemm's canal prevents the free circulation of the aqueous humour which is necessary for the proper metabolism of the eye. When the cribriform ligament is sclerosed the aqueous has to get away mostly by the veins of the iris through the iris crypts, and thus it comes about that atropine induces an attack of glaucoma by dilating the pupil and closing the orifices of the crypts of the iris. Iridectomy, on the other hand, relieves glaucoma by opening up new channels for escape of the aqueous, as the surface of the iris never scars up, but remains open and unaltered after it has been cut (Thomson Henderson).

The œdema of the tissues of the eye which occurs in glaucoma may be ascribed to the deficient circulation of aqueous, leading to altered metabolism and increase of osmotic pressure. The congestion of the blood vessels must be also set down to the irritant effect of the products of disordered metabolism. A rise of general vascular pressure may, it is said, precipitate an acute attack of glaucoma; probably by increasing the secretion of aqueous; this finds room at the expense of the veins which are narrowed, *i.e.* the absorbing surface; the excess of aqueous cannot escape again when the general pressure falls, and thus the tension of the eyeball remains heightened, the circulation in the eye lessened and the mischief increased.

The conditions which hold good for the eye and brain also apply in part to the limbs enclosed by the skin, and to the other organs, such as the kidney, which are enclosed in capsules. The writer and M. Flack estimated the capillary pressure in man by pushing a hollow needle into the subcutaneous tissue of the arm or leg, and connecting this with a glass tube containing an air bubble, and the tube with an Hg manometer and a pressure bottle. The air bubble indicates when the pressure is sufficient to overcome the capillary pressure and drive the water in, and as the subject feels the smart of the water, he can give a confirmatory signal. The observations made in this way showed that a pressure of 10 to 20 mm. H_2O was sufficient to overcome the capillary

pressure in the arm placed at the heart's apex level. In the leg at a level 380 mm. below the arm 90 mm. H_2O sufficed, giving a difference of 70 mm. H_2O against a gravity difference of 380 mm. H_2O. On supplying the armlet and raising the pressure in it to 910 mm. H_2O, the capillary pressure in the forearm rose to 45 mm. H_2O, at a time when the venous pressure had risen to that in the armlet. On another occasion it was 57 mm. H_2O, and in the armlet and veins 910 mm. H_2O.

These observations only prove what any one can feel for himself by holding a limb motionless and dependent for some time and then estimating with his finger the pressure in the veins and the capillary areas of the skin. Every movement that occurs under the varying conditions of active life squeezes on the capillary and venous blood. The tissues and pressure sense organs are thus protected from any great increase of vascular pressure. After an area of capillaries has been squeezed empty, the blood pressure for a time must be nil within it. The blanching effect of clenching the fist demonstrates this. Thus in spite of the hydrostatic pressure due to gravity, equal to 140 mm. Hg in a man six feet high standing vertical, in spite of this the same bristle will blanch the capillaries of his feet and hand, so long as he does not keep the parts for long immobile, but by contractions of his muscles every now and then expresses the blood from the capillaries onward past the venous valves. The vaso-motor system by constricting the arterioles—the arteries constrict of themselves to increased pressure—prevents over rapid filling of dependent parts, so that it takes some little time for the dependent and warm *immobile* hand to become greatly congested, and still longer the foot, while in a cold atmosphere, owing to vaso-constriction, congestion is only very slowly produced by the dependent posture.

So that while arterial and venous pressure in a relaxed limb exactly follow the variations of hydrostatic pressure on change of posture, the capillaries do not. Likewise on obstruction of the veins, while the venous pressure rapidly rises to the pressure of the obstructing armlet, the capillary pressure rises only very slowly. This fact which seems at first sight contrary to physical laws, in that the pressure is high in the artery which feeds and in the vein which drains but not in the capillary area which joins together the two, this fact is explained if we suppose that the capillary bed is a sponge work emptied by every movement, and

taking time to fill up again, and that there are wider channels connecting the arteries and veins through which the pressure is transmitted to the veins. The existence of such wide channels is recognised by histologists. Inspection of the hand and foot when kept still, and held first in the dependent, and then in the horizontal position, when held in the dependent position and before and after contracting the muscles of the part (*e.g.* clenching the hand), teach the enormous importance of movement in maintaining the circulation of the blood.[1] Muscular exercise, by increasing the combustion of food stuffs, and by furthering the circulation of the blood, and so elimination of tissue waste, is the greatest source of vigorous bodily and mental health.

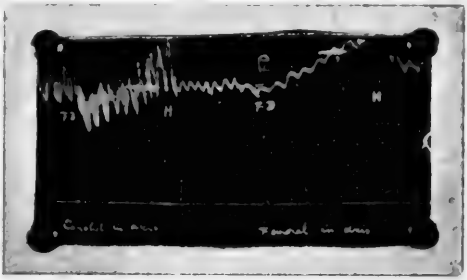


FIG. 17.—Arterial pressure recorded in carotid and in femoral artery, each artery in turn being placed in the axis of rotation of the animal holder. H, horizontal; F, D, vertical feet-down posture. The difference between the pressures in this posture was equal to the column of blood separating the two arteries. Note increased action of respiratory pump.

Standing erect and with a leg relaxed the arterial and venous pressures in this leg become higher than those in the arm by the column of blood separating the two points of measurement. In students hanging head downwards by their feet, M. Flack and the writer found the arterial pressure in the arm little altered from the normal taken in the horizontal posture. Thus—horizontal, brachial 126, post-tibial artery 126; standing, 140 and 204; head down, 116 and 42. The pressure in the circle of Willis was about 20 mm. less than in the brachial in the standing, and about 10 mm. more in the head-down posture. Now the column of blood above the point of observation is then in the six foot man almost equal to the normal arterial pressure taken in the horizontal position. The heart by lessened output and the vaso-motor mechanism by increased dilatation can compensate for this hydrostatic pressure, and it is clear that the heart and brain are so protected from a greatly increased arterial pressure. In the standing

[1] Butchers say it is easy to bleed all the tissues of an ox if it is pole-axed after being driven off the road into the yard, but difficult if it has lain down for some hours.

posture the column of blood in the vessels of the limbs can be broken up into segments by muscular action, and the blood permitted to circulate by alternate and appropriate contraction and relaxation of the muscles. A most important and hitherto almost unexplored reflex mechanism is here engaged, a mechanism in which the skeletal muscles and the muscular wall of the arteries each take a part, and in which sensory "receptors" are engaged, tuned in sensitivity to capillary blood pressure.

To sum up then, the function of the heart is to drive the blood into the capillary bed, the function of the arterioles is to regulate the distribution and switch the current on to one or other part of the capillary bed and limit the pooling of the blood under the stress of gravity; the function of the skeletal muscles and respiratory pump, aided by the valves in the veins, is to drive the blood back from the capillary bed to the heart, to prevent hypostatic congestion, and to act as a pump to the vascular system of no less importance than the heart. The respiratory pump even may drive the blood through the right heart and lungs.

The Action of the Respiratory Pump

The writer's argument that the circulation is largely maintained by bodily movement and varies continuously with every change of posture and muscular contraction, and is liable to an extent which defies analysis in the living active animal, is borne out by recent researches of T. Lewis on the effect of respiration on the blood pressure of man.

To determine this on man the sphygmograph can be used, but it must not be fixed by a band encircling the wrist, because this entails a serious fallacy due to the swelling of the volume of the arm. A sphygmograph applied with a band acts like a plethysmograph. T. Lewis fixed the sphygmograph by a suspension method and controlled the results with a sphygmomanometer. The effect of pure intercostal or pure diaphragmatic breathing in a trained subject he found to be as follows :—

	Inspiration.	Suspended Inspiration.	Expiration.	Suspended Expiration.
Thoracic . .	−	+	+	−
Abdominal . .	+	−	−	+

If both abdomen and chest participate in the breathing, intermediate results will be obtained,—one effect will counteract the other; and if abdomen or chest do not participate to the same relative extent during different instants of a particular act, complex curves will result which are beyond analysis. When a patient is asked to take a deep breath, the breathing is often disorderly

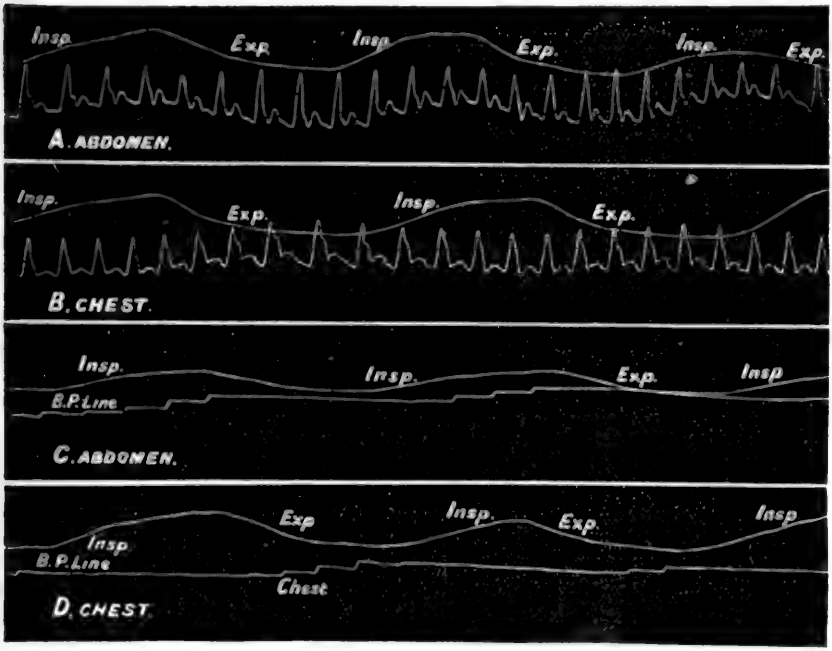


FIG. 18.—Influence of chest and abdominal breathing on the pulse (Lewis).

in character, starting perhaps as intercostal and finishing as abdominal.

In man a deep intercostal respiration, if not prolonged, yields a fall of pressure, and conversely a deep diaphragmatic inspiration yields a rise. But as the normal respiratory curves of blood pressure are of very complex origin, and the different factors involved vary widely, it is not possible to state what the effect on blood pressure will be, unless the conditions and nature of the respiratory act are known. The ordinary statement in the textbooks that inspiration raises and expiration lowers blood pressure is altogether unjustified by the records. The pressure almost

always falls when the patient is told to take a deep breath, and thus what has been termed the pulsus paradoxus and considered of pathological import, turns out to be quite a normal event.

In animals, says Lewis, under deep anæsthesia, the abdomen plays no part in the production of respiratory curves. The inspiratory rise is due to the lessened pressure in the pericardium and consequent increased filling of the heart. It is abolished by allowing free access of atmospheric air to the pericardial sac. The varying intra-pleural pressure affects intimately the filling of the heart, while its influence on the resistance and capacity of the pulmonary vascular area is a matter of assumption rather than of experimental proof. We are at present, says Lewis, justified by experiment in ascribing the inspiratory rise in animals on intercostal breathing to the effect on the heart only.

Tigerstedt found that ligation of the vessels of the left lung, out of thirty-one observations, produced in eighteen no noticeable effect on the output per second of the heart. In eleven cases it produced a decrease of 6 to 10 per cent., and in two cases a decrease of 18 to 20 per cent. In twenty-three cases the arterial pressure was unaltered by this operation, in seven it was decreased 6 to 10 per cent., and in one case over 10 per cent. Thus the pulmonary circuit can be shut off to a very large extent—at least in the animal with artificial respiration—and the remainder suffice to deliver an unlessened quantity of blood to the heart. Tigerstedt's observations also show that the arterial pressure may sometimes remain constant when the output of the heart varies considerably; the explanation of this is that the arterial system contracts down on the blood that it contains.

In Valsalva's experiment—a deep expiration with the mouth and nose shut—the abdominal pressure rises very greatly, and this is the chief cause of the rise of arterial pressure which then occurs. If a stiff-walled rubber tube is used as a rectal sound, and is connected to a manometer, an estimate of intra-abdominal pressure may be obtained, and this can be compared with the expiratory pressure obtained by expiring against a mercurial manometer. In one case the rectal pressure rose to 94 mm. Hg, and the tracheal pressure to 87 mm. Hg. The same conditions occur in coughing.

In deep abdominal breathing the rectal pressure may rise to 30 mm. Hg, and frequently shows a range of 20 mm. Hg, a fact

which shows what an effect such deep breathing has both on the return of venous blood and on the resistance in the splanchnic area. The action of abdominal breathing on the return of venous blood may be easily demonstrated by opening the thorax of a cat just above the diaphragm, and cutting a hole in the vena cava inferior. With each descent of the diaphragm the blood spurts out. The muscles of the abdomen and the levator ani support the abdominal pressure, and the avoidance of prolapse of the viscera depends on the proper exercise of these muscles and on the presence of an adequate amount of fat in the belly.

Effect of Mental Work and Emotion

In curarised animals excitation of the cortex cerebri in the motor areas of the limbs and trunk muscles raises the arterial

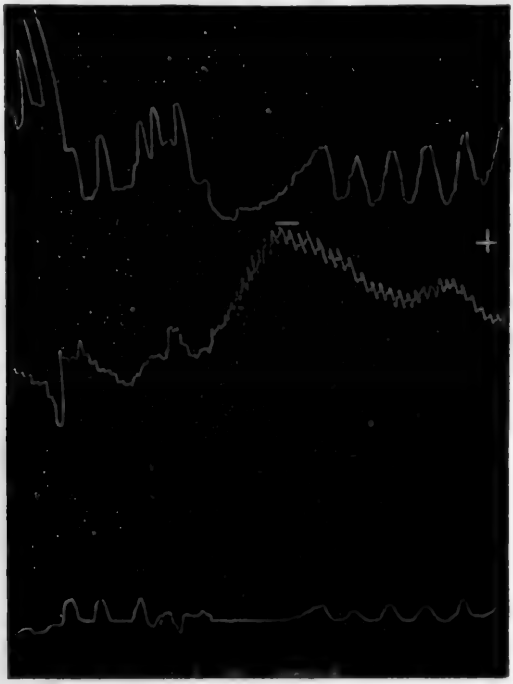


Fig. 19.—1, Volume of abdominal organs; 2, volume of arm; 3, respiration; +, pleasant; ,– unpleasant taste.

pressure, by causing contraction of the splanchnic area, and dilates the blood vessels of the limbs. Dilatation of the splanchnic area

similarly is accompanied by constriction of the vessels of the limbs. The cortex discharges motor impulses and alters the circulation in accordance with the needs of the moving parts. E. Weber has recorded in man the volume of the arm by means of a plethysmograph, and the volume of the abdominal organs by a rectal sound with balloon attached to the end of it, the sound

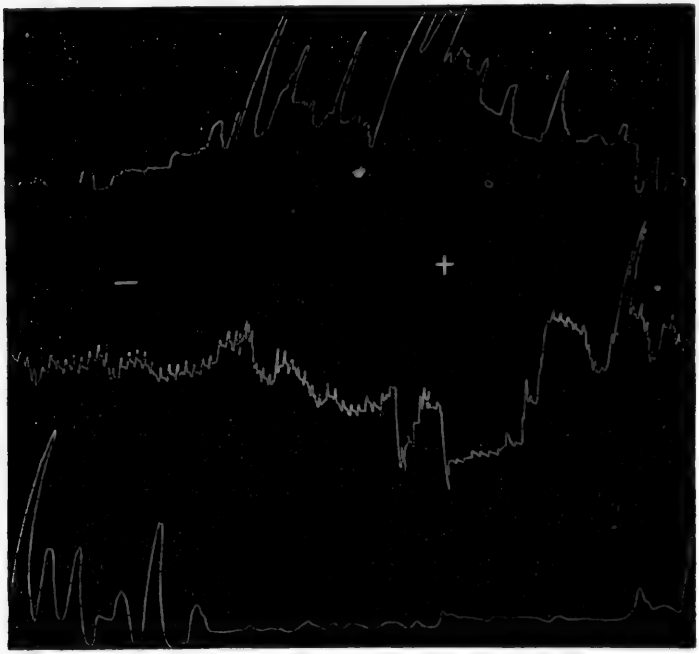


FIG. 20.—1, Volume of abdominal organs; 2, volume of arm; 3, respiration. From — to +, suggestion to hypnotised subject of his execution.

being connected to a strong tambour. He also has repeated Mosso's experiment of placing a man in the horizontal posture on a long balanced board and seeing whether the head or feet end becomes heavier in different emotional states. Weber put the abdomen mostly on the foot side of the axis, instead of on the head side as Mosso, and balanced by weights on the head side. He found that mental work and painful emotions determine blood to the abdomen, while pleasurable ideas and those of active movement send blood from the abdomen into the peripheral parts.

Pleasurable feelings are accompanied by relaxation of the muscles of the limbs and dilatation of the vessels of the limbs—*relaxation* in contrast to the strained taut condition of *work*. It is not the brain, as Mosso supposed, but the belly within which the blood collects during mental effort. The brain, limited in its expansion by the rigid cranial wall, contains a quantity of blood which can vary but little, except when the tissues of the brain actually lose or gain water, and so shrink or swell. Rise of arterial pressure produced by the contraction of the splanchnic area does not expand the brain so much as increase the proportion of arterial blood to venous blood within it and accelerate the velocity of flow. In muscular exercise the limbs receive more and the venous cistern in the abdomen contains less. The stagnation of the blood in the abdominal veins and liver during mental work and the sluggish circulation caused by the arm-chair posture must have a direct bearing on the irritable dyspepsia of brain-workers. Was not Thomas Carlyle cured of his by horse riding? Exercise sweeps the body clean of unoxidised food stuffs by the swirling current of blood and the greatly increased rate of metabolism. The breathing volume of a boxer after a three minutes bout may go up from the resting volume 9 to 40 litres per minute. How the muscles must squeeze the blood in his organs and drive it to the right heart!

The Filtration Hypothesis

In the explanation of physiological and pathological processes capillary pressure has been since the teaching of Ludwig constantly evolved as a *deus ex machina* for producing filtration. Thus the glomerular capillaries have been generally supposed to filter water and salts into the renal capsules under the pressure of the blood, which is supposed to be higher than that of the urine in the renal tubule. Similarly in dealing with the formation of lymph, filtration by capillary pressure is supposed to be an important factor, by a school of physiologists of whom Starling and Cohnstein in the past have been chief exponents. Dropsy and œdema, such as occur in cardiac incompetence, have been attributed to filtration brought about by increased capillary pressure; an altered permeability of the capillaries being admitted as an accessory pathological factor in the explanation of the fact that increased vascular

pressure does not *per se* produce œdema in the healthy tissues. To show to what an extreme limit this view may be carried, the following example may be cited. Asher, a chief opponent of the mechanical theory of lymph formation, has sought to overthrow it by a number of ingenious experiments, of which the following is one. He injected into the vein of a dog a concentrated solution of sugar, and immediately killed the animal. The lymph flow from the thoracic duct was measured, and this, in spite of the animal being dead, increased from 4 to 37 c.c. per 10 minutes. In this case, says Asher, there can be no question of a filtration pressure because the animal is dead and the circulation at an end. In an argument upholding the filtration hypothesis, Bainbridge suggests, however, that the sugar, by raising the osmotic pressure of the blood, drew water from the tissues into the blood, and thereby increased the volume and the mean (residual) hydrostatic pressure in the vascular system. "The capillary pressure after death will therefore," he says, "be unusually high, and there will be an excessive transudation of lymph, so that on analysis, the experiment is seen to support, rather than to oppose, Starling's views."

Now to make the mechanical theory possible we must suppose that the blood is driven through a system of rigid tubes with a sieve-like structure. If water be driven under pressure through a coil of hose which leaks, and the coil of hose be sunk in a tub of water, then it is true water will filter through and the tub will overflow. But in an organ of the body the conditions are quite otherwise, and an effective filtration pressure cannot exist because, as the writer has proved in the case of the brain, the blood in the capillaries, the tissue cells and lymph are at one and the same pressure, viz. the capillary-venous pressure.

Let us take the example of the salivary gland. Asher has pointed out that while lymph flows in increased amount when the gland is thrown into secretory activity, from an atropinised gland no lymph flows when the chorda tympani is excited, although the arteries dilate, and the capillary pressure is raised. Here is an experiment, he says, which is against the filtration hypothesis, for capillary pressure is raised and yet lymph does not flow. The experiment may prove Asher's chief contention, that it is functional activity with the consequent production of metabolites of high osmotic pressure which determines the flow of lymph, but is not

required to disprove the filtration hypothesis because the conditions are the same both in the resting and the excited gland, in as far as the whole of any lobule of the gland must be at the same pressure, and therefore no filtration pressure exists in the one state more than in the other.

The gland is composed of a connective tissue framework, holding together tubules full of secreting cells, whose protoplasm contains some 80 per cent. of water, the tissue spaces surrounding the tubules are full of lymph, the capillaries of blood, and the tubules of saliva. The wet films of protoplasm which form the walls of the tubules, the capillaries, and the lymphatics, may act as colloidal surfaces separating fluids of different chemical constitution, but cannot possibly act as rigid sieve-like structures. There cannot be a difference of hydrostatic pressure on either side of the films, as is required by the mechanical theory. Molecular not molar forces are here at play. The salivary cells are endowed by their colloidal structure with the power of linking up or setting free crystalloids brought to them in solution, and are thus the seat of the play of complex forces of surface and osmotic energy, and at the same time are the seat of chemical reaction, selective in character and depending on the ferments they contain—the keys which fit the locks of chemical constitution. These living cells control the passage of fluid in one or other direction, and the mystery of the secretory process requires the same solution as in the case of the unicellular organism, and this solution at present is just as far from attainment in the one case as in the other.

The comparative study of the structure of the nephridial tissues shows how far away from the truth are the mechanical theories of renal secretion which have held their ground in physiological text-books for the last fifty years. The writer has condensed the following passages from the work of Dahlgren and Kepner.

In the unicellular animals the excretory organ is formed by contracting vacuoles which form channels leading from the endoplasm to the exterior of the cell. The fluid that the vacuoles throw out by their rhythmic expansion and contraction is drained from the cell and is charged with uric acid. The contractile vacuoles of Paramœcium are two in number and permanent features of the cell. Their inner surface dips into the endoplasm and their outer surface opens through the ectoplasm to the exterior.

Into each contractile vacuole a radiating series of drainage channels lead. The channels are filled as the contractile vacuole discharges its contents. In the higher animals tissues, selected for the secretion of urates, form the nephridia. In the lowest Metazoa, so far as is known, any surface cells may take on nephridial functions. The higher forms of nephridial tissues are usually mesodermal structures. These tissues are always epithelial; one face of the epithelium is directed towards the fluids from which waste products are being taken, the other face forms the surface of a retaining or conducting cavity. In the Ascidians the renal epithelium is a vestigial cœlomic epithelium. Into this blind space waste products are excreted and stored as solid particles. All other nephridial sacs or tubules deliver the waste products to the exterior through nephridial pores or ducts. In all the simpler forms where the nephridial tubules have a small lumen, the latter is intracellular. In invertebrates where the lumen becomes larger, and in all vertebrates it is intercellular.

The fluids from which the waste products are taken may be intercellular fluid, cœlomic fluid or blood. Intercellular fluid and cœlomic fluid when associated with nephridia bathe them on their proximal surfaces. The blood supply is effected in two ways. In a few types the nephridial tissues are merely bathed in the blood (Insecta). Blood is usually supplied to the nephridial tissues through the capillaries of a circulatory system. In the simplest tissues there is but an ordinary supply. In the vertebrates there is a general capillary supply as well as a terminal supply. The terminal capillary structure is a more or less distorted plexus which is supported upon a connective tissue framework at definite terminal regions of the nephridial tissues, forming a "glomus."

We may rest assured that the nephridial tissues act in much the same way in every class of animal, viz. form vacuoles containing granules of excretory substances and expel the contents of these into tubules. Examination of the kidneys of hibernating and thirsting animals show evidence of secretory granules and vacuoles forming in the resting kidney. These disappear when diuresis is established. There is no question of filtration pressure in the excreting vacuole of Paramœcium, none in the case of Insecta where the nephridia lie in a bath of blood, and consideration of the structural conditions which pertain in

the mammalian kidney will show that there can be no question of a capillary pressure which can produce filtration therein.

The formation of glands in the embryo displays the same progressive evolution from the simple to the complex state, as is observed in ascending the animal scale. The most perfect and complex glands of the higher animals resemble in embryo the secretory organs of the lower animals. The arborescent ramifications of the blood vessels accompany the ducts in their development, and in proportion as the development of a secreting plane surface into a cæcum and ramified cæca proceeds, the vascular layer of the originally simple membrane spreads as a closely investing network around them. The ramified secreting tubes, which, when the structure is simple as in Insecta and Crustacea and in the pancreas of the rabbit, lie free freely and unconnectedly, in proportion as their evolution is carried further acquire a common covering or capsule; and thus a solid organ is produced. The vascular conditions in the simple and the complex are the same. No one would be rash enough to suggest that filtration of fluid could occur from the capillaries of the rabbit's pancreas through the ramified tubules exposed in the mesentery in a thin sheet. The tubules and the capillaries here are obviously at one and the same pressure, that of the abdominal cavity, alike squeezed by the respiratory muscles, and pulsed by the wave of blood which distends the abdominal arteries at each cardiac systole. There is barely a positive pressure in the capillaries, but this, aided by the rhythmic squeeze of the respiratory muscles, is sufficient to maintain the onward flow of blood. The gland cells when excited at times secrete their juice at a positive pressure, which with the help of the peristaltic wave of the muscular wall of the tubules drives the fluid into the intestine. Similarly in the case of the kidney, the blood in the capillary networks, the tissue lymph, and the urine in the tubules are all at one and the same pressure—the capillary-venous pressure. The whole kidney is expanded by each arterial pulse, and drops of urine may be squeezed thereby into the pelvis from the mouths of the tubules. The whole kidney is rhythmically squeezed by the respiratory muscles. The tubules are formed of watery cytoplasm, surrounded by lymph spaces full of fluid, and networks of capillaries full of blood. There is nothing of a rigid structure here, nothing of the nature of membranes which can separate fluid at one pressure in one system of tubes from

fluid at another pressure in another system. If the capillary-venous pressure were higher than the pressure in the tubules, the latter would be obliterated until the pressures became the same, likewise if the pressure in the tubules were higher than that in the veins. If the ureter be obstructed so that the pressure rises within it to say 40 mm. Hg, the capillary-venous pressure and tension of the whole kidney rises to this amount, and it takes a pressure of 40 mm. Hg to drive water through a hollow needle into the kidney substance. If the renal vein be obstructed till the pressure in the renal venules rises to 40 mm. Hg, the same must hold good, and the pressure of the urine in the renal tubules become the same. If the arterioles of the kidney be dilated the whole organ swells in its capsule, and the tension of the whole rises, the vascular system and the tubular system together approximating towards the rigid condition, but both at the same pressure, viz. the capillary-venous pressure. Under these conditions the velocity of blood flow is greatly increased, and if the kidney be enclosed in plaster of Paris, so that it cannot expand, it makes no jot of difference, because the arteries dilate at the expense of the veins, which are narrowed until a rigid system with a rigid flow is produced. When the blood reaches the glomerular capillaries, three courses are open to the fluid part, the capillary wall retaining the corpuscles. It may pass on by the efferent venules or by the lymphatics, or into the capsular ends of the renal tubules. Which course it takes depends on the play of such forces as surface tension, adsorption, and osmosis. Filtration has nothing to do with it, for the fluid pressure must be the same on either side of the wet films engaged, which are of a tenuity comparable to that of the bubbles of a soap lather.

Confirmation of the above views may be drawn from the perfusion experiments carried out by Sollmann on excised kidneys in spite of the fact that the flow he obtained from the ureter was attributed by him to filtration. He perfused 1 per cent. salt solution at arterial pressure through the renal artery, and collected and measured the outflow both from the renal vein and the ureter. He found the venous flow reached its maximum in fifteen minutes, while the ureter flow continued to increase for one to two hours, thus rising slowly to a maximum. As the ureter flow increased the venous flow declined slowly, and then the two flows ran a parallel course. Subsequently undergoing minor oscillations—the

venous flow increasing slightly, and the ureter flow decreasing at first, and then increasing. On altering the arterial perfusion pressure the venous flow and ureter flow, the volume of the kidney, the maximal venous pressure and the maximal ureter pressure all varied in the same sense, but the maximal venous and ureter pressures were at a lower level than the injection pressure owing to leakage through capsular collaterals. If the perfusion pressure were made rhythmically intermittent the venous and ureter outflow were increased. Obstruction of the renal vein caused swelling of the kidney and almost complete cessation of the ureter flow. A graduated increase in the venous pressure, produced by raising the level of the venous outflow tube, diminished the venous and ureter flow and expanded the kidney, especially when the pressure rose above 40 to 60 mm. Hg. The venous and ureter outflow varied with the molecular concentration of the perfusion fluid. Hypertonic solutions caused lessened resistance in, and more flow from, the tubules and vessels, and hypertonic solutions the opposite. In volume a hypertonic solution produced at first a sharp fall, followed by a rise to original level, while a hypotonic solution gave a progressive diminution in renal volume. Many of these results are difficult to explain, but none are in favour of filtration. Vernon has shown that the fluid coming from the kidney under these conditions does not correspond to that sent into the artery. The kidney metabolism continues for days after death in a modified form. At first we see the perfused fluid found its way through the capillary-venous system, and only much more slowly made a passage through the renal tubules. At the start the capillaries were distended with the perfused fluid, the lumina of the capsules almost obliterated; the surface tension of the capillaries therefore was high, that of the capsules low. The surface energy of the latter therefore was high. It may have been these conditions which led to the transference of the fluid from one side to the other of the wet film formed by the capillary and capsular epithelial cells. We may suppose with justice that the epithelium retains the corpuscles and the native colloidal material of the blood. We know some colloids may pass. Sollmann found gum arabic, added to the perfused fluid passed through, and egg albumen passes into the urine of normal people if much be eaten. In the case of the renal tubules at the time when the capillaries become distended with fluid, the epithelium of the tubules contains stores of ex-

cretory products, some in colloidal linkage, some as crystalloidal substance. In these cells there comes about a complex play of the forces of osmosis and surface tension. Supposing the epithelium of the tubules swells owing to their surface energy being great in comparison with the capillaries where the surface tension is great, then the epithelium in its turn will have a higher surface tension than the lumina of the tubules, and this surface energy will cause the transference of liquid from vessel to tubule. We have in the kidney a gelatinous foam-like structure, the meshes of the foam containing fluid, and the meshes being formed of two sets of ramified channels, the one set leading to the venous and the other to the ureter outlet. Blood is driven in pulses into the vascular meshwork. By such forces as adsorption and surface tension the fluid part of the blood pervades the tubular meshwork, while the living cells concentrate, and extrude vacuoles filled with, urinary excretions. The mystery of the whole process is hidden from us, but we may be sure that an excretory cell in a bath of collecting fluid and provided with an excretory channel form the structural basis of the mechanism, and that the mechanical filtration theories may be relegated to the conceits of a science in its more primitive days.

It has always been assumed by those who maintain the defence of the filtration theory that the capillary pressure must be raised not only when the general venous and arterial pressure rise together, but also when the general venous pressure is raised, so long as there is no fall of arterial pressure compensating for this venous rise. No such assumption can be made in regard to a rise of arterial pressure because of the unknown factor—the resistance in the arterioles. Now the experiments of Martin Flack and the writer made on the arterial venous and capillary pressure of their own limbs show that the above assumptions are, at any rate in the case of the limbs, not valid. The capillary system is not filled to distension ; there is a large potential space which only gradually fills when the venous return is impeded, and thus the venous pressure—the veins being filled by broad paths of low resistance—may rise greatly while the capillary pressure in large areas drained by these veins is scarcely altered. The gradual filling of the capillary system, while producing distension of the part, enormously increases the surface exposure of the blood fluid and the surface tension of the capillary films, and these are probably factors of the greatest importance in the formation of lymph,

another factor being the alteration of tissue metabolism produced by the impeded blood flow with consequent want of oxygen, setting free of crystalloids from colloidal combination, and increase of waste products, leading to a rise of osmotic pressure and swelling of the tissues.

In the case of such an organ as the liver a great expansion takes place when the outflow from the vena cava inferior is impeded, or excess of blood or saline is injected intravenously. Here again increase of surface exposure and stagnation of flow are the factors at work which produce the greater outflow of lymph—not the increased capillary pressure. That the capillary pressure is increased in such capsulated organs as the kidney, salivary gland, liver, and brain when the outflow of venous blood (or secretion) is impeded is proved by the increased tension of the organ, but this increase must be uniform throughout each lobule, if not throughout the whole organ, and cannot act as a filtering agent.

The Residual Vascular Pressure in the Dead Animal

The vascular system as a whole is not filled to distension. There is in the dead animal no uniform positive mean pressure throughout the vascular system. If there did exist in the system such a positive "mean hydrostatic pressure" when the heart is arrested and the skeletal muscles are relaxed by death, it must be produced by some secretory power of the vascular epithelium or by the osmotic pressure of the blood. The blood must possess a greater power of holding water than the tissues, and the wet film of the capillary wall must be able to retain the water, so that the whole system is filled to distension. The shrinkage of the face in fainting, and how much more in death, shows the error of this conception. After death there is a residual pressure in the aorta owing to the resistance in the arterioles which contract and do not allow the last of the blood to leak through into the capillary-venous system. There is also a residual pressure in the venæ cavæ produced by the influence of gravity and the post-mortem contraction of the viscera which drives the blood from the capillary areas into the venæ cavæ. These residual pressures are, however, unequal, and cannot be taken as representing a "mean hydrostatic pressure" of the whole system. Thus the writer found in a morphinised dog :—

Aorta.	Vena Cava.	
Mm. Hg. 165 30	Mm. Hg. 3 14	Normal. Heart arrested by vagus.

and in a morphinised and curarised dog :—

Aorta.	Vena Cava.	
Mm. Hg. 80 14	Mm. Hg. 3 6	Normal. Heart arrested by vagus.

In the uncurarised animal the convulsive movements of respiration by compressing the abdominal vessels raise the vena cava and lessen the fall of aortic pressure.

Similarly in Cohnheim's classical experiments, when he injected oil into the pericardium to study the effect of impeding the filling of the heart, there resulted no equality of residual pressures in the aorta and vena cava.

It has been supposed that a general constriction of the arterioles, such as may be produced by the injection of adrenalin, would by reducing the capacity of the vascular system raise the "mean hydrostatic pressure," and therefore the capillary pressure. The writer produced by injecting adrenalin a rise of arterial pressure from 80 to 180 mm. Hg, and then arrested the circulation by clamping the ascending aorta. The vena cava pressure fell to the same residual pressure as when the aorta was clamped before the injection of the adrenalin. A rise of pressure of 1500 mm. of blood in the aorta may be accompanied only by a rise of 50 mm. in the venæ cavæ, and this small rise is due not to diminution of the total capacity of the vascular system, but to a greater return to the venæ cavæ of blood squeezed from the splanchnic area and the failure of the heart to empty itself in the face of the high resistance.

It has been supposed that the intravenous injection of physiological saline, or the injection of concentrated sugar solution—this produces hydræmia by drawing water out of the tissues into the blood—it has been supposed that either of these agents increases

the flow of lymph by adding to the total volume of fluid in the vascular system, and thus increasing the capillary pressure and filtration through the capillary wall. Now in a case of polycythæmia studied by the writer, the arterial, the venous, and the capillary pressure in the arm, held at heart's apex level, were the same as in himself. There was not a sign of congestion, except a redness of the hands and face and fulness of the veins, and not a trace of œdema in this man. And yet he had a hæmoglobin per cent. of 155, 3½ times the normal oxygen capacity, 12,000,000 red corpuscles per c.mm. of blood, and a total blood volume 2½ times the normal as determined by A. S. Boycott.

During the temporary arrest of the circulation in the dog the writer has injected rapidly 30 c.c. and more of physiological saline solution into the venæ cavæ, and observed only a temporary and slight rise of pressure in the venæ cavæ during the injection and no effect at all on the residual pressure in the arteries; an experiment which shows without question that there is no such thing as a positive "mean hydrostatic pressure" in the vascular system, and that the pressure can be raised in one part without influencing another, owing to the unfilled areas of capillaries, and the roomy capacity of the veins.

Dog: Cannulæ, in Aorta and Vena Cava Superior, connected with Manometers filled with 1 per cent. Sodium Citrate Solution.

Time.	Residual Aortic Pressure.	Residual Vena Cava Pressure.	
	Mm. H_2O.	Mm. H_2O.	
3·17	114	89	Pulmonary artery occluded.
3·18–19	114	204	Convulsive respirations.
3·30	70	64	Heart poisoned by chloroform
3·32	70	127	100 c.c. saline injected into femoral vein.
3·35	76	76	
3·45	63	56	

The Effect of Obstructing the Venæ Cavæ

Some remarkable experiments by C. Bolton may be cited here in connection with these experiments of the writer. Bolton

studied the result of totally obstructing and of narrowing the venæ cavæ in order to arrive at the share in the production of dropsy which increased capillary pressure had. He tried at first to produce cardiac deficiency by constriction of the pericardium by means of sutures, so as to prevent the proper diastolic expansion of the heart, but gave up this line of work as he found it very difficult to hit the right amount of constriction. The animals either died or recovered without symptoms. To obstruct the venæ cavæ he made an incision one to two inches long parallel to the ribs in the third right intercostal space for the superior, and seventh space for the inferior cava. Artificial respiration was put on, the ribs drawn apart by retractors and the lung held aside by a spatula, and incomplete obstruction set up by encircling the vein with a short piece of soft rubber catheter of appropriate diameter. The thorax was then closed, after squeezing out the air, and the animal allowed to recover. The venous pressures were measured in some of the animals after varying degrees of constriction had been established, the measurements being taken in the external iliac; at the lower end of the femoral above the ankle; in the splenic branch of the portal; and in the post-auricular branch of the external jugular. Complete occlusion of the superior cava caused the death of the animal in one to six days. There was caused considerable œdema of the mediastinum and exudation of venous fluid in the pericardial and pleural sacs. The animal refused food, wasted, and passed less urine. When the obstruction was made above the azygos vein, one animal survived, efficient anastomoses becoming established by way of the internal mammary, azygos, veins of diaphragm and comes nervi phrenici. There was œdema and fluid in the pleura and pericardium until these anastomoses were established properly. Another animal died eighteen days after operation, and 145 c.c. of fluid were found in the right and 125 c.c. in the left pleural cavity. In the cases of partial obstruction Bolton found constriction to three-fifths of the normal size produces œdema and hydrothorax.

Such obstruction only raises the venous pressure in the external jugular by 20 to 40 mm. of blood, and quite temporarily. Complete obstruction altered the arterial pressure very slightly and raised the pressure in the external jugular by 130 mm. of blood, but within an hour the pressure was normal again. The œdema and dropsy were produced next day long after the pressure had

become normal again. Complete obstruction of the inferior cava caused death in a few hours (as was determined by R. Lower in the days of Charles II.). The arterial pressure at once fell to 30 to 40 mm. Hg, and the venous pressure in the external iliac rose by 100 mm. of blood or more, but within an hour fell back to its old level.

Partial constriction to more than three-fifths caused death. The diameter of the vena cava is about 5 mm., and on constriction to 3 mm. the animal survived, while on 2 to 2½ mm. it might or might not die. The arterial pressure fell about 20 mm. Hg when the constriction was to 3 mm., and the pressure in the external iliac vein rose 20 to 30 mm. of blood, but this rise was quite temporary. Ascites resulted until proper anastomoses were established by way of the veins of the abdominal wall; but the first signs of ascites occurred long after the venous pressure had returned to normal. Constriction of the portal vein from its normal diameter 4 mm. to 1½ mm. gave the same results as constriction of the vena cava inferior. Constriction of both cavæ to 3 mm. produced dropsy of the pleuræ and peritoneum just as in a case of uncompensated heart disease.

Finally Bolton observed that 130 c.c. physiological saline (an amount equal to from two-thirds to the whole blood quantum) might be slowly injected in the course of one and a half hours, the blood pressures remaining normal, and some ascites being produced meanwhile.

In the experiments on the effect of complete obstruction of the inferior vena cava he records that while the pressure in the external iliac vein rose by 100 mm. of blood or more, that in the femoral vein above the ankle only rose by some 60 mm. The writer attributes this to the low pressure in the arteries, the derivation of the arterial blood through the lower resistance channels—the abdominal vessels—and consequent slow filling of the veins of the legs.

Bolton's observations show that the ascites and œdema occur when the general venous and arterial pressures are normal. They must be ascribed, therefore, to altered tissue metabolism, greater filling of and stasis in capillary areas, and consequent change in the conditions of surface and osmotic energy.[1]

[1] The work of B. Moore and his co-workers has shown how the osmotic pressure of the complex of colloids and crystalloids which forms the serum or tissue proteid is altered by slight changes in alkalinity, &c. See *Bio-Chemical Journal*, vol. iii. p. 422, 1908.

The mechanical theory as to the causation of cardiac dropsy has been summed up by Bainbridge as follows :—

" First, in an uncompensated heart, there is a fall of arterial pressure, and a rise of venous pressures near the heart. There is also a fall of capillary pressure, in consequence of the fall of arterial pressure, in the kidneys, intestines, and peripheral parts of the body. The fall of capillary pressure lessens filtration, and for a time upsets the balance between filtration and absorption ; consequently an excess of fluid is absorbed by the blood vessels from the intestines and peripheral tissues.

" Secondly, this continued absorption associated with the diminished urinary secretion, leads to hydræmic plethora, and increases the mean systemic pressure.

" Thirdly, this hydræmic plethora raises the capillary pressure all over the body, and promotes increased filtration, the more so because the venous state of the blood damages the capillaries, and increases their permeability. A further subsidiary factor is the obstruction to the entrance of lymph into the great veins at the thoracic duct owing to the excessive venous pressure."

The writer controverts these views in each particular—the arterial pressure is not altered in uncompensated cases of heart disease unless death is imminent ; neither is the venous pressure altered, nor the capillary pressure.

Neither hydræmic nor blood plethora raises the arterial venous or capillary pressures excepting during the period of intra-venous injection. Even if the capillary pressure were raised it would not cause filtration because the blood in the capillaries and the tissue lymph in any organ are and must be at one and the same hydrostatic pressure.

The Effect of Obstructing the Blood Vessels

While cessation of the blood flow in the " higher level " centres of the brain abolishes consciousness in a second or two, permanent recovery from a complete anæmia may occur which has lasted some minutes, at the outside twenty minutes (Stewart and Guthrie).[1] The heart quickly stops beating when the coronary arteries are closed, but can be recovered by transfusion hours after. Muscle

[1] A temporary recovery may occur after sixty minutes. Guthrie transplanted the head of a dog, and obtained reflex movements of the eyes, &c. The circulation in the brain had been interrupted twenty-nine minutes.

can stand a much longer anæmia than the heart and viscera, and connected tissue and epithelia still longer. After the obstruction of arteries, beyond the possibility of an efficient current being set up by way of anastomotic pathways, the capillary-venous area of the part affected fills by the slow inflow from surrounding areas, the plasma passes out owing to the altered osmotic conditions, and the red corpuscles heap together. Such congestion is seen in the tongue of the curarised frog after tying the artery on either side of the under surface. If the root of the ear of a rabbit be confined by a ligature for eight to ten hours, and the string be loosened, the ear swells and becomes very red, and the tissue lymph and white corpuscles increase in the tissue spaces. After ligation for twenty-four hours, small hæmorrhages occur, the permeability of the capillaries being then seriously altered.

The effect of back congestion has been studied in the frog's tongue after tying the veins which on either side carry the blood from the tongue to the larger veins in the floor of the mouth (Cohnheim, Thoma). The congestion can be observed microscopically as it spreads backwards. *The veins and capillaries widen in the tongue, but scarcely so in the web of the foot where the surrounding tissue is inextensile.* As the plasma escapes into the tissue spaces, the capillaries and veins become choked with red corpuscles. If a cannula is placed in the lymphatics on the outer side of the leg of a dog, and a ligature is drawn round the thigh so as to obstruct the veins, the lymph—before scarcely moving—begins to flow, and the foot may swell, gradually becoming œdematous. Division of the vaso-constrictor nerves increases the effect. This is well seen on obstructing the veins of the root of the rabbit's ear and dividing the cervical sympathetic nerve.

If the veins of the dog's leg are entirely obstructed by injecting plaster of Paris into the vein on the dorsum of the foot—confining the thigh by a ligature during the injection—the leg next day is become cylindrical with œdema. The kidney swells after ligation of the renal vein to double or treble the size, and bloody extravasations appear in its substance. In the frog's tongue the red cells may be seen escaping through bulgings which appear in the capillaries and small veins, that is when the venous obstruction is complete. In all these cases increased capillary pressure is not the prime cause of the phenomena. They result from stagnation, altered metabolism, and altered osmotic energy and surface energy

of the capillary cells and tissues. The appearance of a part in a state of passive hyperæmia is livid and bluish, swollen, pitted by pressure; its temperature is lowered. The degree of swelling depends on the relative in and out flow of blood. It is little in hypostatic congestion because of the feeble arterial supply. Whether the tissues live or die depends on the maintenance of some flow by collateral paths.

When a vein is slowly closed by a thrombus, collateral pathways have time to enlarge. "Thrombosis of the common iliac vein or vena cava inferior produces œdema of the lower limbs and compensatory enlargement of the cutaneous vessels of the legs and abdominal wall. Thrombosis of the subclavian vein can be compensated by collateral paths through the internal mammary and intercostal veins, and even thrombosis of the innominate vein fails to produce œdema if the laryngeal descending veins remain open." The effects depend on the rapidity with which the thrombosis takes place, *i.e.* on the relative damage of the tissues by deficient flow. If the inferior cava is thrombosed rapidly, general œdema occurs below the level, and blood and albumen appear in the urine if the renal veins are involved. Closure of the portal vein by a tumour or of its branches by cirrhosis of the liver, leads to congestion of the intestines, enlargement of the spleen, and ascites. Here again the results are due entirely to deficient flow and altered constitution of blood and tissue cells. The cranial sinuses are liable to thrombosis. They are wide, of irregular lumen, with Pacchionian granulations dipping into them, and in some cases bands crossing them. The current is forwarded by respiration but cannot be influenced directly by muscular contractions. Hence thrombosis occurs in marasmic states, with feeble respiration and deficient cardiac power. Sudden blockage of an artery by ligature or embolus is of little effect so long as there are adequate collateral anastomotic paths. These rapidly dilate, and while the blocked artery shrinks up the anastomotic capillary paths, where the flow is increased, develop the structure of arteries. Retinal, coronary, renal, splenic, and cerebral arteries beyond the circle of Willis behave as terminal arteries. Closure of these and of the superior mesenteric artery in spite of its collateral paths, leads to stasis and necrosis. It seems to be possible for an embolus to be driven by the respiratory and muscular movements in a retrograde fashion down the large veins by coughing or expiratory

effort, for after the injection of emulsions of white sand into the jugular or femoral vein, grains have been found in the veins of the face, liver, kidney, as well as in the venæ cavæ. Thus the old Galenical doctrine that the blood is driven down the veins from the liver to the body has a grain of truth in it.

Plethora

When freshly defibrinated dog's blood, warmed to body temperature, is injected into a dog by way of the jugular vein, the arterial pressure may rise with each injection some 20 to 30 mm. Hg, but quickly returns to its old level. After blood to the extent of 3 to 4 per cent. of the body weight has been injected the arterial pressure may reach the height of 170 to 180 mm. Hg, but much beyond this it cannot be driven. If the transfusion be continued until more than 10 to 12 per cent. of the body weight has been introduced—*i.e.* more than twice the normal blood quantum—significant upward and downward variations of pressure occur, which presage cardiac failure. All the animals die in the course of a day or so who have received over 10 to 12 per cent. of their body weight.

During each period of injection the heart being better filled responds with an ampler output and raises the arterial pressure. The pressure returns to its old level so soon as the injected blood is swallowed up by the capillary-venous reservoirs.

Finally, when so much blood has been introduced that the venæ cavæ and liver have become distended, the heart becomes over-loaded, and having to perform its systole in a dilated state and owing to its greater output against an increased resistance, begins to fail. The share of the vaso-motor system in the restitution of the pressure in the early stages of the experiment is made manifest by dividing beforehand the spinal cord in the lower cervical region. The low arterial pressure, which obtains after such a lesion, is driven up by each injection until the normal arterial pressure is reached and restitution of pressure between the injections then occurs. The falling back of the pressure after that point has been reached is due to the escape of the blood from the arteries into the capacious capillary-venous areas.

It is in the small veins and capillaries and particularly in the abdominal organs that the excess of blood lodges. The pressure

in the venæ cavæ rises during each injection but sinks again owing to the extensibility and large potential capacity of the capillary-venous system. The liver holds a great deal and becomes large and firm to the touch, and when excised a great quantity of blood streams from it. The large abdominal veins and liver by receiving most of the blood injected protect the heart from over-distension, but if the transfusion into the jugular vein be made too rapidly, no time is given for the filling out of the liver and other capillary-venous reservoirs, and the heart becomes over-loaded and fails.

Plethysmographic records of the heart showed Johansson and Tigerstedt that with a sufficiently slow transfusion there is an increase in the systolic output and no passive congestion of the heart occurs. With a more rapid rate of transfusion the heart fails to empty itself and expels a smaller amount of blood than before. Hence the constancy of the arterial pressure during transfusion is to be ascribed largely to the heart's action.

Rabbit: period of transfusion of 30 per cent. of blood quantum marked by the vertical lines:—

Output measured by Stromühr introduced into Ascending Aorta

Arterial pressure .	78	88	99	97	114	131	134	133	140	
Output of heart per minute per kgm. of body weight	18	32	53	39	31	33	32	38	36	
	144	147	148	146	148	147	148	149	147	
	36	36	38	36	32	44	45	51	60	
	145	131	119	112	107	104	101	99	94	90
	66	66	66	61	59	59	59	54	50	51

The following shows the effect of a larger rapid injection = 50 per cent. of the blood quantum :—

Arterial pressure .	78	89	120	130	144	158	160	151	146	136
Minute volume .	33	49	80	71	51	35	32	31	32	33

and so on to $\frac{131}{26}$ and then to $\frac{122}{56}$, the output rising as the arterial pressure fell and the heart recovered as the blood fluid found room in the capillary-venous system and tissue spaces.

After an injection of 69 per cent. of the normal blood quantum in the period of fourteen minutes the heart worked well at first, and the arterial pressure rose from 50 to 125 mm. Hg. After twenty minutes the heart failed, the minute volume sank to half

its original value, and the pressure fell from 117 to 37 mm. Hg. On bleeding the rabbit 12 c.c. and then 20 c.c., and then again another undetermined amount, the pressure rose and reached 40 mm. Hg some twenty minutes after the first signs of cardiac failure. At the end of another twenty minutes it had risen to 79 to 86 mm. Hg.

It is possible that the cardiac failure may be due in part to other causes than the mere mechanical overloading of the heart. Some experiments made by Bier seem to show that defibrinated blood has a toxic influence, for he found that if he transfused the excised limb of a pig with pig's blood, defibrinated and oxygenated, at arterial pressure, an active hyperæmia ensued at first, and the blood flowed from the veins in a full stream. Soon, however, the outflow diminished and became very small, and the limb turned deep blue in colour. Arterial blood transfused directly into the limb from another pig had no such effect ; the limb at each transfusion became hyperæmic for a time and then returned to its natural colour.

Worm-Müller observed that bleeding an animal, to the extent only of that amount of blood which had been injected, killed it, if the transfusion had been a large one. The excess of blood fluid in part pooled in the expanded capillary-venous system and in the tissue spaces, in part excreted, could not be drawn on quickly enough to maintain an adequate supply to the heart.

Much has been made of the increased resistance which is said to occur in plethora owing to transudation and excretion of the blood fluid and the concentration of the corpuscles. To the greater viscosity so produced the overstrain and failure of the heart has been attributed. The researches on surviving organs show on the whole the same proportion between viscosity and flow, as in a glass viscometer. If the viscosity is increased 50 per cent. the flow will be about 50 per cent. slower. Such an alteration of viscosity is, however, of little significance in the vascular system, for a slight excitation of the vaso-motor nerves can alter the flow 100 per cent. or more. In the chewing muscles of the horse the flow may increase four times or more during work owing to vaso-dilatation and the furthering of the blood flow by the alternate relaxation and contraction of the muscles. A drug such as Yohinbim may in the first stage of its action lessen flow 50 per cent. and pressure 18 per cent., and subsequently increase

flow 250 per cent. and pressure 11 per cent., so great is the effect of vaso-dilatation coupled with increased cardiac efficiency (Brodie and Müller).

In polycythæmia, where the blood is more than doubled in quantity and the number of corpuscles twelve million instead of five, there are no signs of high pressure, hypertrophy of heart, &c. The heart continues to circulate about the normal amount, and the excess is stored away in the peripheral capillary-venous areas. Increased viscosity is compensated for easily by dilatation of the arterioles. The toxic conditions which arise in cases of polycythæmia are probably due in part to the long time much of the blood must take to complete the circulation. Thrombosis also results in the cerebral veins. The viscosity of the blood may be increased nearly 100 per cent. by stasis—produced by confining it within a limb for twenty minutes by means of a rubber bandage. The increase is due to the passage of blood fluid into the tissues. In cholera and polycythæmia the viscosity co-efficient has been observed to be as high as 20 in place of 4·8, the normal worth. A current of carbonic acid led through the blood, it is said, increases the viscosity 50 per cent. The maximal effect of hard work or Turkish baths and sweating is an increase of 20 to 30 per cent.

Hydræmia

Extraordinary amounts of physiological saline can be infused without harm—up to 60 to 70 per cent. of the body weight! No bad after effects follow the injection of threefold the fatal amount of blood. The arterial pressure is not notably altered, and the vena cava pressure, while rising by some 200 mm. of blood during the injection, soon returns again to the old level. The velocity of flow in the capillaries is greatly increased, as may be seen in the frog's web, owing to the dilated arterioles and lessened viscosity. The output of the heart is immediately increased, and the heart shows no sign of failure. Thus Tigerstedt found on injecting into the rabbit 25 c.c. Ringer sol. (period of injection marked by vertical lines):—

Arterial pressure .	90	96	99	97	87	92	89
Minute volume per kg.	51	64	78	100	95	122	122

falling in a few minutes to $\frac{81}{61}$.

The greater part of the water passes rapidly out of the vascular system, the glands all actively secrete, watery urine is passed, the saliva drips, the guts become filled with watery solutions, the lymph flows in a continuous stream from the abdominal organs but not from the lymphatics of the limbs. After death the subcutaneous and intermuscular cellular tissues and the central nervous system and usually the thoracic organs are as dry as normal, while the abdominal organs are markedly œdematous and the peritoneal cavity contains fluid. Scalding, toxic agents, temporary anæmia, by altering the vascular tone and conditions of surface and osmotic energy [1] of a limb, render it œdematous when the state of hydræmia is produced. An hydræmia maintained by daily injection has the same effect, so that ligation of the femoral vein, which normally does not produce œdema in the animal, in such case does.

A number of toxic substances are known which have the effect of so altering the relations of osmotic and surface energy that hydræmia causes œdema in the limbs. The œdema which occurs in renal disease is probably to be explained on these lines. The factors to consider are—a scanty output of urine, particularly of solid constituents, retention of salts and other waste products, with consequent alteration in osmotic conditions leading to the passage of fluid into the tissue spaces; excessive metabolism of the muscles resulting from the defect of renal functions; an effort on the part of the tissues to excrete into the body spaces waste substances (this is the normal process in the ascidian) when the nephridial tissue fails. Mellanby maintains that the creatin found in the muscles is a waste product stored therein with advancing life.

The injection into the blood of a concentrated solution of a crystalloid such as sugar produces hydræmia. Water is drawn from the tissue space into the blood vessels and to such an extent that the injection of 45 c.c. of 75 per cent. solution of dextrose may temporarily double or treble the volume of blood fluid in a dog, as measured by the alteration in number of red cells (Starling). The lymph flow which is greatly increased in quantity is ascribed to increased capillary pressure and filtration. In confirmation of this view Starling found that if he drew off an adequate amount of

[1] If a shrunken tissue cell border on a distended capillary, the surface tension of the capillary will be high and its energy low; while the surface tension of the tissue cell will be low and its energy high—the one strives to shrink, the other to swell.

blood beforehand so as to compensate for the incoming of the tissue fluid, no noteworthy increase in the lymph flow occurred. Objections to the filtration hypothesis have already been fully stated; it remains to suggest another explanation for Starling's results. The following hypothesis, for the present, may be found adequate.

The injection of the sugar increases the osmotic energy of the blood above that of the tissues, and draws water into the vascular system. The capillaries are better filled and the surface energy of the tissue spaces is increased in proportion as the surface tension is increased in the capillaries. Sugar passes through the permeable film formed by the capillary wall into the tissue spaces and cells, and thus the osmotic pressure of the blood falls. Surface energy then gets the upper hand and water passes from the distended capillaries into the tissue spaces. This occurs particularly in the highly vascularised abdominal organs where the flow of lymph is furthered by the respiratory pump.

Hyperæmia

The blood supply of each organ is in relation to its functional activity, and thus while half of the whole blood quantum is estimated to be in the viscera, and the blood they contain may be equal to one-fifth of their weight, that within the locomotor organs in the resting state of the animal is said to be not more than 2 to 3 per cent. of their weight. The capillaries of the skin are normally far from filled. The effect of an irritant on the vessels of the skin or conjunctivæ and on the mucous membrane of the lip demonstrates the striking difference in the capillary supply. Hyperæmia may be active and arterial in origin, or passive and due to venous congestion. Active hyperæmia may be caused by increased resistance in other vascular fields—the arterial supply to the brain is increased by constriction of the splanchnic area—or it may result from vaso-dilatation, and this in its turn may be produced by the vaso-motor nerves, or by physical or chemical agents acting locally, *e.g.* effect of heat and cupping on the skin, pilocarpine on the salivary glands and diuretics on the kidneys. It is suggested that the products of secretion cause vaso-dilatation in the salivary gland when the chorda is excited, just as excretory products dilate the renal vessel.

The arterial wall responds to increased tension by contraction, and to diminished tension by expansion, and thus tends automatically to compensate variations in aortic pressure and keep the blood flow constant. That the vaso-motor centres have no share in this is shown by an experiment of Bier. He amputated the limb of a pig, leaving it connected with the body by an arterial cannula only, and found that an active hyperæmia followed a temporary arrest of the arterial supply.

The following is one of the most interesting experiments of Bier. He produced venous congestion of the arm by means of a bandage, then tightened the bandage so as to obliterate the artery, and lastly after five minutes loosened the bandage. The venous congestion was at once replaced by an active arterial hyperæmia. He concludes then while arrest of the arterial flow is followed by active hyperæmia, venosity of the blood causes arterial constriction. To confirm this conclusion Bier rendered bloodless the limb of a pig for ten minutes by means of an Esmarch bandage, and then loosened it. The limb responded by the usual active hyperæmia. He next closed the windpipe of the animal, and noted that the limb first became blue and then paled. On opening the windpipe the active hyperæmia returned, to be abolished once more on closing it.

One more example of the influence of chemical state of the blood on the circulation is the following. Bier exposed the rabbit's intestine in a bath of warm salt solution, and stopped the blood supply to two loops of it, one of which was empty and the other filled with milk at body temperature. On lessening the ligatures, the one filled with milk responded by an active hyperæmia, the other not. Bier says the intestine of a fasting animal does not become hyperæmic after a temporary anæmia, while that of a fed one does, an observation which is of some interest to the surgeon. The stomach of the rabbit does not give the hyperæmic reaction while that of the dog does, so that ligation of the chief arterial supply of the stomach causes necrosis in the one and not in the other animal. Man is like the rabbit in this respect. While obliteration of the mesenteric arteries for a length of only 3 cm. produces necrosis in the small intestine, 10 cm. is the minimum in the colon of the rabbit.

Bier points out that every organ in functional activity is in a state of active hyperæmia, so too where tissue growth is great as

in the regeneration of feathers after moult. The procreative and reproductive functions too are accompanied by active hyperæmia. Hyperæmia is the natural reaction of the tissues to injury, foreign material and bacterial invasion, and this hyperæmia is not to be combated, but regarded as the natural healing agent. Anti-phlogistic treatment, says Bier, may relieve the pain, but it retards the healing process, and may render it less complete. The treatment of Bier and of A. Wright is to promote the flow of plasma into the infected or inflamed tissues. Venous congestion or cupping are the methods employed by Bier.

The knife of the surgeon employed in the opening of abscesses, &c., has the same influence in relieving tension and allowing the free transudation of plasma. Wright employs sodium citrate solutions as a drug or locally as an irrigant to lessen coagulability and thus increase the permeation of the infected part. Chronic disease is chronic because the bacterial excitant does not provoke an active hyperæmia; make this appear and healing follows. Animals infected with anthrax and streptococci have been protected by the induction of venous congestion in the infected part owing to the intensified "antitropic" action of the plasma. The defence lies in the plasma, and hence while blood infection is rare local infection is of every-day occurrence. The plasma is turned on to the infected local area in full stream, and if nature fails to do this, the surgeon must aid the transudation. Salt rubbed into wounds of slaves after whipping by osmotic force has this effect, while hot fomentations produce hyperæmia and soften the skin and so allow more transudation.

Resorption is favoured by the hyperæmia which follows venous congestion, especially if massage be employed. Potassium ferrocyanide solution, introduced into a joint, appears thirty minutes later in the urine. When hyperæmia of that joint is induced the salt appears in the urine in six to ten minutes. Lactose is a good test substance to inject because its presence in the urine can be detected by the polarimeter. The resorption of this is doubled or more in rate by exposure of the animal to hot air and made very slow by packing the limb in ice. When two limbs of an animal, with the bones fractured, are splinted, and one limb surrounded with an air bath at 38° C. and the other at 10° C., a callus forms in six to seven days in the limb which is kept warm, while the regenerative process has just begun in the other. Hence the curative

effect of poultices and stimulating solutions lies in the hyperæmia and greater flow of plasma which they produce. The old ideas underlying the words "derivants" and "revulsants" are entirely wrong. Mustard poultices and turpentine stoups do not draw the blood from the deeper diseased parts into the superficial, but produce hyperæmia of both. The abdominal organs are rendered hyperæmic by exposing the abdomen to a hot air bath. The intra-pleural temperature may be raised slightly (owing to hyperæmia) by applying an irritant to the skin of the chest, and may be raised several degrees by applying hot poultices. The greater warmth of the part not only induces hyperæmia but increases phagocytic and other actions. Herein we find the explanation of the success of these old-fashioned remedies in the treatment of fevers and inflammation. Bleeding likewise may have been effectual by drawing tissue lymph into the blood and so increasing the stock of bactericidal and opsonic substances. It is unlikely that our forefathers bled fever-patients for nothing excepting the fee.

Shock and Collapse

When a large hutch rabbit is held for a few minutes in the vertical position with its limbs stretched out and head uppermost, it may become unconscious and die from cerebral anæmia. The blood collects in the large flaccid abdomen, the animal not being able to return it to the heart by changing its posture. It struggles to maintain a circulation—cerebral anæmia excites convulsions which squeeze the blood from the limbs, &c., into the heart—but the difficulty in face of the circulation is too great and the animal dies. A wild rabbit with taut abdomen is not affected in this way, neither is a cat or dog, but a goat is with its capacious belly. The wild rabbit can, however, be brought into like state by a dose of chloral, and so can the dog by chloroform poisoning or by bleeding. The emotional fainting of a man is due to the inhibition of the nervous system—a neutralisation of all other afferent stimuli by one all-powerful one—the consequent sudden relaxation of muscular tone, collapse of the body and non-return of venous blood to the heart. The horizontal posture or compression of the abdomen immediately restores from syncope the rabbit or the man. The condition of shock which results from division of the spinal cord in the lower cervical region is recovered from and cannot be renewed by

a subsequent section or total destruction of the spinal cord (Sherrington). It is caused by the sudden interruption of the nervous tonic influence which proceeds from the brain to the muscular system. The incessant inflow of visual and labyrinthine impulses no doubt maintain this tone ; just as the wires of a piano-

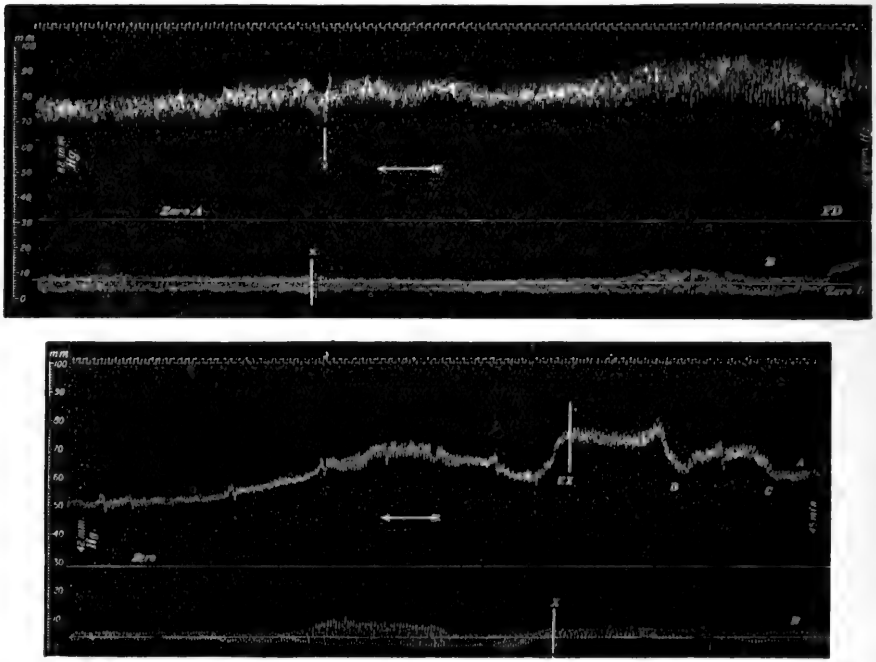


FIG. 21.—Carotid and superior vena cava pressures of dog. FD, animal turned into the vertical feet-down posture with the cannulæ in the axis of rotation. The arterial pressure fell in fifty minutes from 110 to 42 mm. Hg. From C to EX the animal was immersed in a bath which was deepened to the chin at D. Note the increased effect of respiration on the venous pressure after FD, and again after the bath. Note the fall of pressures at FD and the compensatory rise in arterial pressure, which gradually weakens.

forte are ceaselessly kept humming by the noise of the world, so is the neuro-muscular system. Shock may be caused in man by any severe injury, and is generally attributed to paralysis of the vaso-motor centre. The centre is said to be exhausted by the violence of the sensory stimulation (Crile). Porter objects to this view, and says it is disproved by the fact that the centre responds to excitation of a sensory nerve in the usual way, and in an animal

in a condition of shock from injury raises the arterial pressure from its low level by an amount which is no less than in a normal animal. The centre, he says, is able to act quite efficiently. The fault may lie, however, in the sensory synapses. The centre fails to be excited by the usual weak excitation streaming into it, or the usual effect may be reversed—pressor turned into depressor reflexes, and so the arterial tone flags.

Bayliss has brought forward evidence that there exists a

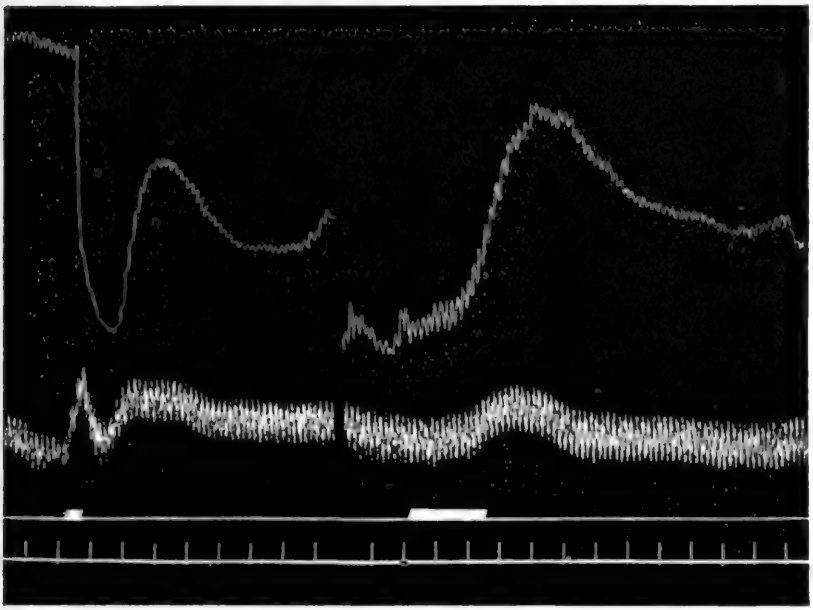


FIG. 22.—Inhibition of constrictors in Lovén reflex. Upper curves, volume of hind-limb; lower curves, arterial pressure. First excitation, median nerve; second, sixth lumbar posterior root (Bayliss).

reciprocal innervation in the case of vaso-motor reflexes as in those affecting skeletal muscle. Under normal conditions the arterioles are in a state of moderate contraction or tone, which may continue even when the vessels are separated from connection with the nervous system. Such tone is a normal property of smooth muscle, and in the case of the vessels it seems to be kept up by the contractile reaction of the arterial wall to the distending force of the pulse, as well as, it is thought, by the internal secretion of the adrenal glands acting on the sympathetic nerve plexus in the

wall (Elliot). This tone can be increased by vaso-constrictor and diminished by vaso-dilator impulses. These impulses may be continuous, resulting from a state of tonic excitation of the respective centres, which is partly of reflex origin and partly depends on the quality of the blood circulating through the centres, *e.g.* by the percentage of O_2 and CO_2 in the blood. Bayliss finds that in depressor reflexes there is, along with inhibition of tone in the vaso-constrictor centres, an excitation of the vaso-dilator centres, and that in pressor reflexes along with excitation of constrictors there is under appropriate conditions inhibition of dilator tone.

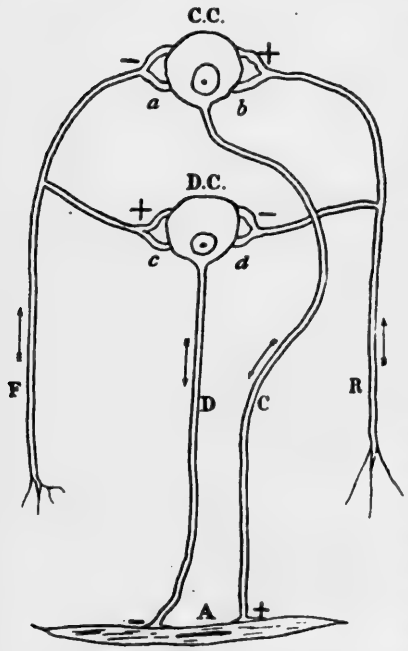


FIG. 23.—F, depressor; R, pressor afferent nerves affecting arteriole muscle through C.C., constrictor, and D.C., dilator centres, as shown by + and − signs (Bayliss).

When an afferent nerve from any particular organ is excited there is produced along with the usual pressor reflex on the general blood pressure a vaso-dilatation in the organ itself. By this means the maximal supply of blood is sent to an active organ. In these local or Lovén reflexes as they are called, Bayliss finds evidence of both excitation of dilators and inhibition of constrictors. Chloral and chloroform convert pressor into depressor reflexes, acting not on the afferent neurone, but on some point in the reflex arc, probably the synapse.

It is not possible to cause a great fall of arterial pressure merely by severe sensory excitation in an etherised and morphinised animal. The pressure falls lower the longer the animal is kept anæsthetised on the table exposed to cold, to chloral or chloroform, or to operations which expose large surfaces and lead to actual loss of blood fluid or to obstruction of venous return, vaso-dilatation, congestion and transudation. Opening the abdomen and exerting

traction on the intestines is the most certain method of producing fall of pressure. The shock produced by severe injuries or operations is probably, therefore, of the same nature as collapse produced by bleeding. In man after a severe injury owing to the shock to the sensory synapses, there is loss of reflex tone, and relaxation of both skeletal and vascular muscle. The entire cessation of movement leads to the pooling of blood in the peripheral fields, and at the same time the injury may entail considerable loss of blood fluid. Toxic products of altered metabolism probably arise in the cooled and stagnant blood which secondarily poison the nervous system. Adrenalin and pituitary extract by constricting the arteries restore the blood pressure, the former for a brief, the latter for a much longer time (Mummery and Symes).

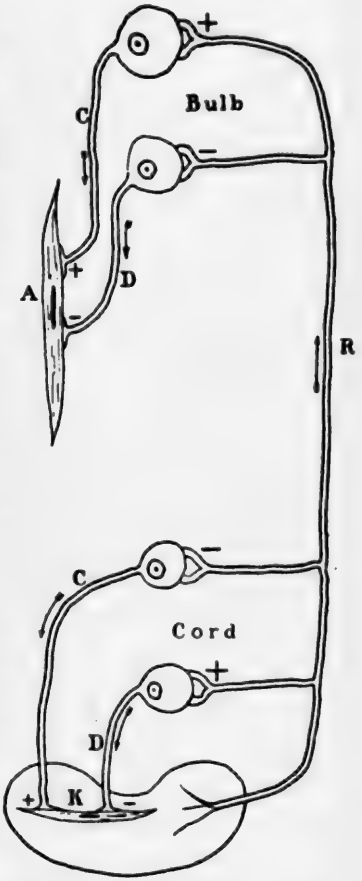


FIG. 24. — C, constrictor; D, dilator neurones; A, arterial muscle cell of body; K, of kidney; R, afferent nerve of kidney influencing bulbar and spinal centres as shown by + and — signs (Bayliss).

Chloroform, says Bayliss, converts pressor into depressor reflexes in the rabbit by reversing the usual excitation of constrictors into inhibition. Strychnine, he says, converts the inhibitory phase of all reflexes into excitation; thus the depressor nerve produces a rise instead of the usual fall under full doses of strychnine. The constrictor centre is excited by the mechanism which normally inhibits it. The first effect of a small dose in the normal animal is to increase the action of the vaso-constrictor centre on the viscera and dilate the cutaneous vessels. The synapses of the pressor fibres with the constrictor centre are the first to show paralysis as the dose is increased. Thus the usual pressor effect which follows excitation of a sensory

nerve then becomes depressor. By increasing the cardiac power, and the action of the skeletal muscles, those of respiration in particular, strychnine may act favourably.

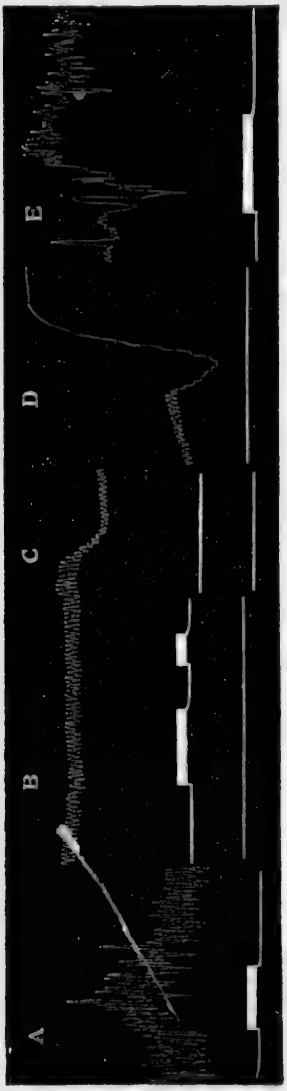


FIG. 25.—Antagonism of chloral and strychnine. Effect of excitation of anterior crural nerve on arterial pressure. A, under ether; B, after chloral; C, effect of first dose of strychnine; D, of second dose; E, after strychnine (Bayliss).

Those who, like Crile, maintain that strychnine is useless as a drug in shock can argue that the constrictor synapses are easily paralysed in this condition by the drug, and thus it may accentuate rather than alleviate the fall of arterial pressure, for it will then excite the vasodilators which supply all parts, and the limbs in particular. The cutaneous dilatation will favour the loss of body heat. Bandaging the limbs and particularly the abdomen partly restores the arterial pressure and cerebral circulation in a rabbit, which has been fixed in the vertical position, as it does in the dog chloroformed or collapsed from loss of blood. Crile has introduced a rubber pneumatic suit for confining the body in states of shock. An equable air pressure is kept up so that the arterial pressure measured with the sphygmometer is restored. Flaps are arranged in the dress which can be removed for the surgeon to operate. The pressure of the air can be reduced gradually as the patient shows signs of recovery. This seems a sound and rational method of treatment. The objects in view are to fill the heart, increase the resistance in the arterioles, and compress the capillary-venous areas of the limbs and trunk

so that the cerebral, coronary, and pulmonary vessels are well filled.

Direct transfusion of human blood from artery to vein has been used by Crile in extreme cases of simple shock. It is unwise to use this in any state of toxæmia, for hæmalysins may then come into play. Injection of physiological saline is found a valuable aid.

In collapse brought about by the injection of bacterial toxins, it is said, the synapses of the vaso-motor centre are at fault, so that neither excitation of a sensory nerve nor asphyxia provoke any rise of arterial pressure, while compression of the abdomen or of the descending aorta provokes it, showing that the heart is not exhausted and can still respond with increase of energy to better filling, and increased resistance to its output (Romberg).

Rabbit : 0·2 *gm. Chloral intra-venously injected.*

Excitant.	Arterial Pressure.
	Mm. Hg.
...	56·5
Sciatic faradised . .	128·0
Abdomen massaged .	147·0
Aorta compressed . .	153·5
Asphyxia . . .	139·5
...	81·5
Splanchnic nerves divided.	
...	34·0
Sciatic faradised . .	34·5
Abdomen massaged .	119·0
Aorta compressed . .	132·0
Asphyxia . . .	27·5
...	33·0
Chloral injected again.	
... .	20·0
Abdomen massaged .	66·0
Aorta compressed . .	52·0
...	23·0

These figures show the relative effect of paralysis of vaso-motor nerves and of damaging the heart by chloral, and with them the following may be contrasted :—

Rabbit: 1·2 *c.m. Diphtheria Toxin injected.*

Collapse after Diphtheria Toxin.

Excitant.	Aortic Pressure.
	Mm. Hg.
...	39·0
Sciatic faradised . .	47·0
Abdomen compressed .	81·0
Asphyxia . . .	31·0
Last stage of collapse	
...	17·5
Abdomen compressed .	62·0
Asphyxia . . .	18·0

Mr. H. P. Dean informs the writer that in spinal anæsthesia produced by Stovain (injected into the lumbar part of the spinal canal), the sensory anæsthesia spreads upwards to a higher level than the motor paralysis, and the medullary centres are unaffected or almost so when the anæsthesia has spread even to the head. The sensory synapses are the first to fail. The blood pressure falls some 20 mm. Hg only, showing that the visceral vaso-constrictor nerves are maintained in good state. To sum up then, the condition of shock or collapse is associated with cessation of the reflexes which maintain the body in a state of vascular tone and muscular activity. Hence the stagnation of the blood, fall of blood pressure, and loss of body heat.

BIBLIOGRAPHY

Carrel, Journ. Exper. Med., ix., p. 226, 1907.
MacWilliam, Proc. Roy. Soc., lxx., p. 109, 1902.
Lister, Brit. Med. Journ., 1899, 1, p. 924.
W. Russell, Arterial Hypertonus, Sclerosis and Blood Pressure, 1907.
G. Oliver, Studies in Blood Pressure, 1908.
Roy and *Adami*, The Practitioner, xlv., p. 32.
Howell and *Brush*, Bost. Med. Surg. Journ., cxiv., 146, 1901.
C. J. Martin, Brit. Med. Journ., 1905, 1, p. 870.
Erlanger, Amer. Journ. of Physiol., x., 1904.
McCay, Lancet, 1907, i., p. 1484.
Dahlgren and *Kepner*, The Principles of Histology, Macmillan, 1908.
Thoma, Textbook of General Pathology, Trans. A. Bruce, 1896.

Roy and *Brown*, Journ. of Physiol., 2, p. 323, 1879–80.
V. Recklinghausen, Arch. f. Exp. Path. in Pharm., 55, 375, 1906.
Lewy, Arch. f. d. ges. Physiol., 65, 447, 1897.
Stewart, Manual of Physiology, 1895, p. 59.
Leonard Hill, The Phys. and Path. of the Cerebral Circulation, London, 1896. Cerebral Anæmia, Trans. Roy. Soc., Journ. of Physiol., xxvii., p. 337, 1901; and xxviii., p. 122, 1902. Article Circulation, Schäfer's Textbook of Physiology, vol. ii., 1900.
T. Henderson, Ophthal. Soc. Trans., xxviii., 1908. The Ophthalmoscope, Oct. 1908.
T. Lewis, Journ. of Physiol., xxxviii., p. 240, 1908.
Tigerstedt, Ergeb. der Physiologie, vi., p. 269.
E. Weber, Arch. f. Physiol., 1907, p. 300.
Mosso, Die Furcht, 1889.
Bainbridge, Practitioner, lxxv., p. 633, 1905.
Sollmann, Amer. Journ. of Physiol., 1905, 13, p. 241.
Bolton, Journ. Path. and Bact., 1903, p. 67.
Stewart, Guthrie, &c., Journ. Exper. Med., viii., 289, 1906; x., 371–490, 1908.
Cohnheim, Vorlesungen über Allgem. Pathologie, 1882.
Worm-Müller, Transf. u. Plethora, Christiania, 1875.
R. du Bois Raymond, Brodie, and *F. Müller*, Arch. f. Physiol., 1907, Suppl. Bd., p. 37.
Starling, Schäfer's Physiology, 1, 285, 1898.
Bier, Hyperamie als Heilmittel, 1903, Leipzig.
A. Wright, The Practitioner, lxxx., p. 600, 1908.
Sherrington, The Integrative Action of the Nervous System, 1906.
Porter and *Quinby*, Amer. Journ. of Physiol., xx., p. 500, 1907–8.
Bayliss, Proc. Roy. Soc., 80, p. 339, 1908.
Elliott, Journ. of Physiol., 32, 401, 1905.
Crile, Blood Pressure in Surgery, 1903.
Mummery and *Symes*, Brit. Med. Journ., Sept. 19, 1908.
Romberg, Pässler, &c., Deutsch. Arch. f. Klin. Med., Bd. 64, p. 652, 1899; Bd. 77, p. 96, 1903.

For a general list of recent literature consult Heinz. Handb. der exper. Path. u. Pharm., vol. 2, p. 283.

THE MECHANISM OF RESPIRATION IN MAN

By ARTHUR KEITH.

The following is a summary of the chief points dealt with in this article :—

(1) The lung is composed of elements of varying degrees of extensibility; hence the expansion of its parts are unequal during inspiration.

(2) The infundibula or air sacs are the essential distensible (inspiratory) elements of the lungs. The distensibility of any part of the lung will depend on the number and size of the infundibula in that part.

(3) The bronchial musculature regulates the tension of the infundibular air and may regulate the distribution of air and blood throughout the lung.

(4) The lungs do not expand equally in all directions, but execute a movement in certain definite directions during inspiration.

(5) The roots of the lungs are not fixed but undergo a respiratory movement.

(6) The great fissure of the lung is of functional significance. The upper lobe is chiefly expanded by a mechanism formed by the upper ribs, the lower lobe by a compound mechanism formed by the diaphragm and lower ribs.

(7) Expiration is controlled by muscular action.

(8) The extensibility and elasticity of the thorax are factors in producing expansion or compression of the lung only when the ribs pass into extreme inspiratory or expiratory positions.

(9) The first pair of ribs and the manubrium sterni are parts of a single mechanism which may be described as the thoracic operculum. The sterno-manubrial joint is of functional importance.

(10) In observing and analysing the respiratory movements of the thorax it is advantageous to treat the costal cartilages

and their musculature as an individual part of the respiratory mechanism.

(11) The diaphragm acts as a true piston, moving the abdominal contents downwards and forwards, the direction depending on the type of respiration. The effect of its contraction depends on the action of its antagonists.

(12) That in describing the movements of the ribs it is necessary to recognise at least two types, one representative of the upper costal mechanism and the other of the lower or diaphragmatic mechanism. The movements of the lower set are correlated with the action of the diaphragm; those of the upper set work independently of the diaphragm.

(13) The floating ribs (eleventh, twelfth, and often the tenth) are functionally parts of the abdominal wall.

(14) The articulations, muscles, movements, and conformation of the ribs of the lower set differ widely from those of the upper set.

(15) The action of the intercostal muscles depends on the antagonists brought into use. Some intercostal spaces are widened and some diminished during inspiration, and the same is true during expiration.

(16) The levatores costarum have no action on the ribs; they are purely spinal muscles.

In this article the writer proposes to summarise certain recent papers dealing with the respiratory expansion and contraction of the human lungs. The evidence contained in these papers is derived from three sources: (1) From measurements of the respiratory movements of the body wall by photography, by X-rays, by recording tambours, by direct measurements, or by tracings taken with strips of lead moulded on the body. When possible the writer has selected those observations which deal with the normal unconscious respiratory movements rather than records made on conscious subjects taking exaggerated breaths. (2) From observations on the anatomy of parts concerned in respiratory movements, for whatever theory be adopted of these movements, it must give a rational and complete explanation of the form and arrangement of the structures concerned in them. (3) From clinical observations made by means of percussion and auscultation. When the evidence from these three sources is summarised it is found

to necessitate a considerable alteration in our current teaching of the mechanism of respiration.

The Extensibility and Elasticity of the Lung

It is usually presumed that the lungs are equally extensile throughout, but an examination of their structure shows that this cannot be so. From an anatomical point of view the lung may be divided into three zones : (1) A root zone containing the bronchus, artery, and vein, and their main divisions, with lymphatic glands and vessels, and much fibrous tissue, all structures offering great resistance to a distending force. (2) An intermediate zone in which vascular and bronchial ramifications radiate towards the surface of the lung with pulmonary tissue implanted between the rays. It is a zone containing structures of varying degrees of extensibility, the veins being the least extensile and the pulmonary tissue the most. (3) An outer zone, estimated roughly at 25 to 30 mm. in depth, which expands much more freely and equally than the intermediate zone. Perhaps the subpleural stratum of the outer zone should be distinguished, for if a lung, which has been removed from the body, be gradually inflated, it will be found that the subpleural stratum is at first elevated at certain points into plateaux about 2 mm. above the surface of the lung, and from these elevated points the process of distension of the subpleural stratum spreads out in all directions. This at first appeared to be due to a more complete collapse of the subpleural air sacs, but microscopic sections show that in the collapsed condition these sacs are still as large as the deeper, so it may be concluded that, when distended, they are larger than the deeper sacs, and collapse to a greater degree. Seeing that the lung is intersected with radiating bronchio-vascular rays, of a much lower degree of extensibility than the pulmonary tissue between them, one must suppose that these rays during the inspiratory expansion of the lung must move apart so as to permit the pulmonary tissue lying between them to expand. A consideration of the anatomy of the lung and of its movement during inspiration shows that the expansion of the lung is not the simple dilatation it was believed to be ; its expansion is a regulated act resembling more the opening of a Japanese fan than the distension of a simple elastic sac. Among recent writers, Tendeloo is the only one to emphasise

the varying degree of extensibility of the structures of the lung. In all mammalian lungs the veins and arteries occupy a definite and constant relationship to the bronchial ramifications—a relationship which must have a functional significance. Amongst the various means the writer employed to estimate the extensibility of the several parts and structures of the lung was that of marking the surface of the partly inflated organ with points placed at regular intervals, and then measuring the distances between these points when the lung was more fully inflated. The parts of the lung which were found to expand most were the central areas of the costal and of the diaphragmatic surfaces. The method was abandoned because it was found that the expansion obtained by inflating the lung did not correspond to the expansion of the lung by means which imitated the normal action of the thoracic walls. Hutchinson discovered long ago that the form assumed by the thorax when the lungs are inflated after death, differs altogether from the inspiratory position of the thorax. His observation, however, has been forgotten, and models of lungs so inflated are at present the only ones on the market. Several anatomical papers have been published recently giving the inspiratory position of the apices of the lungs, that position being determined by artificial inflation of the lung. In the dead body the lung, when inflated, expands in the direction of least resistance.

On the Function and Nature of the Infundibula

Closely related to the extensibility of the various elements of the lung is the question of the function and nature of the infundibula. In the most valuable work recently published by Oppel the use of the term infundibulum is condemned. He prefers to follow Miller in distinguishing the following terminal air spaces in the lung:—

(1) The terminal bronchiole, with its sphincter-like arrangement of musculature; (2) the vestibule; (3) the atrium; (4) the air sacs; (5) the alveoli implanted on the walls of the air sacs.

Such an elaborate nomenclature obscures the functional nature of the final pulmonary elements, for while the terminal bronchus is one functional element, and the alveoli another, the vestibule, the atrium, and air sacs combined form but one element, namely, the essential distensible air spaces of the lung (bellows part), and it is well to retain the term infundibulum to designate the com-

plex space in which a terminal bronchiole ends. In the frog's lung the central space represents the infundibular element of the mammalian lung; in reptiles it is represented by the thin walled posterior part of the lung; in birds it is represented by the air sacs; in the mammalian lung the distensible element is scattered throughout the lung, whereas in all other vertebrate it forms a separate part. If out of a rubber balloon a model of the terminal bronchiole infundibulum and alveoli be made and inflated, it is the central or infundibular space which expands most, the alveoli implanted on its walls being widened but at the same time rendered more shallow. The point which one seeks to emphasise is that it is not the alveoli but the infundibula that should be regarded as the essential expansile parts of the lung; the larger and more plentiful the infundibula in a part of the lung, the more readily will that part respond to any distending force. Oppel gives the diameters of the infundibula in the apical part of the lung as ·12 mm. at the third year and ·45 mm. at the seventieth; in the basal part of the lung as ·38 mm. at the third year and ·85 mm. at the seventieth. They are largest in the subpleural zone and smallest in the root zone. One infers, therefore, that, when a breath is taken, the base expands more readily and to a greater extent than the apical part, and the subpleural more than the part at the root. When emphysema occurs it is the infundibula which first become hyperdistended, and the parts most liable to emphysema are those in which the infundibula have normally the greatest size.

The Bronchial Musculature

The older physiologists regarded the bronchial musculature as expiratory in function; even now most medical writers ascribe the reflex contraction of the lung (Abram's reflex) which follows any stimulation of the chest wall to the action of the bronchial musculature. It is more probable that the retraction of the lung is due to a reflex contraction of the musculature of the body wall. The action of the musculature of the bronchioles in regulating the tension of the air within the infundibula has not received the attention it deserves. The more the calibre of the bronchiole is diminished during inspiration the greater must be the negative tension within the infundibula, a tension which must act on and distend the capillaries and various blood spaces embodied in the

walls of the infundibula. The bronchial musculature by diminishing or increasing the access to the infundibula in various parts of the lung may regulate the distribution of the indrawn air throughout the lung. By regulating the intra-alveolar pressure it may also influence the distribution of blood throughout the lung, and take the part of the vaso-motor mechanism which has not been proved to exist in the lung.

The Necessity of Recognising Surfaces of Direct Expansion and Surfaces of Indirect Expansion on the Lung

The lung is usually regarded not only as being equally distensible in all its parts, but also of expanding equally in all directions during inspiration. This is far from being true of the mammalian lung. Of the five areas which one may distinguish on the surface of the human lung, three are in contact with stationary parts of the thoracic wall, and therefore cannot be directly expanded. These three pulmonary surfaces are—(1) The *mediastinal*, in contact with the pericardium and structures of the mediastinum; (2) the *dorsal surface*, in contact with the spinal column and with the spinal segments of the ribs—those parts of the ribs to which the erector spinæ is attached; (3) the *apical surface*, the pulmonary area lying in contact with Sibson's fascia at the root of the neck. It is not strictly true to say that these three parts of the pleural wall are stationary, for the heart being conical in shape, with its base resting on the diaphragm, it is clear that the mediastinal surface of the lungs may expand inwards with the inspiratory descent of the heart; only the dorsal part of the apical surface is stationary, for the ventral or anterior part is elevated with the first rib, but the fact remains that during inspiration the apical resonance does not extend into the neck but decreases (Colbeck), and by placing a tambour on the neck over the apex of the lung it is found that the apex descends whenever the diaphragm is well in action, even if the first rib remains stationary. The two surfaces of the lung which are directly expanded are the diaphragmatic and ventro-lateral or sterno-costal. Thus if the diaphragm and lower ribs are in action the whole lung is expanded in a downward and forward direction, the apical surface remaining stationary or descending until the structures of the neck become sufficiently tense to resist a further descent.

The negative tension, in such an inspiration, falls first and most in the basal part of the lung; hence one finds very frequently a horizontal groove (Harrison's sulcus) on each side of the thorax corresponding to the level of the domes of the diaphragm and to the zone of greatest negative pressure in those who have had the respiratory passage obstructed. Meltzer found the degree of negative pressure within the thorax of rabbits increased as the diaphragm was approached; it is least along the stationary walls of the thorax. It is thus apparent that a certain degree of the expanding force transmitted by the thorax to the surfaces of direct expansion is lost as it passes through the lung to the surfaces of indirect expansion. Further, the extent to which any part of the lung is expanded depends on the distensibility of that part, being greatest in the superficial zone of the lung and least in the root zone. That the expansion of the lung does not take place instantaneously and equally throughout all its parts is well substantiated by clinical observation. Huggard and Clive Riviere observed independently that if percussion and auscultation of the lung were carried out before a deep breath were taken, the apices of the lungs, especially in those who were regarded as being the subjects of a phthisical tendency, were less in action than the rest of the lungs; Lloyd Jones records that when a breath is taken the resonance of the anterior part of the apex of the lung increases much more than the posterior; Gerhardt noticed that when a pleural effusion was being absorbed the apex of the lung was the last part to regain its normal resonance. It is a well-known clinical fact that a localised consolidation is surrounded by an area of increased resonance, showing that the diminution of one part of the lung is not followed by an expansion of the whole lung but only of the part immediately adjacent. When it is remembered that those who lead sedentary lives use their lungs to only 10 per cent. or even less of the full pulmonary capacity, the importance of recognising that a thoracic movement only affects that part of the lung directly subject to the movement will become apparent. In those who have contracted a lazy habit of body it is possible for the parts of the lung which are the most remote from the surfaces of direct expansion and at the same time of a low degree of distensibility, to pass into a condition of partial or almost complete disuse; such a part is that region of the apex where phthisis so frequently commences.

Respiratory Movements of the Roots of the Lungs

The root of the lung has hitherto been regarded as the most fixed part of the lung, the part from which the expansion of the lung takes place. Were this so it is manifest that those parts of

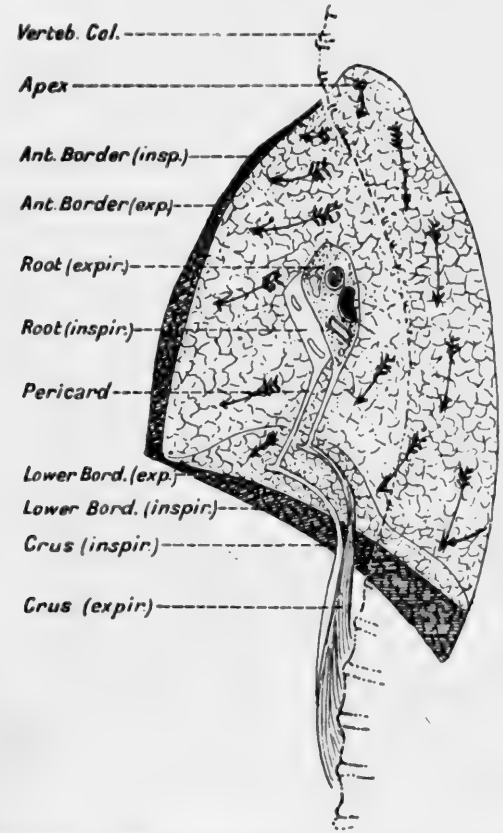


Fig. 1.—Mediastinal aspect of the right lung to show the respiratory movement of the root. The crus of the diaphragm is also indicated, and its attachment to the root of the lung through the pericardium. The arrows indicate the direction of the inspiratory movement of the various parts of the lung.

the lung which lie between the root and the stationary walls of the thorax could undergo no expansion. The truth is that during a complete inspiration the whole lung, root included, undergoes

a definite movement. In the normal mixed inspiration, where diaphragm and ribs co-operate equally or almost equally, the lung expands in three directions—downwards, forwards, and outwards, the root sharing in the combined movements. When the abdominal breathing is well marked, the trachea can be felt descending in the neck as the epigastrium comes forwards. By the use of X-rays the heart, and therefore the roots of the lungs, for the heart is bound firmly to them, can be seen to follow the movements of the chest wall; with a thoracic breath, the heart follows the movement of the sternum; with a diaphragmatic breath, it descends with the diaphragm. The great muscular crura of the diaphragm, forming one-third of that muscle, can act directly on the roots of the lung through the pericardium and heart. In cases where the roots of the lungs are bound to the posterior or stationary wall of the thorax through adhesions set up by mediastinitis, Wenckebach observed that both the respiratory and circulatory movements were abnormal in character.

The Functional Significance of the Division of the Lungs into Lobes

It is usually said that the division of the lungs into lobes has no functional significance. This opinion is founded on the fact that they may be only partially developed or completely obliterated by disease without altering the functional capacity of the lung. The obliteration of the pleural cavity by adhesions has so little apparent effect on the respiratory movements that their presence cannot be detected during life. In one case, where the lungs were completely adherent, Hutchinson found the vital capacity to be 680 cc. above the average amount. This method of reasoning is liable to lead one into great error, for there are many functional organs in the body which may be removed without any marked disturbance of the bodily economy. When the normal respiratory movements of the lung are fully understood it will be found that the great fissure, which divides the upper from the lower lobe, is functional in its significance. The upper lobe is normally expanded by one mechanism, the lower by another. When the lung is removed from the body and slightly inflated there will be seen marked out on the lateral and anterior aspects of the upper lobe—especially in the lungs of women—

the impressions of the first, second, third, fourth, and fifth ribs and costal cartilages. These impressions are marked in two ways: the part of the lung lying under the rib is less pigmented and is grooved; the zones corresponding to the intercostal spaces are more pigmented and are elevated above the level of the costal zones. To obtain such results, for these marks cannot be post-mortem effects, the relationship of the upper lobes to the upper ribs must have been stationary during life; there could have been no gliding of the lung across the ribs and spaces during inspiration and expiration. But on the lower lobe, except for an occasional impression of the seventh costal cartilage, at the anterior angle, these costal impressions are absent; the pigment is evenly distributed, or if not, does not correspond to spaces. The inference one draws is that the lower lobe glides beneath the ribs during the respiratory movements; there is not, as in the upper lobe, a constant relationship between ribs and spaces. But it must be noted, too, that the dorsal surface of the upper lobe does not show these costal impressions; here, too, there must be a downward and upward movement, one which I had inferred to take place before my attention was drawn to the costal markings as a guide to the respiratory movements of the lung. When dealing with the movements and mechanism of the ribs it will become apparent that the lower lobe and the dorsal part of the upper lobe are chiefly expanded by a diaphragmatic mechanism, and the upper lobe by the upper five ribs. It must not be supposed that these markings are to be found on the lungs of every individual; they are constant in the lungs of women, and their frequent absence on men's lungs can be understood when one remembers how many there are that obtain their chief inspiratory expansion by a moderate use of the diaphragmatic mechanism alone. Pleuritic sounds and pleuritic pains are most intense over the lower lobe; Fowler and Pasteur have recorded cases of paralysis of the diaphragm where the collapse was confined to the lower lobe. The upper lobe is always relatively larger in women than in men, a result to be expected from their manner of breathing. It is true that pleuritic friction can frequently be detected over the upper lobe; this fact must certainly be taken into consideration, but it must be remembered that a localised pleurisy has a powerful reflex influence on the respiratory musculature corresponding to that part, and it is therefore probable that

there is a grave disturbance of the normal respiratory movements in such cases.

The Action of the Respiratory Musculature in Normal Expiration

A consideration of the evidence now at our disposal makes it difficult to believe that normal expiration is merely the result of an elastic recoil. The recoil is evidently under muscular control. The antagonist of the diaphragm is the musculature of the belly wall; it is difficult to believe that the replacement of the diaphragm and the abdominal viscera at the end of an inspiration is merely an elastic recoil of the abdominal musculature. One cannot deduce the elasticity of a living muscle from the study of the dead, but I may put on record here the following observation. A piece of the human rectus abdominis 135 mm. long stretched to 180 mm. when a weight of 10 kilos was attached to it; on removing the weight it had retracted in five minutes to 150 mm. It is improbable that the muscles which are attached to the ribs are carried by the ribs as passive burdens during expiration. The reflex co-ordination which Sherrington has shown to exist between so many antagonistic groups of muscles, probably holds true also for the inspiratory and expiratory groups of muscles. Duchenne found that the abdominal musculature was brought into action when the phrenic nerve is stimulated. Spina and Mislawsky observed that stimulation of the apparent fibres in the phrenic had an inhibitory action on the abdominal musculature. Baglioni obtained an expiratory movement of the body wall when the diaphragm itself was stimulated. At least one can feel the upper part of the rectus abdominis harden under the fingers during expiration, as if it were in action. The observation of Treves, the Italian physiologist, also points to expiration being a muscular act. He found that if an inspiration is arrested, it is followed by an expiration of normal amount. Mosso observed that the respiratory movement became thoracic in type when the horizontal position was assumed, a result which cannot be ascribed to an alteration in the elastic recoil of the lung. Mosso concluded that the assumption of the thoracic type of respiration in the supine position is brought about through a reflex action of the vagus, but in the writer's opinion the change is due to an alteration in the

action of the expiratory muscles. The erect posture necessitates an increased action of the musculature of the belly wall in order to balance the body, the ribs being thus more firmly fixed than in the supine position; with the assumption of the supine position the musculature of the belly wall is relieved of its postural function, thus lessening the strain on the ribs and allowing them to move more freely. If expiration were an elastic recoil uncontrolled by muscular action one would expect the thorax to diminish simultaneously in all its parts; this is not so, for expiration like inspiration is a definite movement commencing in the upper or lower part of the thorax and spreading gradually to the rest. Those who regard normal expiration as a result of the elastic recoil of the lungs cite as conclusive evidence of their opinion those cases of fracture of the spine or section of the spinal cord where the diaphragm is the sole respiratory muscle in action. In such cases the writer has observed that the patient lies on the back or turned somewhat on the left side; the epigastric movements are greater than normal; pressure of the hand applied to the epigastrium gives immediate distress and completely alters the type of respiratory movement, the lower ribs being then raised and the lower part of the chest expanded. Further, the writer observed that the diaphragm in such cases is kept in a condition of over-action; in one case the diaphragm worked some 25 to 30 mm. below its normal level, thus compressing the abdominal contents and obtaining a recoil from the weight and tension of the abdominal viscera. To what extent the tonus of the abdominal and thoracic musculature is lost in these cases has not been determined. Mosso has shown that tone varies independently of the contractibility, and that the abdominal musculature possess a high degree of tone. The parietal layer of the peritoneum is highly extensile and elastic to preserve its smoothness in the various states of movement.

The Respiratory Value of the Elasticity of the Thorax

The degree of elasticity of the living thorax has to be estimated from experiments made on the dead. We now know, from observations made by the use of X-rays, that the diaphragm is

in a position of ultra-expiration after death, and we infer that if the elasticity of the thorax is in antagonism to the elasticity of the lungs at the end of expiration, then the elastic recoil of the thorax in the dead is an exaggeration of that in the living. Sir Douglas Powell made observations on ten subjects; he noted the expansion of the thorax when the pleural cavity was punctured and the lungs allowed to collapse. In six of these there was no expansion of the thorax; in four the average expansion forwards of the chest wall was 2·3 mm. When it is remembered that the lateral or antero-posterior thoracic expansion varies from 1 to 2 mm. in normal respiration, even in men with the thoracic type of breathing, it is evident that the elasticity of the thorax can play but a slight part in normal expiration. Any observation made on the dead body is vitiated by the rigor mortis and post-mortem changes of the muscles. I observed that when the muscles are removed from the thorax that the weight of the ribs and sternum was enough to cause the thorax to assume an expiratory position when the body was turned in the feet-down position, and to pass into the inspiratory position when the body was inverted. One must conclude from a study of the thorax of the dead that the rib movements are so free that elastic recoil of the thorax comes to be a factor in expiration and inspiration only towards the extreme limits of respiratory movements.

Recently the writer had reason to compare the elasticity and collapsibility of the thorax in living subjects with that of dead subjects. The matter has some importance in determining the best method for performing artificial respiration on the apparently drowned, and also in selecting the position of patients in performing intra-thoracic operations. Elsberg, for instance, asserts that the pleura may be opened without collapse of the lung if the patient be placed in the prone position; it is certainly possible to reduce the capacity of the thorax in adult human beings to a point when it is too small to contain the collapsed lungs, and hence a part is extruded as a hernia. The writer's investigations show that the living and dead thorax react quite differently when compressed, the difference being due, in his opinion, to the reflex action of the respiratory musculature. The following table gives the results of his experiments; the measurements for the living are the average for ten students varying from eighteen to twenty-four years of age; those given for the dead are the averages from five

dissecting-room subjects varying in age from fifty to seventy-two years, in whom the compressibility of the thorax is expected to be greatly diminished.

Results of Compression of the Thorax.	*Living.*	*Dead.*
1. The front-to-back diameter of the thorax was diminished in turning from the supine to the prone position	17·4 mm.	21·4 mm.
2. The side-to-side diameter in the same experiment increased	22·1 mm.	13·5 mm.
3. The front-to-back diameter decreased on placing 10 kilos. on the thorax (subject supine)	23·7 mm.	29·6 mm.
4. The transverse diameter increased in the same experiment	5·6 mm.	13·5 mm.
5. The front-to-back diameter of the thorax decreased on placing 10 kilos. on the thorax (subject prone)	12·8 mm.	4·6 mm.
6. The transverse diameter increased in the same experiment	3·0 mm.	8·6 mm.

These experiments show that the compressibility of the thorax is largely modified by the action of muscles during life, and that in the prone position a very great degree of the natural elasticity of the thorax is lost.

Freund, whose observations are receiving active attention in Germany, after many years of neglect, is of opinion that the elastic torsion which occurs in the cartilage of the first rib during inspiration is one of the chief active forces in producing an expiratory recoil of the thorax; he also regards emphysema as a result of loss of elasticity of the costal cartilages. His opinion concerning the expiratory recoil of the cartilage of the first rib will be referred to in dealing with the sterno-manubrial joint; as regards the loss of elasticity of the cartilages causing emphysema, it may be said that surgeons have put Freund's belief into practice by section of the costal cartilages in such cases, but the results of such experiments have not yet been determined. Certainly calcification of the costal cartilages frequently occurs without emphysema.

The First Rib, Manubrio-sternal Joint, and their Respiratory Significance

The first rib has always been treated as merely one of the costal series. Its articulation to the spine, its ligaments, its muscles, its shape, its costal cartilage, its intimate union with the manubrium sterni, differ so markedly from the corresponding features of other ribs, that were only the anatomical evidence available, one would conclude that it differed from all the others in its respiratory function. An examination of its movements and of the part it plays in expanding the lung shows this is so. The first pair of ribs and the manubrium sterni are bound intimately

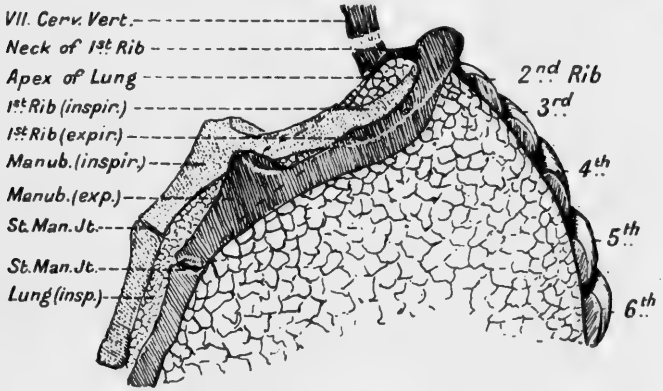


Fig. 2.—Diagram to show the respiratory movements of the first pair of ribs and manubrium sterni, and the effect of these movements on the expansion of the apex of the lung.

together by the broad and short first pair of costal cartilages, and form with the manubrium, a united structure which may be described as the lid or operculum of the thorax. Behind, this lid is articulated to the spinal column by a joint which is set more transversely and is wider in the extent of its attachment than any other of the costal arcs; in front the lid is articulated with the body of the sternum at the manubrio-sternal joint. The manubrio-sternal joint must be counted amongst the important respiratory joints. Anchylosis of this joint is rarely seen before the fiftieth year, and it is uncommon before the sixtieth. The respiratory movement which occurs at it varies with the individual, with the type of respiration, being greatest in those with

the thoracic type, and with the extent of the respiratory movement. Braune estimated its movement at 5° to 13°, Rothschild, who regards limitation in the movement of this joint as a cause of consumption, estimated the average movement (in full inspiration) to be 15·85° in the male and 12·85° in the female; while the writer, who was unaware of Rothschild's observations, found it varied from 1° to 16°. The degree of movement depends chiefly on the inspiratory behaviour of the body of the sternum, which is extremely variable. In some individuals the lower end of the sternum during the elevation of the thorax during inspiration may be drawn towards the spine or move forward to a less degree than the upper end of the body of the sternum; in such, the sterno-manubrial movement is free. If, on the other hand, the lower end of the sternum moves more freely away from the spine than the upper end, the movement at the joint is less extensive. At the sterno-manubrial joint, the operculum or lid of the thorax articulates with the anterior thoracic wall. The prominence of this joint on the surface of the thorax is extremely variable—so many conditions may render it unduly prominent. Ludwig, the Parisian physician, is said to have regarded an undue prominence of the articulation (Angulus Ludovici) as an indication of phthisis; but researches made by recent German writers have failed to trace such a statement in Ludwig's writings. Rothschild found that the sterno-manubrial movements were limited or absent in phthisical subjects, and ascribed the susceptibility of the apex to phthisis as due to an anchylosis or limitation of movement at this joint. In his opinion a free manubrio-sternal movement is necessary if the apex of the lung is to be properly expanded. Freund attributes the incomplete expansion of the apex in the phthisical action to a congenital shortening and ossification of the cartilage of the first rib. It is true that the necks of the first pair of ribs are so articulated to the spine that with the elevation of the manubrium sterni there is some degree of torsion of their cartilages, but the amount of the torsion is slight in extent because of the particularly loose manner in which the heads of those ribs are bound to the first dorsal vertebra. The writer, unaware of the observations and theories of Freund and Rothschild, had concluded that the ossification of the first costal cartilage and limitation of the sterno-manubrial movements were consequences rather than causes of a limited expansion of the apices of the lungs. In

dealing with the significance of the division of the lungs into lobes, the direct influence of the diaphragm on the apices of the lungs has been already pointed out. The upward movement of the first pair of ribs and manubrium expand chiefly the anterior or ventro-lateral part of the apex of the lung; the movement has but an indirect influence on the dorsal part of the apex, especially that part lying in front of the necks of the first and second pair of ribs. It is the dorsal part of the apex of the lung that is the common initial site of pulmonary tuberculosis. To secure a free expansion of that area of the lung a full diaphragmatic contraction is much more effective than any movement of the upper thorax.

The Respiratory Movements of the Costal Cartilages

In man, and it is true of nearly all mammals, the costal cartilages progressively increase in length and in their declivity to the sternum as one passes from the first downwards. The following are the lengths of the cartilages in millimetres of a well-built man from the first to the ninth ribs :—first, 25; second, 37; third, 50; fourth, 62; fifth, 75; sixth, 87; seventh, 112; eighth, 137; ninth, 160. Although the eighth and ninth cartilages do not directly reach the sternum, yet for functional purposes they really do through their close union with the seventh costal cartilage, and hence their length is estimated as if they did reach the sternum. The costal cartilage of the first rib descends to reach the sternum; that of the second normally lies horizontal and joins the sternum at a right angle; the third ascends to the sternum, and the degree of ascent becomes greater with each succeeding cartilage until, at the lower end of the sternum, the seventh pair of costal cartilages form together the subcostal angle which varies from 45° to 90°, 65° being a common size in well-formed adults. In observing the respiratory movements of any individual it is well to regard the costal cartilages as a separate part of the respiratory mechanism; they have their own muscles; during inspiration the interchondral muscles (anterior part of the internal intercostals) and the anterior digitations of the diaphragm raise them into a more horizontal position, increasing the transverse diameter of the thorax and the size of the subcostal angle. The cartilages are depressed and the subcostal angle decreased by the upper part of

the transversalis and triangularis sterni; the rectus abdominis also depresses the cartilages, but its action, owing to its peculiar insertion, is really that of a depressor of the whole thorax. Measurements of the respiratory movements of the subcostal angle are useful in distinguishing between an inspiratory movement effected by an upward movement of the thorax as a whole, and one in which the upward movement is accompanied by a tilting upwards of the outer ends of the cartilages. For instance, during a forced inspiration, in three individuals, selected at random, the increase at the subcostal angle was 6°, 9°, and 30°. Unfortunately nearly all the observations published on the movements of this angle relate to forced inspiration; in quiet inspiration the increase is about 1·5° for those with an abdominal type of respiration, and about half that amount in those with a thoracic type. The writer, from observations made by the aid of X-rays, has come to regard a free movement of the subcostal angle as an index of a free action of the diaphragm.

The Action and Movements of the Diaphragm

In recent years anatomists have had an opportunity, thanks to the discovery of Rontgen, of correcting their inferences as to the action of the various parts of the diaphragm by direct observation on the living. When tested in this way the elaborate deductions of Hasse as to the internal respiratory movements have proved to be remarkably near the truth. He inferred that the central or pericardial part of the diaphragm must also participate in all respiratory movements, that the diaphragmatic movement as a whole must be in a forward as well as in a downward direction, and that all diaphragmatic movements were accompanied by a definite movement of the abdominal viscera. The writer has shown that the diaphragm is made up of two parts which are different in origin, different in their nerve supply, and different in their action. These two parts are the spinal or crural part, the fibres of which arise from the spinal column and arcuate ligaments, and ascend to be inserted into the posterior or concave margin of the central aponeurosis; these fibres are normally from 125 to 150 mm. long, and weigh about 60 grammes. The other part of the diaphragm—the sterno-costal—weighs about 96 grammes; its several digitations vary in length, that from the ninth costal car-

tilage being longest; the fibres pass backwards as they ascend. Thus while the spinal segment of the diaphragm tends to elongate the thorax in a vertical direction, the sterno-costal part pulls forwards and downwards the abdominal viscera, increasing the back-to-front diameter in the lower part of the thorax. The resultant movement of the diaphragm is one in a downward and forward direction; the more the thorax is elevated the greater is the forward visceral movement; the more the downward movement, the more are the abdominal viscera depressed. The writer has observed in patients who were described clinically as neurasthenic, that the spinal part of the diaphragm may act forcibly while the sterno-costal part is almost passive. Duchenne showed conclusively that if descent of the abdominal viscera is restrained the diaphragm spent its force in elevating the thorax. Dally observed, and the observation has been frequently verified, that the curvature of the domes of the diaphragm is scarcely altered during even a profound inspiration. We have come to see that the diaphragm, rendered semi-solid by the abdominal viscera and having its circumferential zone kept constantly applied to the inner wall of the lower part of the thorax by the negative intra-thoracic pressure, acts as a true piston—a piston moving in a downward and forward direction, the lung expanding into the space it vacates. The action of the diaphragm depends on which group of muscles comes into play as its antagonists. If the abdominal contents are rendered fixed by the abdominal musculature, the lower margin of the thorax moves towards the domes of the diaphragm; if, on the other hand, the ribs are fixed by the intercostal muscles, and the abdominal musculature is reflexly relaxed, the domes of the diaphragm move towards the lower aperture of the thorax. In subjects of extreme visceroptosis Wenckebach observed that the diaphragm was thrown out of action by its visceral fulcrum being lost, and breathing was carried on by an elevation of the upper part of the thorax. Seeing how variable the action of the diaphragm is in the same individual, and how much it differs in its action from individual to individual, it is rather misleading to make any precise statement of the amplitude of the movements of its domes. In quiet breathing Dally found, by the use of the orthodiascope, that the mean descent of the right dome in 100 individuals was 12·5 mm.; the left dome, 12 mm.; the central part rather less than the left dome.

Hultkranz estimated the average inspiratory descent of the whole diaphragm at 10·5, Guillemot at 15 to 18 mm. About half an inch is its ordinary descent, the right dome moving rather more than the left, and the left more than the central part. From Hutchinson's, Dally's, and my own observations the area of the diaphragm in contact with the lungs may be estimated at 250 sq. cm. A descent of 10 mm. all over gives an increase of 250 c.c. of thoracic space; if one estimates an average quiet breath at 400 c.c. it will be seen that the diaphragmatic movement plays a larger part than the costal movement. Hultkranz estimated that in taking a breath of 490 c.c. 170 was the result of the diaphragmatic, and 320 of the thoracic movement. Sewall and Pollard found that a larger breath could be taken by a thoracic inspiratory movement than by an abdominal one. R. T. Mackenzie has again verified Hutchinson's observation that there is no relationship between the extent to which the chest can be expanded in circumference and the amount of breath that is thereby taken in. The thorax can be enlarged so that the abdominal viscera instead of air is drawn into the thoracic cavity. At the London Hospital there was an old acrobat who could draw in this way all his abdominal viscera up into the thorax, so that the abdominal aorta was felt pulsating under the fingers from the epigastrium downwards. When the thorax is expanded beyond the extensibility of the lungs the abdominal viscera are drawn upwards to occupy the thoracic space; highly trained gymnasts at the army schools invariably obtain their great chest expansions in this way.

The Respiratory Movements of the Ribs

In describing the respiratory movements of the thorax most teachers restrict their description to a typical rib, in order to secure simplicity of description. Two movements are recognised, one round an axis corresponding to the spinal articulation of the rib, and another round the spino-sternal articulation. The first movement gives increase of the back-to-front diameter, the other of the side-to-side. Now, although in a general sense this description is essentially true, yet when one comes to study the costal movements in the living and the arrangement of parts in the dead, it is found to afford a very imperfect explanation of what is seen. The ribs vary in size, shape, inclination, articula-

tion, and action from the first to the twelfth; to describe the action and movement of each would cause the student to be lost in detail. It is enough, in the writer's opinion, to recognise that in the thorax there are two parts which are functionally independent; these are (1) the upper mechanism connected with the expansion of the upper lobe of the lung (the part above the great fissure), consisting of the second, third, fourth, and fifth ribs, and their attached muscles; and (2) the lower mechanism, consisting of the sixth, seventh, eighth, ninth, and tenth ribs, and their attached muscles, designed for the expansion of the lower lobe. In this lower mechanism the diaphragm is the dominating part. The lower set of ribs is specially adapted to act with the diaphragm; they are an intrinsic part of the diaphragmatic mechanism. The floating ribs, the eleventh and twelfth, and in 40 per cent. of bodies the tenth also belongs to this group, are, from a functional point of view, essentially a part of the abdominal wall; their articulations and movements are peculiar. The peculiar shape and action of the first rib has already been described. In the writer's opinion it is necessary, for a full analysis of the respiratory movements in health and in disease, to distinguish four parts in the costal series—(1) The first rib, part of the thoracic operculum; (2) the upper costal series (second to fifth); (3) the lower costal series (sixth to tenth), an intrinsic part of the diaphragmatic mechanism; (4) the floating series, functionally a part of the abdominal wall.

The Respiratory Movements of the Lower Costal Series

The muscles and movements of the lower series are totally different from those of the upper. The dominating muscle is the diaphragm; the other muscles are so arranged in their attachments as to act either as synergic muscles (the ilio-costalis, the external intercostals, the interchondrals) or as antagonists (the external oblique, the internal oblique, the internal intercostals, and the transversalis). The ribs of the lower series are articulated to the spinal column in such a manner that the lateral and anterior part of each moves outwards more than the one above it during inspiration. The spinal part of each (50 to 70 mm. in length)—the part to which the erector spinæ is attached—rotates and actually moves forwards (sternal-wards) during inspiration. The

tubercle of the rib glides downwards and forwards on the flat upper facets on the transverse processes. The axis of the movement in the lower set does not correspond to the neck of the rib; it corresponds to its spinal segment and is determined by the action of the muscles rather than by the shape of the articulations and ligaments. Anteriorly the diaphragmatic set of ribs is inserted to the lower end of the sternum by the strong peculiar complex formed by the costal cartilages of the sixth, seventh, eighth, and ninth ribs. As the diaphragm and external intercostals elevate the lower costal series, they also raise the sternum upwards through the cartilage complex. The ilio-costalis, rising from the iliac crest, steadies the spinal segments of the ribs, or during an energetic inspiration actually draws them downwards. The result of a movement of the lower ribs—or better, of the action of the diaphragmatic mechanism—is to increase the transverse and back-to-front diameter of the lower thorax and the vertical diameter of the whole cavity.

Respiratory Movements of the Floating Ribs

As already mentioned, the eleventh and twelfth ribs are functionally parts of the belly wall. Sibson observed that the tenth and eleventh intercostal spaces widen during inspiration, and diminish during expiration, an observation which the writer has frequently verified. The opposite is true of the other spaces. The twelfth rib is not only controlled by the quadratus lumborum and erector spinæ muscles, but also by a strong and constant ligamentous membrane, the function of which has been entirely overlooked. This membrane, really an extension of the middle layer of the lumbar fascia, anchors the lower border of the twelfth rib to the transverse processes of the first and second lumbar vertebræ; it is continued up between the spinal parts of the lower five ribs. Thus the lower five ribs at and near their angles are bound to the spinal column in such a way as to strictly limit the upward movement of the spinal segments of the ribs. On the other hand, the lateral and anterior parts of the ribs are not so limited; the whole arrangement is designed to secure the movements of the lower ribs round an axis, not corresponding to their necks, but to their spinal segments, the parts to which the erector spinæ is attached.

Respiratory Movements of the Upper Ribs

The upper ribs differ from the lower set (1) in their musculature; (2) in their articulation and ligaments; (3) in their shape and arrangement; (4) in their movements. Their movement is designed for the expansion of that part of the lung which lies above the great fissure. The musculature of these ribs is the intercostal and interchondral. The first rib and its muscles provide a fulcrum towards which the upper set of ribs may be raised, while the lower set of ribs, fixed by the abdominal musculature, affords a fixed base towards which they may be depressed during expiration. Now the spaces between the ribs of the upper set are peculiarly wide on the anterior and lateral aspect of the chest—the area covered by the pectoral muscles and the upper part of the serratus magnus. It is in these spaces that most observations on the action of the intercostal muscles have been made. Duchenne noted that during life the musculature of these spaces was tense during inspiration and lax during expiration in the living, and inferred that both external and internal intercostals were in action during inspiration, and out of action during expiration. That was also Haller's opinion. Rutherford and many others also drew that inference from experiments on the articulated thorax. Sibson, who was an accurate observer, also agreed that the internal intercostals of the subpectoral region of the chest are inspiratory in function. Both internal and external muscles have the power of diminishing the intercostal spaces, and may therefore act as inspiratory or expiratory muscles according to whether they act from the first rib or from the sixth. One must receive with caution the inferences drawn from experiments which involve a wide disturbance of the circulatory and reflex mechanisms—such as those of Martin and Hartwell. They found the interchondral as well as the internal intercostal muscles were expiratory, a conclusion altogether at variance with the fact that these cartilages are elevated during inspiration. In other parts of the thorax, with the exception of the anterior and lateral aspect of the upper part of the thorax, the internal intercostals are normally expiratory muscles.

The spinal articulations of the ribs of the upper set differ from those of the lower set. The articulation on the tubercle is a con-

vex ovoid facet, and fits into a corresponding hollow facet on the transverse process unlike the flat facets of the lower rib. Each transverse process from above downwards is tilted a little more backwards than the one above, so that the angle at which the ribs are set to the spine increases as one passes down the series. The double articulation of each rib to the spine by its head and by its tubercle prevents any rotation of the rib round a sterno-spinal axis. There can be no " bucket-handle " movement. The axis on which the upper ribs move corresponds to their necks. The only part of the erector spinæ which can influence their movement is the accessorius. The series of slips included in this muscle rises from the lower set and is inserted into the upper set of ribs. It is physically possible for this muscle to act on the upper set during expiration. The muscles named levatores costarum increase in size from first to twelfth, being thus largest to the rib which is in least need of elevation; they are so inserted to the ribs as to be unable to influence the movements of the ribs; they are not concerned in respiration but in lateral movements of the spine.

One can see from the shape of the upper ribs that their mechanism is totally different to the lower set. The ribs of the upper set have a concave upper margin, the lower convex; the upper ribs are shaped like the blade of a sickle; each successive rib from second to fifth making a greater lateral and forward sweep than the rib above it. The ribs of the lower set form a vertical series, the one situated vertically above the other. The upper set is designed for the expansion of the conical upper lobe, the lower set for the expansion of the lower lobe which is a segment of a cylinder.

Recently Dally has again directed attention to extension of the spine as a normal means of expanding the thorax. He has studied the spinal movements by means of the othodiascope. Hutchinson and Hasse have each demonstrated a normal inspiratory extension of the spine. Extension of the spine causes an increase in all three diameters of the thorax.

It would carry this article to an undue length were the writer to deal fully with other matters connected with the mechanism of respiration, such as its influence on the circulation (see Wenckebach and T. Lewis); with the changes which set in soon after adult life and gradually increase until old age (see Mehnert). He feels he has scarcely done justice in his review to the articles of

du Bois Raymond, Boruttau, and Hart, the last named having compiled a most useful summary of German literature treating of the relationship of phthisis to the mechanism of respiration.

BIBLIOGRAPHY

Abrams, Lancet, Oct. 10, 1903, p. 1052.

Du Bois Reymond, Mechanik der Atmung. Ergebnesse der Physiol., Bd. 1 1902, Abth. Bio-physik., p. 277.

H. Boruttau, Die Atembegwegungen und ihre Innervation. Handbuch der Physiol. der Menschen, Nagel, Braunschweig, 1905, Bd. 1, Abth. 1, pp. 1-56.

Braune, Der Sternelwinkel, Angulus Ludovici, in Anatomische und Klinische Beziehung. Archiv. fur Anat. und Physiol. Anat. Abth. 1888, p. 306.

Colbeck and *Pritchard*, An Explanation of the Vulnerability of the Apices in Tuberculosis of the Lungs. Lancet, June 8, 1901.

E. H. Colbeck, The Phenomena of Tidal Percussion at the Apices of the Lungs. Practitioner, March 1903.

J. F. H. Dally, A Contribution to the Study of the Mechanism of Respiration. Proc. Roy. Soc., Feb. 6, 1908; Lancet, June 27, 1903, p. 1802.

Duchenne, Physiologie des Movements, Paris, 1867.

Elsberg, Zentralbl. fur Chirur., No. 10, 1908.

W. A. Freund, Der Zusammenhang gewisses Lungen Krankenheiten mit Primaren Rippen Knorpelanomalien Erlanger, 1859, p. 127. (For references to Freund's later papers see Hart.)

K. Gregor, Die Entwickelung der Atemmechanik in Kindesalter. Anat. Anz., Bd. xxii., p. 119, 1902.

C. Hart, Die Mechanische Disposition der Lungen spitzen zur tuberkulosen Phthise, Stuttgart, 1906, p. 267.

C. Hasse, Die Formen des menschlichen Korpers und die Formveranderungen bei der Atmung, Jena, 1888–90, parts i.–ii.

C. Hasse, Ueber die Atembemegungen des Menschlichen Korpers. Arch. f. Anat. u. Physiologie, 1901 and 1903.

W. R. Huggard, Brit. Med. Journ., Oct. 14, 1905.

J. Hutchinson, article on "Thorax." Todd's Cyclopædia of Anatomy and Physiology, vol. iv., 1852.

E. Lloyd Jones, The Physical Examination of the Upper Regions of the Chest. Brit. Med. Journ., Oct. 24, 1903.

A. Keith, A Variation which occurs in the Manubrium Sterni of Higher Primates. Journ. Anat. and Phsyiol., vol. xxx., 1896.

A. Keith, A Contribution to the Mechanism of Respiration in Man. Proc. Anat. Soc. of Great Brit. and Ir., May 1903.

A. Keith, Why does Phthisis attack the Apex of the Lung? London Hospital Gazette, Nov. 1903.

A. Keith, The Nature and Anatomy of Enteroptosis. Lancet, March 7, 1903, p. 634.

R. T. Mackenzie, The Relationship of the Thoracic Type to Lung Capacity. Montreal Medical Journ., vol. xxxiii., 1904, p. 237.

Martin and *Hartwell*, On the Action of the Intercostal Muscles. Journ. of Physiol., vol. ii., 1879, p. 24.

E. Mehnert, Ueber topographische Altersveranderungen des Atmungsapparates, Jena, 1901.

Meltzer, The Respiratory Changes of the Intrathoracic Pressure. Journ. of Physiol., vol. xiii., 1892.

H. von Meyer, Der Mechanismus der Rippen. Archiv. fur Anat. und Entwickel, Leipzic, 1885, p. 253.

A. Mosso, Action des centres spinaun sur la Toncite des Muscles Respirateurs. Archiv. Ital. de Biol., t. xli., 1904, p. 111 ; also t. vii. p. 93.

A. Mosso, Le Movements respiratoires du Thorax et du diaphragme. Arch. Ital. de Biol., t. xl., 1903, p. 43.

A. Oppel, Lehrbuch der mikroscopischen Anatomie der Wirbeltiere: part vi., Atmungs Appar., Jena, 1905.

W. Pasteur, Massive Collapse of the Lung. Lancet, Nov. 7, 1908, p. 1351.

Sir R. Douglas Powell, On some Effects of Lung Elasticity in Health and Disease. Medico-Chir. Soc., vol. lix., 1876, p. 165.

A. Ransome, Observations in the Movement of the Chest. Journ. of Anat and Physiol., vol. iv., 1870, p. 140.

Clive Riviere, Lancet, June 8, 1907, p. 1603.

Rothschild, Ueber die physiologische und pathologische Bedeutung des Sternelwinkels. XVII. Kongr. f. inn. Med., Karlsbad, 1899. (Hart gives full references to his later papers.)

Rutherford, Note on the Action of the Intercostal Muscles. Journ. of Anat. and Physiol., vol. x., 1876, p. 608.

Sewall and *Pollard*, On the Relationship of Diaphragmatic and Costal Respiration to Phonation. Journ. of Physiol., vol. xi., 1890, p. 159.

F. Sibson, On the Mechanism of Respiration. Philosophical Trans., vol. cxxxvi., 1846, p. 501.

N. Ph. Tendeloo, Studien ueber die Ursachen der Lungen Krankenheiten, Wiesbaden, 1902, p. 480.

K. F. Wenckebach, Ueber Pathologische Beziehungen Zwischen Atmung und Kneislauf beim Menschen. Sammlung klinischer Vortrage, Neue Folge, Leipzig, 1907.

THE PHYSIOLOGY OF MUSCULAR WORK

By M. S. PEMBREY

CHAPTER I

Introduction

Although muscular work has always been one of the most important factors in every-day life, it has not received sufficient attention from medical men. It has been the subject of much writing, numerous casual observations, but few scientific investigations. The practical importance of a knowledge of the influence of muscular work was never greater than it is at the present time. The migration from the land to the towns has deprived the youth of this country of many of the opportunities for healthy muscular exercise which their forefathers possessed. The increasing use of machinery in all occupations has reduced the demand for healthy muscular labour, and has thrown an extra strain upon the nervous system of the working man. The much-vaunted advances of medicine and surgery have prevented oftentimes the beneficent action of the law of the survival of the fit, and a morbid sentimentality under the guise of charity has pampered the degenerates of the country. The bad must be taken with the good, but this necessity does not make any thinking man satisfied with the conditions of modern civilisation. Its defects are well recognised, and for this reason the outlook is hopeful. The fear of a physical deterioration of the race found expression recently in the appointment of a departmental committee of inquiry, and serves at the present time as a strong argument in the hands of the advocates of compulsory military service. If degeneration is to be prevented, the public must recognise more fully the vanity of luxury and the benefits of healthy muscular exercise, whether it be as work or play, and must insist that the population is not weakened by immoral efforts to diminish the birth-rate and a healthy struggle for existence.

Physiologists have often neglected the question of muscular work or have devoted a vast amount of time and ingenuity to

experiments upon the isolated muscles of frogs. This has been reflected in the teaching and training of medical students. The underlying idea of the supporters of the school of muscle and nerve appears to be or to have been that a thorough investigation of the properties of two tissues would solve the problem of vital activity. The mystery is greater than ever it was. The day of that school of physiology is passing. A reaction set in some years ago, has not waned, but has steadily gained in strength. Some extremists would maintain that the investigation of isolated muscles and nerves is strictly not physiology; that a muscle and nerve under such abnormal conditions is pathological and pathological to a degree which does not obtain under the ordinary conditions of life. It cannot, however, be denied that such experimental work has its value, for all knowledge is useful if it be properly appraised. Muscle and nerve are not units of life; the unit is the living organism. Muscular activity under natural conditions is exhibited only by the organism, and under such conditions it should be studied.

Athletes and the trainers of men and animals for sport have done much for the practical study of the physiology of muscular work. The practice of training is even at the present time ahead of the theory, and each year physiological investigations show the value of the methods introduced by athletes. Experience has been the guide of athletes, and experience is the result of numerous physiological experiments upon a large number of men. The diversity and gradation of the muscular exercise involved in the numerous forms of sport render it suitable for all men, young and old, strong and weak. In these and many other respects sport is far superior to physical drill and gymnastic exercises, and as such deserves even more recognition and study than it already receives.

The main purpose of this article is the physiology of muscular work in man. It will be necessary, however, to glance at some of the elementary facts concerning the structure and properties of muscle considered as a tissue.

The Structure of Muscle

There are many interesting differences in the naked eye and microscopical structure of muscle, and these must be considered in relation to the various functions of the different kinds of muscular

tissue. In muscle the power of contraction, which is present in the primitive cell, has been especially developed in the process of division of labour and differentiation of structure. Three kinds of muscle are recognised—voluntary, cardiac, and involuntary. Their minute structure, which has given rise to much controversy, is strictly a question of anatomy, and will not be discussed here. There are not only differences in the structure, composition, and properties of voluntary muscles in different animals, but also in the same animal. The best known example is the red and the white muscle of the rabbit (1). Simple inspection of the muscles of a rabbit directly its skin is removed detects a marked contrast in the colour of the different muscles; the masseters and some of the muscles of the hind limbs, such as the soleus and semi-membranosus, are red in colour, but most of them are pale. This difference is not due solely to variations in the vascular supply, for even after the blood has been removed a contrast remains. The red muscle fibre contains hæmoglobin and myohæmatin within its substance, and these pigments are probably of some importance in the process of internal respiration. The capillary blood vessels have dilatations, which are not present in the case of the pale muscles. The red fibres are thin with nuclei in their substance as well as under the sarcolemma, and the transverse striation is less regular. Functional differences can be easily demonstrated. The red muscle contracts and relaxes slowly, in marked contrast to the rapid wave of contraction in white muscle; red muscle is more easily tetanised, and does not pass into rigor mortis so rapidly.

The Physical and Chemical Properties of Muscle

One of the most important characteristics of muscle is its elasticity. A muscle fibre regains its original length after it has been stretched within certain limits; it possesses perfect elasticity and conforms to Hooke's law; the successive increments in length produced by equal increments of weight are equal. It is only when the muscle has been extended beyond the limits to which it is exposed in the living body that its perfect elasticity is impaired (2).

In the normal condition muscles are stretched between their points of attachment and by the action of antagonistic muscles;

if a muscle be cut across its ends retract in the wound. The practical importance of this elasticity is found in the more prompt performance of work; the muscles are taut and have not to take in slack when they begin to contract. The extensibility of a muscle is greater during contraction than in the condition of rest. This is a further safeguard to the muscle in any sudden or vigorous contraction against a great resistance; the shock and strain are lessened and rupture of the muscle is prevented. It is more common to find bones fractured than muscles ruptured by violent contraction. Later it will be shown that in addition to this elasticity the muscles have a condition of tone or tonic contraction, which increases their efficiency in the performance of work.

Muscle consists of 25 per cent. of solids and 75 per cent. of water; twenty parts of the solids are proteins, and the remaining five parts are extractives and inorganic salts. From the muscle can be expressed a viscid alkaline juice which soon becomes acid and clots. The chief constituents of this muscle plasma are the *proteins* investigated and named by Halliburton ([3]) para-myosinogen and myosinogen; they correspond respectively to the myosin and myogen of Von Fürth ([4]). These proteins in most respects resemble the globulins; para-myosinogen is coagulated by heat at 47°, myosinogen at 63°. The myosinogen gives rise to soluble myosin in the process of clotting, and this substance, which is coagulated by heat at 40°, is a normal constituent of the muscle plasma of cold-blooded animals.

The statements made concerning the proteins of muscle plasma may soon need revision, for in a recent preliminary communication Mellanby ([5]) has maintained that there is only one protein in muscle and that it is not a globulin.

A comparison of the protein constituents of the different kinds of muscle brings out an interesting difference. Nucleo-protein is most abundant in plain muscle, and least abundant in voluntary or striated muscle; cardiac muscle occupies an intermediate position in this respect. In simple cells nucleo-protein is a typical constituent; plain muscle is the least and voluntary muscle the most differentiated of the three kinds of muscle; thus changes in function and structure have been accompanied by a corresponding gradation in the amount of nucleo-protein.

Another point of great interest has been discovered by a comparison of the temperatures at which the different protein con-

stituents coagulate (6). When an excised voluntary muscle of a mammal is heated, it begins to shorten at 43°, shortens more at 47°, and again when the temperature reaches 58°. The excitability of the muscle is destroyed when the shortening occurs at 47°, and this corresponds with the temperature at which paramyosinogen is coagulated. The internal temperature of a healthy mammal is about 36° to 37°, and it is well known that life is endangered when owing to fever or some other cause the temperature of the body rises to 44°. Birds are also warm-blooded animals, but their internal temperature is several degrees above that of mammals; the temperature of a sparrow is 42°, that of a hen 41° to 43°. There must therefore be some difference in the heat-rigor of the proteins of their muscles; experiments on this point have proved that the coagulation of the protein does not occur until the temperature is raised to 53°.

The temperatures at which coagulation begins are not rigidly fixed, for prolonged heating at a lower temperature will produce that change of state; it is necessary also to remember that the excised muscles are devoid of a circulation of blood, and no doubt are in a condition which is not the same chemically as the normal muscle. These criticisms do not invalidate the practical importance of heat-rigor in connection with the effects of hyperpyrexia and the pathological changes which occur in muscle during prolonged fever. It is necessary, however, to exercise care in any argument from the part to the whole body.

The next constituents of muscle which must be considered are the *extractives;* these can be divided into two classes, the non-nitrogenous and the nitrogenous. The former group is represented by glycogen, dextrin and sugars, inosite, fat, and lactic acid.

Glycogen or animal starch $(C_6H_{10}O_5)_n$ is a polysaccharide which appears to be intimately associated with the source of muscular energy. The amount of glycogen which can be extracted from a muscle varies according to its activity, and this fact will explain the lack of agreement in the percentages found by different observers. Resting muscle contains from 0·1 to 2·5 per cent. of glycogen. The amount not only varies in different animals, but also in different muscles of the same animal: the more active muscles contain less. By prolonged activity the glycogen of the muscles can be removed, but it disappears from the liver first; poisonous doses of strychnine which cause violent convulsions

bring about a loss of about 90 per cent. of the glycogen of the muscle. During starvation glycogen disappears from the liver sooner than from the muscles. These facts raise the question whether glycogen is supplied to the muscles by the blood-stream which has taken up glycogen from the liver or whether it can be formed by the activity of the muscles themselves. There is no conclusive evidence to show that the latter is the case, but it will be better to defer the consideration of this point until the sources of muscular energy are discussed in detail.

Dextrin and Sugars.—Between these bodies and glycogen there is a close relationship. Glycogen appears to be the form in which carbohydrate is stored up, probably in loose combination with the proteins of the muscle ; dextrin, maltose, and glucose represent the stages through which the reserve material passes on its way to yield energy during combustion. The glycogen of an excised muscle rapidly decreases and the sugar at the same time increases. This conversion can be effected by the ferments which are found in muscle ; there is an amylolytic enzyme and a maltase, and by their action dextrin, maltose, and finally dextrose are formed. The relation of sugar to muscular activity will be considered later.

Inosite is found in small quantities in the muscles. It was formerly known as muscle sugar, owing to the fact that it has the same molecular formula ($C_6H_{12}O_6$) as glucose. It is not, however, a sugar, but a crystallisable substance belonging to the aromatic series. Nothing appears to be known of its physiological importance, although it is found in other parts of the body besides muscle.

Fat is constantly present between the muscle fibres, but it is uncertain whether it is a normal constituent of muscle ; there is no definite evidence of its presence within the substance of the fibre. Leathes ([7]) found that the red muscles of the rabbit contain considerably more fat than the white muscles.

Lactic acid, paralactic or sarcolactic acid, $CH_3(CH.OH)COOH$. There has been a great conflict of opinion upon the question whether the normal muscle contains lactic acid, which is always present in dead muscle. Recently, however, the discrepancies have been explained by Hopkins and Fletcher ([8]) in an important research upon lactic acid in amphibian muscle ; by this work the knowledge of the conditions under which lactic acid is formed in muscle has

been greatly extended. Their results are given in the following summary taken from their paper :—

" Freshly excised resting muscle is found to yield very small quantities of lactic acid, and these small amounts are possibly not more than can be accounted for by the unavoidable minimum of manipulation prior to extraction.

" A large increase of the yield of lactic acid is found as the result of mechanical injury, of heating, and of chemical irritation.

" Lactic acid is spontaneously developed under anaërobic conditions in excised muscles. During the survival periods of subsisting irritability, and not after, equal increments of acid arise in equal times. After complete loss of irritability the lactic acid yield remains stationary.

" Fatigue due to contractions of excised muscle is accompanied by an increase of lactic acid. The amount of acid attainable by severe direct stimulation is found, with notable constancy, to be not more than about one-half of that reached in the production of full heat-rigor, or by the action of other destructive agencies than heat.

" In an atmosphere of oxygen there is no survival development of lactic acid for long periods after excision.

" From a fatigued muscle, placed in oxygen, there is a disappearance of lactic acid already formed.

" This disappearance of lactic acid due to oxygen does not occur, or is masked, at supra-physiological temperatures. It is not found in muscle which has suffered mechanical injury ; one essential condition for this effect of oxygen appears to be the maintenance of the normal architecture of the muscle.

" The amount of lactic acid produced in full heat-rigor is constant for similar muscles. This ' acid maximum ' of heat-rigor is not affected by a previous appearance within the excised muscle of lactic acid due to fatigue, or by a previous disappearance of acid in the presence of oxygen, or by alternate appearances and disappearances several times repeated."

It will be necessary later to consider this work in its bearing upon the effects of muscular activity, upon hyperpnœa and muscle soreness ; at the present time only the chemical characteristics of muscle have to be discussed.

The nitrogenous extractives of muscle form a large group ; the chief ones are creatin, carnic acid, inosinic acid, carnosin and purin

bodies. It is impossible to give a satisfactory account of their significance in the physiology of muscular work, but an attempt will be made to pick out the observations of most interest.

Creatin is a substance which crystallises out when an aqueous extract of meat is allowed to evaporate. It has the formula $C_4H_9N_3O_2$. E. Mellanby ([9]) has found that it is present in different amounts in the muscles of various animals; as a general rule there is a greater quantity in the muscles of animals in an ascending scale of development from the cold-blooded to the warm-blooded. This is illustrated by the following table:—

Lamprey	·25 per cent.	Hedgehog (winter)	·2 per cent.
Skate	·24 „	„ (summer)	·2 „
Cod	·3 „	Rats (two months old)	·3 „
Frogs	·26 „	Bullock	·3 „
Fowl	·31 „	Pig	·33 „
Guinea pig	·32 „	Rabbits	·44 „

A further interesting difference was discovered by an analysis of the muscles of similar animals during several stages of development.

Rabbits (fœtal, 21 days)	a trace.
„ 7 days old	·191 per cent.
„ 9 „	·228 „
„ 12 „	·283 „
„ 19 „	·316 „
„ 25 „	·300 „
„ 39 „	·390 „
„ 46 „	·373 „
„ adult	·435 „

Chick embryo, before 12th day	no trace.
„ „ weight 6·1 grms. 12th day	a trace.
„ „ „ 11·3 „ 14th „	3·8 mgrs. total.
„ „ „ 17·3 „ 16th „	6·6 „
„ „ „ 26·0 „ 18th „	11·8 „
„ „ „ 30·25 „ 20th „	13·25 „
Chick, weight 36·0 grms. 1 day after hatching, but no food taken	23·0 „

In the embryo chick creatin is absent at a stage of development when muscle is present; in hedgehogs the quantity of creatin in the muscles remains constant throughout the year, notwithstanding the great differences in the metabolism of these animals during the periods of hibernation and activity.

Creatin is absent from invertebrate muscle, although morphologically and physiologically the cross striated muscle of these animals is identical with that of vertebrates. The closely related substance creatinin, $C_4H_7N_3O$, is not present in muscle, and is not formed from creatin during prolonged work. Creatin has apparently no influence on muscular contraction or the passage of a nervous impulse into muscle. From a consideration of these and other facts, Mellanby suggests that creatinin is formed into creatin and stored in the muscle, and that the development of the liver in the vertebrates may account for the presence of creatin in their muscles; the gland of the mid-gut of invertebrates, although it has been called a liver by some biologists, has no morphological or physiological connection with the liver of vertebrates. The urine of young children is almost free from creatinin, and chicks do not excrete creatinin until about a week after hatching, by which time their muscles are saturated with creatin.

The other nitrogenous extractives found in muscle are *carnic acid*, $C_{10}H_{15}N_3O_5$, combined with phosphorus to form phosphocarnic acid; *carnosin*, $C_9H_{14}N_4O_3$; *inosinic acid*, $C_{10}H_{13}N_4PO_8$; small quantities of *urea*, $CO(NH_2)_2$; and of the following purine bodies—*hypoxanthine* or oxypurine, $C_5H_4N_4O$; *xanthine* or dioxypurine, $C_5H_4N_4O_2$; and *uric acid* or trioxypurine, $C_5H_4N_4O_3$. The significance of these substances in the metabolism of muscle is unknown.

The Inorganic Salts of Muscle

There are considerable variations in the quantity of the inorganic salts which are present in the muscles of different animals, but in all the samples analysed potassium and phosphorus are the most abundant constituents. The following results expressed in parts per 1000 were obtained by Bunge [10]:—

	Lean Beef.	Fat Beef.
K_2O	4·654	4·160
Na_2O	0·770	0·811
CaO	0·086	0·072
MgO	0·412	0·381
Fe_2O_3	0·57	...
P_2O_5	4·674	4·580
Cl	0·672	0·709
SO_3	...	0·010
S	...	2·211

In the above table the sulphur is represented in two divisions; the first gives the sulphate which can be extracted by water, and the second the total sulphur after incineration. The difference is due to the large quantity of sulphur which is set free by the destruction of the proteins of the muscle.

Interesting observations upon the distribution of potassium in muscle have been made by Macallum ([11]), who precipitated the potassium as the hexanitrite of cobalt, sodium, and potassium. In striated muscle there is a condensation of the potassium in the dim bands, the rest of the fibre remaining free from the precipitate; in involuntary muscle it is smaller in amount and is diffused throughout the cytoplasm, and in cardiac muscle it is distributed as in voluntary muscle. Macallum suggests that the potassium is associated with the rapidity of contraction.

The Pigment of Muscle

The exact nature of the pigment, which is present in muscle after the blood has been washed out, has given rise to much controversy. MacMunn ([12]) found associated with hæmoglobin in the muscles a pigment which gave a different spectrum; this he named myohæmatin. He observed it in a compressed fresh muscle when it was held before the slit of a spectroscope, and on account of its capacity for oxidation and reduction he considered it to be a respiratory pigment. It was maintained on the other hand by Hoppe Seyler and his pupils that the pigment was either hæmoglobin or a derivative produced by putrefaction. After the lapse of some years the subject has been reinvestigated by Mörner ([13]), who confirms MacMunn's view, and suggests that the pigment differs from hæmoglobin in the combination of its hæmatin with some other protein or in a different linkage of the components.

The Ferments of Muscle

Modern investigations have demonstrated the great importance of unorganised ferments in physiological processes ([14]); the living cell may be compared to an organised ferment which produces unorganised ferments or enzymes. In voluntary muscles there have been found amylolytic, glycolytic, and peptic enzymes, or in other words, ferments which act upon glucose, glycogen, and protein

respectively; there are also present maltase and an oxidising ferment, or oxydase. These ferments doubtless play important parts in the exchange of material in the muscle, for in addition to their definite action there is the probability of a reversible action; the breaking down process may, according to the condition of the tissue, be replaced by the building up or synthetic process.

CHAPTER II

Facts concerning the structure, and the physical, chemical, and physiological properties of muscle, have been given as an introduction to the physiology of muscular work. It is now necessary to study the effects of muscular exercise or work upon the living organism, especially man.

The origin of muscular activity we cannot trace, nor can we think of its beginning in the offspring of any animal. Muscular activity is a specialised form of protoplasmic movement, and the capacity for such movement is an attribute of the minute male and female cells from the union of which the offspring arises. There has been a continuity of life from parent to offspring through countless generations, and this carries with it the potentiality of muscular movement. Heredity has a far-reaching influence upon muscular development and activity; even at birth the power of co-ordination possessed by some animals is remarkable. A guinea-pig is born with its eyes open and its body covered with fur, and it is able to run about; a calf within a few minutes of first seeing the light is able to walk and seeks its mother's teats. These young animals do not learn to walk, but learn by practice to make perfect the power of walking which they possess at birth. A marked contrast is seen in the newly born rabbit, rat, and mouse; they are blind, naked, and helpless. A study of birds reveals a similar difference. Within an hour or two of hatching the chick is able to run about and peck up its food; the pigeon, on the other hand, is for several days blind, naked, and helpless. The maturity or immaturity of different classes of animals at birth is related to the natural habits of the race and to adaptation.

The condition of the newly born child is intermediate between the extreme examples just given; its muscular development and power of co-ordination are considerable, and are especially seen

in its capacity to grasp with the hands and feet. Most interesting observations have been made upon this subject (15), which affords strong support for the Darwinian theory of evolution. Infants at the very beginning of their separate existence possess a remarkably strong grip; they can hang by their hands from a horizontal bar and support their own weight, and the strongest may maintain their position for two minutes. Most adults would find it difficult to support themselves in this way for a quarter of the time. Infants possess also a power of grasping with the foot; the great toe is abducted and the foot is held more in the position of a hand. This power is gradually lost as the child grows up, and is only found greatly developed in the adult in those rare cases of congenital absence of the arms and hands. These prodigies may be seen at fairs exhibiting their skill in using their feet for all the purposes for which an ordinary man uses his hands.

For these characteristics of the infant there appears to be no adequate explanation except the one suggested by Dr. Louis Robinson. He considers that they are examples of atavism; that the infant of primitive man was carried in a manner similar to that seen in apes, the offspring clinging to the parent by grasping with its hands and feet the hair under the arms and over the pubes. Grasping their parents' hair is well known to afford infants their earliest form of amusement. Dr. Robinson has also pointed out that his view would offer an explanation of the great development of hair over the pubes and in the axillæ at the time of puberty.

It is well known that the fœtus often makes active movements in the uterus; these movements are known as "quickening with child," and by one of those subtilties in which the legal mind delights have acquired some importance, for they entitle any pregnant woman who is condemned to death to at least a temporary reprieve. In many cases, however, no active movements may be detected even in the last days of pregnancy.

There is another striking example of muscular power and co-ordination in the infant. Within a few seconds of its birth it draws its first breath, and continues to ventilate its lungs by alternate contraction and relaxation of its respiratory muscles, although up to this time its respiration has been entirely carried out by the placenta. Ahlfeld (16) maintains that this activity of the respiratory muscles is not suddenly assumed at birth, but that slight respiratory movements can be detected in the fœtus

inside its mother's womb during the last months of pregnancy. These movements he has studied both by palpation and by a graphic record; they resemble the respiratory movements of a newly born infant in their irregular rhythm and in periods of waxing and waning. The criticism that such respiratory movements would draw the amniotic fluid into the lungs is not a serious one, for the movements are slight, and even if the fluid were drawn further than the naso-pharynx it would be rapidly absorbed, and being sterile and isotonic, would not injure the fœtus. It would appear, therefore, that all the muscles of the body are exercised during fœtal life for the work which they have to perform after birth. It is impossible to say that muscular contraction appears at any definite time.

Great advances have been made in the study of muscular movements in man and animals since the introduction of instantaneous photography. Before that time too much stress had been laid upon the anatomical aspect of muscular movements. It is impossible to analyse movement in the living by an examination of the points of origin and insertion of the different muscles acting upon the joints of dead subjects. Such imperfect knowledge could only be partly corrected by careful observation of the natural movements; for the eye is not able to follow the real sequence of events; the impression given to the observer is a composite one of several movements. It is owing to this fact that many instantaneous photographs of men and animals in motion do not appear true to nature and are inartistic. The credit of first analysing movements by relays of instantaneous photographs is due to Muybridge; his work has been greatly extended by Marey and others. If such photographs are seen in rapid succession the observer receives the impression that the objects are in motion; this is due to the persistence of visual impressions, and is the principle involved in the bioscope.

Another method introduced for the analysis of movements is the graphic one developed by Marey. It may be explained as an extension of the simple method of footprints. A man skilled in woodcraft can tell the nature and pace of an animal from its spoor or footprints, and by the examination of the fossils of such impressions geologists have been able to study the movements of animals which became extinct before the time of man.

It would be outside the scope of this article to pursue this

subject further, but it may not be amiss to point out how efficiently movements are carried out; the means are adapted to the end in view, and by practice the man or animal unconsciously learns to perform the movement in the most economical manner. "Practice makes perfect"; natural movements cause less fatigue than conventional ones, and herein lies the explanation of the fact that the pace and style of one man may be quite unsuited for another. An adult experiences more fatigue when he adjusts his pace to that of a child than when he walks the same distance at his usual speed. A child learns to crawl, walk and run, even if it receives no assistance from its mother; healthy exercise is all that is needed, and the experience thus obtained is a far better guide than any system of teaching or drill. A movement which is suitable for one individual is unsuitable for another; some men have long legs, some short legs, and each walks most efficiently at his own pace. This is not sufficiently recognised by many trainers, but the records of many a contest on land and water show that style is a personal factor which can never be rigidly fixed.

Muscular work is not a localised expenditure of energy; all parts of the body are involved in a greater or smaller degree; it is useless to attempt to simplify the analysis of the process by experiments upon the isolated muscle. Such a preparation is artificial, and the issue is confounded. A recognition of the complexity of the changes involved in muscular work enables us to understand how far reaching are the effects which can be produced by exercise. Anatomical changes are produced in the body; not only do the muscles become larger, but the pull exerted by them causes changes in the size and shape of the bones. In certain cases such great changes are produced by the repeated contractions of certain groups of muscles that the occupation of a man may be determined by an examination of his skeleton ([17]).

The law of the conservation of energy shows that without an adequate supply of energy in the form of food there can be no transformation into the energy of muscular work. The food must be adjusted to the work obtained from a man or beast, a truth which is constantly neglected with disastrous results. A man or horse works best when he is well fed, and feeds best when he is well worked. This is recognised by those who have extracted the greatest and most prolonged efforts from each. Napoleon is credited with the saying that "a soldier fights on his belly." A

man who takes enough active exercise does not overfeed and become corpulent, even if the supply of food is unlimited; his appetite is the expression of the needs of his body, and when these are satisfied the desire for food ceases.

The digestion and assimilation of the food involve the activity of the alimentary canal and its various glands. Muscular work produces hunger, and " hunger is the best sauce " ; healthy exercise enables a man to enjoy and digest food which otherwise he could not eat. Pity for the labouring poor on account of the plainness of their fare is misplaced.

The muscles are thrown into activity in response to various impulses, and in this way the whole of the nervous system, including the special senses, is influenced by muscular work. It is not a question of the discharge of motor impulses alone, but a general effect upon the whole system, so that a man overwrought by sedentary mental work often finds the best restorative in muscular exercise.

The respiratory system is thrown into greater activity to supply the increasing demand for the intake of oxygen and the discharge of carbon dioxide. The heart and the vaso-motor system must likewise respond with increased activity to maintain an adequate supply of blood and to adjust the flow to the different organs according to their relative needs. The sweat glands are stimulated by the increased heat of the body, and the kidneys will be influenced by the waste products of muscular activity and digestion.

It may be said that it is unnecessary to lay so much stress upon the value of muscular activity. It is not so. The benefits of muscular work cannot be overestimated. It is a physiological need of a primitive kind, and cannot be eliminated by civilisation. If all men were well worked and well fed many of the great social problems of the present day would be solved. Physiological truths might be carried with advantage into the consideration of social questions. Would there be any danger to the race if those who did not work were not well fed? Do not those who have not to earn their bread show their recognition of the virtue of muscular work by their devotion to manly sports?

Muscular exercise is a necessary condition of a healthy existence; it is difficult to find the man who has been injured by muscular work, it is easy to procure many who have been ruined

by the lack of it. The child or young animal which is not active for the pure love of activity is unwell. The belief that progress lies chiefly in mental training is less rampant than formerly. The compulsory education of young children has increased the infectious diseases to which they are liable, has stunted the growth of their originality as well as their bodies, and has in many cases produced that mental instability which has revealed itself at a later stage of life in crime, insanity, or suicide. The suppression of the instinct to play has gone so far that it has become necessary to found societies for the purpose of teaching children how to play. Even the believers in compulsory education of young children have taken alarm, and think they can undo the harm by compulsory systems of monotonous drill, unnatural postures, and breathing exercises. The irony of it is that this kind of physical training is said to be based upon the teachings of physiology. It is a false physiology which does not recognise that natural exercise is the best, that instincts in healthy children ought not to be unduly suppressed, and that heredity is more potent than systems of education.

Types of Muscular Exercise

Notwithstanding the numerous gradations of muscular exercise between the slightest and the most severe and prolonged exertion, it is convenient to recognise three types ([18]) : (1) Exercises of speed are those in which each individual effort is produced rapidly, but the maximum contraction of any single skeletal muscle is not reached ; (2) exercises of endurance are characterised by long and continuous efforts of moderate strength ; (3) exercises of strength are those in which the muscular exertion is very great for a brief period, such as the lifting of a heavy weight. In these different forms of exercise it can be shown that the effects produced upon the body are not the same, and a different type of physique ([19]) is found in men and animals who excel in any one of them. This is well seen in a comparison of a runner with a navvy or of a racehorse with a dray-horse. It is necessary to remember the importance of build and heredity in this respect, and to avoid an overestimate of training.

The general effects of muscular activity have been sufficiently indicated ; its influence upon the different systems of the body must now be considered.

The Effects of Exercise upon the Muscular System

The muscles of the body are in a condition of partial contraction even during apparent rest. This so-called tone is related to the motor and sensory nerves which supply the muscle. If these nerves be divided and do not regenerate the muscles will first waste or atrophy, owing to disuse, and then degenerate. Destruction of the motor cortex of the brain will cause atrophy of the muscles, but they do not degenerate, for through their motor and sensory nerves they are still under the influence of the spinal cord.

The tone of the muscles is diminished by sleep; the observant mother knows when her child has fallen to sleep in her arms by the relaxation of its body. A far greater decrease in tone is produced by the action of anæsthetics; the arm of a patient drops in a limp and lifeless manner when he is deeply anæsthetised.

From time to time the tone of the muscles varies in response to impulses from the skin and other parts of the body; it is increased by cold, diminished by heat, and herein appears to lie the chief explanation of the effects of different climates. The body is invigorated by a bracing atmosphere, it is depressed by a relaxing one. The tone of the muscles is accompanied by chemical changes and the production of heat; in a stagnant moist and warm atmosphere the body does not lose heat rapidly, and therefore in the maintenance of a constant internal temperature produces less heat by diminishing the activity of its muscles, and as far as possible favours the loss by a dilatation of the blood vessels of the skin. The opposite effects are produced by a cold dry atmosphere, or even by warm air if it be sufficiently dry and in motion. European children afford a good instance of these influences; they will not flourish in the hot moist districts of India. Two more examples will be sufficient. The value of a cold bath on getting up in the morning lies not in its cleansing properties so much as in the bracing or stimulating effect which it has upon the whole muscular system, including the muscles of the cutaneous arterioles. The contrast between the walk of a man on a cold frosty morning and on a damp warm day is known to every one who lives in this country.

The tonic contraction of the muscles may be so greatly increased

that it passes into visible contractions of an involuntary nature; shivering thus arises, and in most cases appears to be a protective response to the effects of cold. It is true that it may occur apart from external cold during nervous excitement, but even in this case observations may show that the temperature of the skin has been lowered by a sudden and vigorous contraction of its blood vessels.

Voluntary contraction is the shortening of the muscles produced by an effort of the will. This is only a general definition, for movements such as walking may be performed unconsciously. During ordinary movements the change of state is not confined to a single muscle; others are also involved, it may be in active contraction or in relaxation. The important researches of Sherrington [1] upon reciprocal innervation have shown how the muscles can influence the activity of one another by means of their motor and sensory nerves: the contraction of one muscle brings about the relaxation of its antagonist. The muscle possesses in its muscle spindles a special sensory ending which is stimulated by the stretching produced by the contraction of its antagonistic muscle; in this way not only can reflex effects be produced upon the muscle, but also upon the vaso-motor and respiratory mechanisms.

A simple movement, such as removing the finger from a key at a given signal, may or may not, according to the individual's type of reaction, be preceded by a movement of the opposite kind. This may be called the antagonistic form of reaction in contrast to the ordinary form in which the lifting of the finger is carried out at once ([20]).

Such a movement of the finger can only be repeated about eight to twelve times a second by the ordinary man, but a pianist by practice and by using muscles in relays can press the keys at a faster rate. In short, sharp, and rhythmical movements of the fingers the rate may be as rapid as forty a second.

The nature of a voluntary contraction, whether it be a single twitch or a spasm, requires consideration. It has been studied in two ways, by a determination of the note of the sound produced by the contraction of the muscle, and by graphic records. The muscle note corresponds to forty vibrations a second, but the difficulty in such a determination by the ear lies in the fact that it

[1] Article Spinal Cord, "Textbook of Physiology," edited by Schäfer, vol. ii., 1900.

cannot perceive a note much lower than one of that frequency. It is probable that the muscle note really represents the overtone corresponding to the second octave of the vibration ten a second.

The work of Horsley and Schäfer ([21]) shows that the rate of contraction is determined chiefly by the rate of discharge of the nerve cells concerned in the movement. A muscle can contract at a faster rate, a nerve can conduct impulses more quickly than ten a second, if they be stimulated artificially. An interesting contrast is revealed by a comparison of the rates of contraction of a muscle when it is stimulated respectively through the cortex of the brain, the corona radiata, the spinal cord, and the motor nerve. In the last case only is the muscle thrown into such rapid contraction that complete tetanus is produced.

The rhythm of the muscular response ([22]) to volitional impulses in man is about eight to thirteen per second, the number of waves varying in different individuals and in the same individual under different conditions of work. A voluntary contraction is an incomplete tetanus, in which each component is a single contraction prolonged long enough to produce imperfect fusion of the waves.

The conditions which affect the activity of the muscles engaged in a simple movement can be studied by the apparatus introduced by Mosso, and called the ergograph. The movements of a finger or limb are transmitted by a system of levers to a writing point which marks a graphic record of the movement upon a piece of smoked paper fixed to a revolving drum. With this instrument many observations ([23]) have been made to determine the influence upon the performance of work of practice, the rate of contraction, load, rest, hunger, mental activity, various foods and drugs. Many of the results, however, must be accepted with caution, for there is one source of fallacy which has not been sufficiently recognised by some investigators; complications can be readily introduced during an experiment by the influence of suggestion upon the subjects of the research, and it is not possible to eliminate these entirely by employing as subjects men who have no special knowledge of, or interest in, the research.

Ergographic studies have shown that general or local fatigue and hunger diminish, while previous practice, rest, sleep, and food increase the power of voluntary muscular contraction. These results are in accordance with the general experience of mankind,

and it is doubtful if a more exact measurement or analysis has been obtained by such experiments limited to a small group of muscles.

The ergograph is a convenient instrument for demonstrations, but the conditions are so different from those of ordinary life that it is safer to rely upon experience and special experiments, such as those [1] of Zuntz and Atwater, upon men marching or performing some other kind of general muscular work.

Upon the physical and chemical changes which occur in an isolated muscle during contraction a vast amount of work has been done.[2] Here it is only necessary to mention briefly those facts which have a bearing upon ordinary muscular work. The extensibility of the muscle is increased during contraction, and its temperature is raised. Even in the resting condition the muscle is about 0·1° to 0·6° warmer than the blood which supplies it, and during contraction an increase of 1·15° has been observed in the muscles of a dog after the blood vessels had been ligatured. Under normal conditions, however, the rapid circulation of the blood distributes the heat so efficiently that the internal temperature of the body is only raised a degree or two by hard work.[3]

The blood supply is greatly increased in the active muscle; according to Chauveau and Kaufmann's observations the flow is 4–5 times as rapid as during rest. The causes of this change will be considered later in relation to the effect of exercise upon the heart and circulation.

The chemical changes are shown by an increased absorption of oxygen and an increased discharge of carbon dioxide; a muscle paralysed by section of its nerve uses 0·003 c.c. of oxygen for one gramme of its weight per minute, but this is raised to 0·006 or 0·020 c.c. by tonic activity.[4] The glycogen of the muscle decreases, owing apparently to its combustion for the supply of energy. These and other similar questions, including the increased growth of muscle, must be discussed in a later portion of this article, which will deal with the general changes in metabolism during muscular work.

[1] See page 233.

[2] See article by Burdon-Sanderson, "Textbook of Physiology," edited by Schäfer, 1900, vol. ii., p. 352; and one by v. Frey in Nagel's *Handbuch der Physiologie des Menschen*, 1907, Bd. iv., s. 427.

[3] See page 243.

[4] Barcroft, *Ergebnisse der Physiologie*, vii. Jahrgang, 1908, p. 699.

The Effects of Muscular Exercise upon the Heart and Circulation

There is little doubt that the heart is the organ which is most easily damaged by exercise unsuited to the weak and untrained. Trainers of both men and animals rightly attach the greatest importance to the condition of the heart, and a vast medical literature upon cardiac strain, the athlete's heart, and the soldier's heart bears witness to the importance of the subject to the medical man.

It will be well therefore to indicate the most practical methods for the examination of the *heart* in relation to the effects of exercise. There is no question here of a consideration of a heart in a condition of disease, and nothing will be said about inspection, palpation, percussion, and auscultation, which are recognised methods in an ordinary clinical examination. In order to test the capacity of a heart to bear the strain of muscular work the most useful method appears to be a comparison of the rate of cardiac contraction at rest, directly after moderate exercise of a few minutes' duration, and again after periods of five, ten, or more minutes' rest. The effect of exercise is an augmentation of the rate; during the rest which follows the work the beats rapidly decrease in the case of a strong well-trained heart, but slowly in the case of a weak and untrained one. The following example of such an observation ([24]) will show the contrast:—

	Trained Man.			Untrained Man.		
	Rest.	Just after Exercise.	Five Minutes later.	Rest.	Just after Exercise.	Five Minutes later.
Pulse-rate for ¼ minute	16	33	15	17	38	24
	14	30	14	21	40	24
	15	26	13	17	38	23

The exercise lasted thirty seconds, and consisted in running down and up stairs.

In some special cases examination of the heart by means of the Röntgen rays may elucidate certain questions, but the method is of limited application and is beset with sources of error. The same remarks apply to the cardiograph, the records of which may be so complicated as to be misleading.

The *pulse* not only furnishes information on the rate and force of the beat of the heart, but also on the condition of the peripheral circulation. The sphygmograph affords a graphic record of the

pulse wave, and in some cases extends the information which may be obtained by the hand alone. By palpation it is possible for the practised hand to gauge the pressure of the blood, but for accurate determinations the Riva Rocci sphygmometer is generally used.

The *circulation* can be studied in several ways; by inspection the colour of the skin affords a guide to the flow of blood in the peripheral parts, and the information so obtained may be checked and extended by the use of flat bulb thermometers with which the temperature of the surface of the skin can be determined. The plethysmograph will measure the changes in the volume of a limb which are due to alterations in the supply of blood, and modifications of the sphygmometer, which indicate the pressures at which the arterioles, capillaries, and veins are blanched, will measure the pressure of the blood in those vessels.

This is not the place for details of the practical use [1] of the various instruments which have been mentioned, but it will not be amiss to point out that the simplest are the best. The striving for exact results by the use of complicated pieces of apparatus often defeats the aim; it is far better to multiply simple observations under different conditions than to spend much time and labour in obtaining a record with a complicated instrument, however exact it may appear to be. For this warning there are two strong reasons. The effects of muscular exercises upon the heart and circulation quickly disappear when a healthy man takes rest; the recovery begins at once, and during the seconds and minutes spent in the adjustment of apparatus great changes may occur. The second reason is a practical one. The medical man engaged in a busy practice has not the time, means, or experience necessary for the successful use of many scientific instruments, and it is far better that he should rely upon his own powers of observation by sight and touch.

In the study of the effects of muscular exercise upon the heart and circulation it is always necessary to know the normal conditions of the subject during rest. The personal variations in different individuals are so great that data are deprived of a great part of their value unless they combine the results of observations both before and after exercise.

It is desirable that a writer should give the results of investigations conducted by himself or in conjunction with others. The

[1] See "Practical Physiology," by Beddard, Edkins, Hill, Macleod, and Pembrey, second edition, 1905.

following table contains the results of observations[1] made by Captain L. E. L. Parker, R.A.M.C., and the author as part of the work of a committee appointed to report upon the physiological effects of food, training, and clothing on the soldier.

Individual Variations in the Pulse during Rest.

Number of Men.	Number of Observations.	Number of Days.	Time of Day.	Pulse.				
				Maximum.	Minimum.	Average of Maxima of each Day.	Average of Minima of each Day.	Average of Mean of each Day.
A. 6 men 6	60	10	9–10 A.M.	110	55	93	68	80
A. 6 men 3	6	2	2–3 P.M.	100	77	99	85	92
B. 5 men 4	4	1	10–11 A.M.	90	72	90	72	78
B. 5 men 4	4	1	2–3 P.M.	100	90	100	90	93
B. 5 men 5	50	10	10.30–11.30 A.M.	92	68	87	72	80
B. 5 men 4	12	3	10.30–11.30 A.M.	88	60	83	68	75
C. 4 men 5*	15	3	10–11 A.M.	104	60	99	65	78
C. 4 men 4	20	5	10–11 A.M.	104	52	95	59	76
C. 4 men 3	3	1	8–8.30 A.M.	88	76	88	76	82
15	174	36		110	52	93	71	81

* Including one of Group B.

The next table gives the results obtained after marching; the figures are arranged so that the same groups of men may be distinguished, but are not classified to indicate the influence of distance, external temperature, clothing, and load.

Individual Variations in the Pulse after Marching.

Number of Men.	Number of Observations.	Number of Days.	Pulse.				
			Maximum.	Minimum.	Average of Maxima of each Day.	Average of Minima of each Day.	Average of Mean of each Day.
A. 6 men 6	245	10	150	70	115	89	101
B. 5 men 4	8	1	112	88	108	93	101
B. 5 men 5	50	10	160	72	123	100	112
B. 5 men 4	12	3	114	72	105	85	95
C. 4 men 5	15	3	126	70	119	78	98
C. 4 men 4	20	5	126	80	112	88	101
C. 4 men 3	3	1	138	84	138	84	117
D. 6 men 6	6	1	120	93	120	93	106
21	359	34	160	70	118	87	104

[1] Second Report of Committee, 1908.

The figures for the pulse in the last table are certainly somewhat under-estimated, for it was not possible to take all the observations immediately after the march; the rate of the pulse begins to decrease directly the work is at an end, and this is especially the case in the well-trained man.

These results represent the condition which probably obtains in active healthy men of the physique of the ordinary infantry soldier; the men were not picked men, and the data are not to be considered as rigidly exact, for it was not always possible to guard against the influence of nervousness in the first examination and of a brief rest directly after marching.

The next table gives the results of observations in the pulse of healthy men before and after running:—

Subject.	Distance in Miles.	Pulse at Rest before Run.	Pulse just after Run.	Pulse after Rest for stated Periods.
C.	1	68	164	98 (15 min.)
	2	70	164	128 (10 min.), 100 (30 min.). 82 (60 min.)
B.	¼	76	152	...
	½ more	...	144	112 (5 min.)
	1	56	160	124 (1 min.)
	2	66	140	120 (2 min.), 106 (33 min.) 84 (77 min.), 74 (107 min.)
	2	56	136	104 (15 min.), 88 (45 min.) 86 (75 min.)
P.	¼	70	84	...
	½ more	...	104	92 (5 min.)
	¼	76	120	...
	½ more	...	140	100 (5 min.)

The heart beats more quickly during muscular work. The object is clear, but the means whereby it is attained are complex. It has already been shown that a more rapid circulation is necessary to meet the various demands of muscular activity: the blood supplies these needs, and the heart is the pump which forces it to circulate through the various parts. The adjustment begins with the performance of work, and it is necessary to study the means whereby this is brought about.

The heart and the arterioles are under the control of the nervous system; by the action of the vagus nerve the beats become slower; they are quickened by impulses passing down the sympathetic nerve. During rest the vagus nerve appears to exert a constant inhibitory action upon the heart, but directly impulses pass from

the motor cortex of the brain down to the muscles the inhibitory action is diminished and the accelerator nerve is stimulated. This is important, for it throws light upon the great influence of training upon the orderly contraction of the heart, and in relation to that subject it will need further consideration later. In addition to this nervous control, it would appear that other influences are at work. The products of muscular activity act upon the heart directly and indirectly through the nervous system; carbon dioxide is one of the most important of these metabolites, and it quickens the beat of the heart (25). Muscular work raises the pressure of carbon dioxide in the alveolar air of the lungs, as Haldane and Priestley [1] have shown; the breathing becomes more rapid or deeper for the maintenance of a constant level in the pressure of that gas in the alveolar air and presumably in the blood of the lungs. Thus there is a mutual dependence of the heart and lungs upon one another, and an insight is afforded into the close association between the heart and lungs which is expressed by a "good wind." Sarcolactic acid is another metabolite formed during muscular activity, and directly or indirectly may influence the heart.

The temperature of the body rises during muscular activity, it may be as high as 102° F. in a healthy man, and it is known that the heart responds to an increased temperature by a more rapid beat. In addition vaso-motor changes occur, more blood goes to the active muscles and more to the skin when the temperature rises, and in some cases at least a more rapid beat of the heart appears to be an effort of compensation for the fall of blood pressure which may arise from the dilatation of the vessels in those parts.

The response of the heart to muscular work and to rest is so extremely rapid that it would appear to be due in the first place to nervous influences; the effects of metabolites and of the rise in the temperature of the body develop more slowly and persist for a considerable time after the work has ceased.

The heart is a muscle, and resembles the skeletal muscles in its response to work. Gradually increasing work with good nutrition and periods of rest strengthens it. There is an increased growth, a physiological hypertrophy which is more or less proportional to the development of the skeletal muscles. The untrained muscle

[1] See page 240.

is overstretched and injured by severe and prolonged exertion, but the damage is more easily done and less easily repaired in the case of the heart. The skeletal muscles become fatigued and painful during movement, and the enforced rest gives them time to recover; the heart cannot take such a profound rest, it must continue to beat, if life is to be maintained, and can rest only by beating less frequently and less vigorously. In the case of the untrained heart over-exertion produces palpitation, overdistension, and dilatation. The duration of systole to diastole, that is, of work to rest, may be less than 1 : 1 in the fatigued heart, whereas in the normal heart the proportion is 1 : 3.

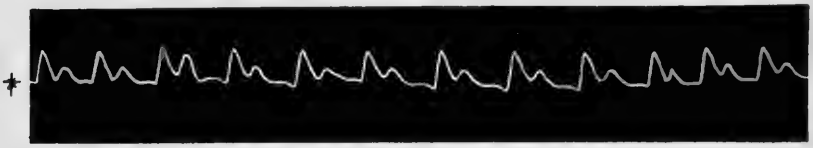
The increase in the rate of the heart beat is within certain narrow limits proportional to the work done. The pulse rate may be readily doubled by running down and up stairs for thirty seconds, but such vigorous exercise rapidly produces dyspnœa and cannot be maintained. The heart not only works more rapidly, but it has to pump the blood into the aorta at a pressure which may be one-half greater than the pressure at rest. Thus a healthy well-trained man who had performed such an exercise showed the following changes in the pulse and blood pressure; the pulse was increased from 56 to 124, and the blood pressure in the brachial artery from 126 to 142 mm. Hg. A high blood pressure is not maintained, for during the continuation of exercise the cutaneous arterioles dilate.

The limit of efficiency as regards the rate of the heart beat appears to be reached at about 160 per minute, but there are doubtless individual differences.

The influence of marching with a load has been especially investigated by Zuntz and Schumberg ([26]); they not only found an increase in the rate of the contraction of the heart but also evidence of engorgement of the liver and heart with blood. The frequency of increased hepatic and cardiac dulness on percussion was 56, 70, and 87 per cent., when the soldiers marched carrying loads of 22, 27, and 31 kg. respectively. The average increase of cardiac dulness was 1 cm., that of the liver 2·3 cm.; the highest figures were 3·5 and 5 cm. respectively. The cardiac dilatation involved the right ventricle on sixty-two occasions, and the left also on thirty-one occasions. The engorgement did not coincide with the increase in the rate of the pulse, but with the increased breathing and the rise in the temperature of the body. In such experiments the belts and

straps of the equipment as well as the load produce a hindrance to free breathing, but nevertheless the engorgement of the liver must be considered as a means of relieving the heart from still greater distension. The tendency to strain upon the heart is diminished by its increased beat, for the area of the inner surface of the ventricle exposed to the pressure of the blood is diminished during its contraction.

After severe exercise the pulse shows an exaggerated dicrotic notch; this has been observed in a considerable number of healthy men, and is no doubt a normal sign of the reaction to the high blood pressure during work. The following figure is a reproduction of a tracing obtained from the radial artery of an athlete on the day following a severely contested game of Rugby football in a "cup-tie" match.



The rate of the pulse was 72 per minute.

The *blood pressure* is the force exerted by the blood upon the walls of the blood vessels, and is dependent upon the pumping action of the heart and the resistance of the vessels, especially of the arterioles. The blood pressure will be raised by a more rapid or more powerful contraction of the heart, if the peripheral resistance remains the same or does not diminish in proportion to the increase in the work done by the heart. During muscular work it is known that the peripheral resistance varies; the vessels supplying the muscles are dilated, and, if the exercise is continued and the temperature of the body rises, the cutaneous arterioles expand. This statement applies to those forms of exercise or work in which there is no prolonged straining effort; directly the muscles of a limb are rigidly contracted and the thorax is fixed in order that a better purchase may be given to the contracting muscles, as, for example, in lifting a heavy weight, or in wrestling, a great peripheral resistance may be introduced. During some efforts the pulse may disappear at the wrist owing to the compression of the arteries by the forcible contraction of the muscles

and to the hindrances offered to the free passage of the blood through the heart. For these reasons it is necessary to consider the nature of the muscular exertion in any discussion of its effects upon the blood pressure.

M'Curdy ([27]) has drawn special attention to this question; he recorded the blood pressure in seventy-seven experiments upon twenty-three men before, during, and two or three minutes after an exercise of strength or effort. The exercise consisted in the maximum lift for each man; the weight lifted varied from 118 to 249 kilos., and the time of an average lift was five seconds. The following are the average values of all the measurements :—

Blood Pressure in Mm. Hg.

Before Lift.	During Lift.	Two to Three Minutes after Lift.
111	180	110

The highest blood pressure before the lift was 127 mm. Hg., the lowest 93; the maximum during the lift was 210 and the minimum 146. The rise in blood pressure was not accompanied by any great change in the pulse rate; some men showed an increase, others no change, and others a decrease. Such exercises subject the heart and blood vessels to a great and sudden strain, and cannot be considered beneficial. A man must be carefully and progressively trained to lift great weights; otherwise there is a great danger of overstrain of the heart.

These results may be compared with those obtained by Bowen ([28]), who investigated the changes in the beat of the heart and the blood pressure during bicycling. He found that there was a rapid rise in the blood pressure when the work began; the maximum was reached in about four minutes, but during the continuation of the exercise the pressure declined slowly. The extent of this fall depends upon the dilatation of the blood vessels of the skin, and this in turn depends upon the temperature of the body and its surroundings. This factor does not come into play during an effort such as a lift; the powerful and sustained contraction of the muscles during the lifting of a weight nearly obliterates the lumen of the blood vessels, and thereby increases the peripheral

resistance enormously; the increase in the volume of the blood driven out of the heart raises the blood pressure quickly to a great height, because the blood already in the arteries is prevented from escaping.

The changes in the blood pressure are effected very rapidly, as is shown by the following examples taken from a series of observations ([29]) upon two men, one well-trained, and the other untrained. The exercise lasted only thirty seconds, and consisted in running down and up stairs.

Trained Man.			Untrained Man.		
Rest.	Just after Exercise.	Five Minutes later.	Rest.	Just after Exercise.	Five Minutes later.
110 mm. Hg	134	118	104	134	108
122 „	134	126	110	140	106
132 „	152	132	118	126	110
126 „	142	130	116	148	103
116 „	136	129	122	148	116

The blood pressure does not remain at a high level during the prolongation of exercise, but falls gradually and may become lower than it was before the beginning of the work. Such a condition has been observed during a march of seven miles; the fall in the blood pressure was associated with a dilatation of the cutaneous blood vessels, which was shown by the increased colour and temperature of the skin.

The causes of the quickening of the heart beat during muscular work are to be sought, as already mentioned, in nervous regulation, effected reflexly or directly by the products of muscular activity, and in the action of those metabolites and the rise of temperature upon the heart itself. It might be expected that the control of the blood vessels is similarly effected, for the heart is developed from blood vessels. The evidence from experiments upon the flow of blood through muscles is conflicting. Gaskell's ([30]) work led him to the conclusion that vaso-dilator fibres are stimulated reflexly when muscles contract, but Bayliss ([31]) obtained only slight dilatation on stimulation of the dorsal nerve roots. Lactic acid was found by Gaskell to produce a dilatation of the arteries of a frog, but Osborne and Vincent could not obtain a similar result in mammals; carbon dioxide dilates the blood vessels in

the muscles of frogs, as Bayliss has shown. There is no doubt about the close association of dilatation of the cutaneous vessels with a rise in the temperature of the body produced by muscular work. Further observations, however, are necessary to explain the means whereby muscular work influences the heart and circulation.

Influence of Muscular Work upon the Respiration

Even during rest the differences in the rate and depth of breathing of healthy men are considerable; some men breathe slowly and deeply, others take rapid and shallow respirations. The "tidal air" may vary from 100 to 1000 c.c., and the total volume of air breathed per minute shows a similar wide range, the determinations ranging from 3000 to 9000 c.c. These figures have been taken from the results of different observers;[1] in addition may be given a series ([32]) recently made upon sixteen subjects, all of whom, with two exceptions, were medical students:—

Subject.	Age in Years and Months.	Weight in lbs.	Height in feet and inches.	Volume of Air Breathed per Minute in Litres.	Number of Breaths per Minute.	Average Volume of each Breath in c.c.
1	21·2	154	5·11	6·560	22·5	291
2	18·4	132	5·7	7·867	19·34	406
3	27·1	144	5·11	7·660	16·5	465
4	18	115	5·5	9·234	21	441
5	21	155	5·11	9·150	17·7	517
6	14·8	91	4·8	6·030	14	431
7	22·9	173	6·2½	9·753	10	981
8	20·4	140	6·0	5·113	17	300
9	20	133	5·7	5·008	14·7	341
10	19·5	129	5·6	6·350	10	638
11	21	131	5·6	5·168	19	271
12	22·1	123	5·5	7·570	19·4	392
13	20	140	5·10	9·504	24	396
14	21·6	126	5·7	5·560	13·5	416
15	19·5	134	5·5	7·900	17	463
16	21·9	126	5·6	5·458	12·4	450
Average	20·5	134	5·7	7·118[2]	16·7	449[2]

[1] See article Chemistry of Respiration, by M. S. Pembrey, in "Textbook of Physiology," edited by Schäfer, vol. i., 1898, p. 748.

[2] Measured at 15° moist.

These results compare very well with those obtained by Haldane and Priestley ([33]) upon fifteen men; the means of their results were :—

Weight in lbs.	Height in feet and inches.	Average Volume Breathed per Minute at 37° Moist in Litres.	Average Frequency per Minute.	Average Depth of Respirations in c.c. at 37° Moist.
154	5·11	8·55	15·2	604

There is little doubt from the results shown in these two tables that many of the older estimates, which give much lower figures, are incorrect.

The composition of the alveolar air is not the same in different adult subjects, for FitzGerald and Haldane ([34]) found that the percentage of carbon dioxide varied from 5·86 to 4·29 in men and from 5·40 to 3·99 in women. From this the conclusion must be drawn that there is a personal variation in the response of the nervous system to the stimulating action of carbon dioxide.

The effect of muscular work is always an increased respiratory exchange and increased ventilation of the lungs to meet the greater demand for the supply of oxygen and the removal of carbon dioxide. The breathing becomes quicker or deeper, or more often is affected in both ways; hyperpnœa is produced and, if the work be severe, laboured breathing or dyspnœa may follow and give rise to so much discomfort that the man will pant and stop work to "recover his breath."

At rest the healthy man breathes through his nose; the inspired air is warmed, moistened, and cleansed of foreign particles by passing over the moist surface of the nose and naso-pharynx. During vigorous exercise, however, mouth-breathing constantly replaces nasal breathing, for there is then less resistance to the entry and exit of the air, and the exposure of the moist vascular surface of the mouth assists in the cooling of the body. The man who resists the inclination to breathe through the mouth during active exercise throws an additional and unnecessary amount of work upon his respiratory muscles, and thereby increases his discomfort and distress.

The increase in the ventilation of the lungs during exercise

may be shown by the following examples from experiments upon three healthy men :—

Subject.	Ventilation in Litres per Minute.	No. of Respirations.	Pulse Rate per Minute.	Remarks.
B.	$10\frac{1}{2}$	18	60	At rest.
	$15\frac{3}{4}$	31	124	After running $\frac{1}{8}$ of mile.
P.	$9\frac{3}{4}$	29	70	At rest.
	12	22	84	After running $\frac{1}{4}$ of mile.
C.	$10\frac{1}{2}$	20	72	At rest.
	$14\frac{1}{2}$	25	110	After running $\frac{1}{4}$ of mile.

The causes of hyperpnœa and dyspnœa have been the subject of many experiments and much controversy, and even at the present time it is impossible to maintain that the question is closed. It is generally admitted that the work of Haldane and Priestley ([35]) has shown that the factor which regulates the respiratory movements during rest is the pressure of the carbon dioxide in the blood, as gauged by the pressure of that gas in the pulmonary alveoli. The rate of breathing may be altered, but the subject of the experiment will also change the depth, so that the mean pressure of the carbon dioxide remains almost the same, as shown by the following results obtained by these authors :—

Subject.	Respirations per Minute.	Percentage of Carbon Dioxide in Alveolar Air.		
		At End of Inspiration	At End of Expiration.	Mean.
J. S. H.	9	5·59	5·87	5·73
	19	5·56	5·70	5·63
J. S. H.	9	5·33	5·47	5·40
	20	5·44	5·60	5·52
J. G. P.	10·5	5·95	6·74	6·35
	30	5·98	6·05	6·02

During muscular work Haldane and Priestley found that there was a slight but distinct rise in the percentage of carbon dioxide in the alveolar air. Their results are given in the next table.

Effects of Work on the Percentage of Carbon Dioxide in the Alveolar Air

Subject.	Work in Foot-Pounds per Minute.	Calculated Respiratory Exchange. Normal = 1.	Alveolar CO_2 per Cent.		Mean.
			End of Inspiration.	End of Expiration.	
J. S. H.	1880	...	5·10	5·80	5·45
	4140	...	5·56	6·51	6·085
	4850	...	5·20	6·19	5·695
	3380	...	5·42	5·78	5·60
	3160	...	5·79	5·88	5·835
	2530	...	5·48	6·15	5·815
Mean J. S. H.	3320	49	5·44	6·05	5·75
Mean J. S. H.	Rest	1	5·54	5·70	5·62
J. G. P.	2420	...	6·53	7·13	6·83
	1940	...	6·61	6·51	6·56
	2460	...	6·60	7·04	6·82
	2540	...	6·06	7·26	6.64
Mean J. G. P.	2340	3·8	6·45	6·98	6·72
Mean J. G. P.	Rest	1	6·17	6·39	6·28
Mean of J. S. H. and J. G. P.	2800	4·3	5·945	6·515	6·235
	Rest	1	5·855	6·045	5·95

From these data they conclude that the hyperpnœa of muscular work is due to a rise in the pressure of carbon dioxide in the respiratory centre, but it is necessary to bear in mind that they measured the pressure of carbon dioxide in the alveolar air, not in the blood.

The history of the different views upon the causation of the hyperpnœa produced by muscular work illustrates extremely well those fluctuations between old and new theories which are so constantly observed in the biological sciences. Muscular activity increases the ventilation of the lungs, the intake of oxygen and the output of carbon dioxide. It was but natural, therefore, that the hyperpnœa should be attributed to a deficiency of oxygen or to an excess of carbon dioxide in the blood due to the greatly increased metabolism. To these causes hyperpnœa was generally attributed until Geppert and Zuntz [36] found that muscular activity was accompanied by an increase in the oxygen and a decrease in the carbon dioxide of the blood. These observers considered that

the hyperpnœa was produced by some product of muscular activity which was absorbed by the blood, and thus carried to the medulla oblongata, where it stimulated the respiratory centre. Loewy [37] also maintained that carbon dioxide was not the factor, for he found that, whereas the rate of respiration was doubled by muscular work when the increase above the normal amount of carbon dioxide in the expired air was only 0·5 per cent., the same amount of dyspnœa could be produced during rest only by artificially raising the percentage of carbon dioxide to a much higher point, about 5 per cent.

The alkalinity of the blood is diminished during muscular activity, and this observation revived the question whether products of activity stimulated the respiratory centre. Forty years ago Pflüger [38] suggested that lack of oxygen might act indirectly as a stimulus to respiration; products such as lactic acid unoxidised owing to the deficiency of oxygen in the tissues might be the exciting agents.

The work of Haldane and Priestley effected a return to the view that carbon dioxide was the chief factor which increased the respiration during muscular work. But quite recently the whole question of muscular hyperpnœa and dyspnœa has been reopened, and it is necessary to consider the possible action of such factors as lack of oxygen, metabolites such as lactic acid, increased temperature of the body and nervous impulses from various parts. The muscular work performed by Haldane and Priestley was slight, and their analyses of the alveolar air do not include the amount of oxygen. After vigorous exercise the alveolar air sometimes shows a considerable rise in the percentage of carbon dioxide, and at other times a fall below the normal [39]. It becomes important, therefore, to determine the respiratory quotient, the ratio of the carbon dioxide discharged to the oxygen absorbed. Such analyses show quotients as high as 1·2 during muscular dyspnœa.

It is necessary to consider whether the lack of oxygen produces dyspnœa directly or indirectly through metabolites which remain unoxidised owing to the lack of that gas. A man at rest breathes with practically the same frequency and depth whether he be breathing air or pure oxygen [40], and his response to an increase of carbon dioxide in his lungs appears to be unaffected by breathing oxygen [41]. Directly after exercise, however, breathing oxygen diminishes the dyspnœa, and enables the man to tolerate a higher

percentage of carbon dioxide. The following are examples of the results obtained :—

Composition of Mixture in Spirometer at Breaking Point.

Subject.		Started with Air.	Started with Pure Oxygen.
		Per Cent.	Per Cent.
A. B.	Rest	6·21 CO_2 4·3 O_2	6·35 CO_2 21·3 O_2
	After exercise	7·73 CO_2 11·6 O_2	10·02 CO_2 30·0 O_2

The complexity of muscular dyspnœa is shown by the fact that it does not increase if the exercise be continued, but on the contrary decreases. This is well known to athletes. During the first quarter of a mile run the hyperpnœa increases until panting and distress are experienced, but if in spite of the discomfort the run be continued the difficulty of breathing disappears and the exercise can be maintained with comfort at the same or even at a greater pace. The runner has now "got his second wind." This interesting phenomenon has not been thoroughly investigated, but it would appear that the distress is associated with a high respiratory quotient, with a relative deficiency of oxygen (42).

Composition of Alveolar Air before and after the Advent of "Second Wind."

Subject.	Percentage of Carbon Dioxide.	Percentage of Oxygen.	$\frac{CO_2}{O_2}$	Pulse Rate in 15 Seconds.	Remarks.
P.	5·11	...	...	19	Rest.
	5·55	15·49	1·0	30	After 8 laps ($\frac{1}{4}$ mile); panting; pulse irregular.
	5·50	15·39	0·99	35	After 18 further laps; "second wind" at 10th lap; pulse more regular; sweating.
R.	5·27	14·32	0·79	...	Rest.
	7·36	14·03	1·06	...	After 6 laps.
	5·91	14·62	0·93	...	After 8 further laps; "second wind"; sweating.
B.	6·04	14·48	0·93	19	Rest.
	8·13	13·17	1·04	38	After 8 laps.
	7·39	12·8	0·90	36	After 19 further laps; "second wind" at 16th lap; sweating.

Other factors are probably involved in these conditions; the contraction of the heart is often irregular during the period of distress, and becomes regular when the "second wind" has arrived. A rise in the temperature of the body, vascular changes and sweating, also accompany "second wind," and further experiments are necessary to determine their significance in relation to the respiratory movements.

Ryffel has found lactic acid in the sweat and urine after muscular exercise, but no pronouncement can be justly made for or against the theory that lactic acid stimulates the respiratory centre.

It is known that a rise in the internal temperature ([43]) of the body quickens the respiratory movements; this is especially marked in the dog; the rate of its respiration may be increased from 28 to 230 per minute when it is necessary for it to cool its body by the evaporation of moisture from its tongue and mouth ([44]).

It is probable, moreover, that nervous impulses from various parts of the body, especially from the heart and lungs, may influence the activity of the respiratory centre and produce such a co-ordination of the respiratory movements that an adequate supply of blood is maintained through the lungs. The sensory nerves of muscles may take part, for the respiratory movements are altered in type, rate, and depth by the nature of the exercise performed. During rowing a well-trained man adjusts his breathing to his stroke.

The quantitative changes in the respiratory exchange during exercise will be considered later in connection with the exchange of material, of which they form an essential part.

Influence of Muscular Exercise upon the Temperature of the Body

It is necessary here, equally with the other systems of the body, to consider the normal variations in the temperature of the body. One might maintain that it is more necessary, for on thermometers and temperature charts the point 98·4° (36·89°) has been marked as the normal; this practice has had the unfortunate result of preventing the full recognition of the daily and personal variations in the temperature of man. Confusion is still greater when it is remembered that many physicians rely upon the temperature of the mouth, others upon that of the axilla, and a

small number upon that of the rectum. It is easy to appreciate the reasons of delicacy which prevent the determination of the temperature in the rectum in the case of most patients, but there is no excuse for the constant neglect on the part of clinicians to mention in their reports the time and place where the temperature was taken. Accurate results can only be obtained by the determination of the temperature in the rectum or stream of urine, for the cavity of the mouth is bounded by such thin walls, and is so readily cooled by exposure, breathing, and sweating, that it often does not indicate the true internal temperature of the body.

The temperature of man shows a daily variation; it rises during the day, the time of activity, and falls during the night, the time of rest and sleep. The range is from 36·0° (96·8°) to 37·8° (100·0°); these are average figures for the temperature of the rectum and urine, and do not include the absolute physiological range.

The temperature is raised during muscular work ([45]); it may be as high as 38·9° (102°) in a healthy man. This truth is now generally accepted, although a few years ago, owing to observations based upon temperatures taken in the mouth, it was generally denied or contested. The explanation of the disagreement is found in the fact that the temperature of the mouth may fall during the time that the temperature in the rectum and urine is raised.

The heat of the body depends upon the production and loss of heat. During muscular work the production is greatly increased, owing to the vigorous combustion of material in the tissues, especially in the active muscles. This combustion is indicated by the great rise in the discharge of carbon dioxide and in the absorption of oxygen. The loss of heat also undergoes an augmentation, otherwise the temperature of the body would steadily rise, and would soon reach a height incompatible with the performance of work and even with life itself. Indeed this does occur under special conditions, when a man is forced to work in a hot atmosphere so laden with moisture that the cooling of his body by the evaporation of sweat is prevented.

Under ordinary conditions the effect of muscular work is to cause a rise in the internal temperature; the increased production of heat is not compensated by a corresponding loss. It appears that a rise of temperature, within certain narrow limits, is bene-

ficial. The chemical changes associated with muscular work are probably facilitated by a temperature a degree or two above the temperature during complete rest, and it may be that the dilatation of the blood vessels of the skin relieves the heart from too great a blood pressure. Most men find that they can work more comfortably and efficiently when they have "warmed up" to the work, and some maintain that they work better when they begin to sweat. The first half mile of a walk is not so well performed as the later portions. Such evidence, however, would not justify a statement that the improvement is solely due to a rise of temperature, for there are other factors to consider. Among these should be mentioned the adjustment of the heart and respiration, the increased flow of blood through the muscles, and probably an increased secretion of synovial fluid in the joints. This much, however, may be said. Muscular work both in the case of man and other warm-blooded animals is constantly accompanied by a rise in the internal temperature; the time of activity coincides with the rise in the daily variation of temperature, the time of rest and sleep with the fall to the minimum. Moreover, the daily variation in temperature is accompanied by corresponding changes in the pulse and the respiratory exchange.

The following table will show the effect of various forms of exercise upon the temperature of man :—

Subject.	Temperature before Exercise.			Temperature after Exercise.			Remarks.
	Mouth.	Urine.	Rectum.	Mouth.	Urine.	Rectum.	
	Degrees.	Degrees.	Degrees.	Degrees.	Degrees.	Degrees.	
P.	36·00	37·22	37·67	35·45	37·94	38·00	Walk of about 4 miles.
P.	36·80	37·22	37·55	36·32	37·83	37·94	Digging for 45 minutes.
P.	...	...	...	36·60	38·35	38·70	Work for about 2 hours in snow.
P.	37·6	37·2	37·6	37·3	38·0	38·1	Bicycle ride for 3½ miles; temperature of air in shade, 33·6 degrees.
A.	...	...	36·22	...	...	38·40	Ascent of Simelihorn (2752 m.).
B.	36·83	37·21	37·53	36·67	37·72	38·13	Bicycle ride for about 20 miles.
R.	...	...	...	36·78	...	39·00	Game of fives for 30 minutes.
E.	...	...	...	36·22	...	38·89	

In addition to the above data may be given the results of observations upon soldiers after marching :[1]—

Number of Men.	Number of Observations.	Number of Days.	Maximum.	Minimum.	Average of Maxima of each Day.	Average of Minima of each Day.	Average of Mean of each Day.
21	359	34	102·4° (39·11)	98·8° (37·11)	101·4° (38·56)	100·2° (37·89)	100·7° (38·17)

In observations upon the temperature of the body it is necessary to determine both the deep and surface temperature, for there is no doubt that the greatest discomfort arises when the temperature of the skin is abnormal. It is in the skin that the sensations of heat and cold arise. A rise in both the deep and surface temperature shows that the body is warmed in all its parts, and discomfort is then experienced : if, on the other hand, the skin be kept cool by sweating or exposure, no discomfort and no bad effects are experienced by a healthy man whose internal temperature has been raised a degree or two degrees by hard work. After exercise the temperature of the body falls, and the reaction is generally seen in a temperature below the normal for a day of rest.

All men know that it is easier to work hard if the clothing be sufficiently light and loose to allow of the free evaporation of sweat. Work can only be performed efficiently under such conditions on a warm and damp day. When a labourer keeps on his coat he does not mean to do a fair day's work, and there is very little doubt that he is being paid by the day and not by the piece.

A man who is not forced to work finds in his sensations of heat a safeguard against overwork and heat-stroke ; he works more slowly when he feels too hot, or, if he wishes to continue to work hard, he increases his loss of heat by the removal of his coat or waistcoat and by turning up his sleeves. The evaporation of sweat is thus facilitated, as shown by the following comparative observations[2] upon soldiers after a march of seven miles :—

[1] Committee on Physiological Effects of Food, Training, and Clothing on the Soldier, Second Report, 1908.

[2] Ibid., Fourth Report, 1908.

Number of Men.	Increase in Pulse.			Increase in Rectal Temperature.			Loss of Moisture from Body in Grammes.			Increase in Weight of Clothes in Grammes.			External Temperatures.	
	Max.	Min.	Aver.	Max.	Min.	Aver.	Max.	Min.	Aver.	Max.	Min.	Aver.	Dry Bulb.	Wet Bulb.
5*	52	16	28	1·6° F.	0·6°	1·0°	1430	1000	1200	250	0	109	67°	58°
„†	48	24	41	1·8	0·8	1·5	2000	1200	1500	480	90	254	69	59

* Drill order without jacket. † Drill order with jacket.

When the temperature of the air is high both by the dry and wet bulbs the evaporation of sweat must be greatly increased in order to cool the body. This is shown by a comparison of the results obtained upon the same men, when they performed the march on hot and cold days with the same clothing, equipment, and load.[1]

Number of Men.	Increase in Pulse.			Increase in Rectal Temperature.			Loss of Moisture from Body in Grammes.			Increase in Weight of Clothes in Grammes.			External Temperatures.	
	Max.	Min.	Aver.	Max.	Min.	Aver.	Max.	Min.	Aver.	Max.	Min.	Aver.	Dry Bulb.	Wet Bulb.
4	84	52	62	2·3° F.	0·6°	1·4°	2390	1140	1816	640	60	320	79°	67·5°
„	24	8	14	1·6	0·0	0·8	555	300	419	40	0	27	45	38

The limits of the regulation of temperature are passed when a man is obliged to work under unfavourable conditions of clothing in a very hot and moist atmosphere; the temperature of his body rises to an abnormal height; the production of heat exceeds the loss, and a point is soon reached at which the metabolism becomes extravagant; more and more heat is produced, and heat-stroke (46) is the result. This condition is seen in soldiers forced to march carrying a load, and wearing unsuitable uniform and equipment in a hot and humid atmosphere.

[1] Committee on Physiological Effects of Food, Training, and Clothing on the Soldier, Second Report, 1908.

The Influence of Muscular Work upon the Exchange of Material

It has already been pointed out that the law of the conservation of energy applies to the performance of muscular work,[1] and data have been given to prove the great increase in the intake of oxygen, the output of carbon dioxide and the production of heat. The respiratory exchange represents only a portion of the total exchange which must be determined in any experiment upon the total income and output. The nitrogenous exchange must be estimated from the total nitrogen of the food ingested and of the urine and fæces excreted. In addition, the composition of the food in terms of carbohydrate and fat as well as of protein should be known, and also the amount of water taken in by, and discharged from, the body.

It is impossible in this article to consider this subject fully, but attention may be directed to the chief results of experiments. The nitrogenous output is dependent upon the intake of nitrogenous food, not upon the performance of muscular work; the intake of oxygen and the output of carbon dioxide are immediately raised by muscular exercise, and under normal conditions are proportional to the work done. It will be understood that the term work is here used in the sense of physiological work which may or may not be immediately apparent as physical work expressed in foot-tons or kilogrammetres. The first time a man performs work, to which he is unaccustomed, he expends more energy than he will do in performing the same work after frequent practice. One of the most important effects of training is the economical performance of work.

The fact that the nitrogenous output is not increased by work would suggest that the energy is supplied by carbohydrates and fats. It is necessary to give briefly the evidence upon these points. In the first place the experiments of Pettenkofer and Voit ([47]) show that the excretion of nitrogen in the urine is the same whether a man does work or is at rest; the output of nitrogen is determined by the amount of that substance taken in the food. In their first series of experiments the mean excretion of nitrogen in the urine during hunger was 12·4 grms. during a day of rest and 11·8 grms.

[1] See Atwater, *Ergbenisse der Physiol.*, 3ter Jahrgang, Abtheilung 1, 1904, s. 497.

during a day of work, the time of labour being nine hours. In the series of experiments when the man received food the figures were 16·8 grms. during rest and 17·1 grms. during work. There is no increase in the discharge of nitrogen on the days following the work, provided that the man started with stores of energy in the form of glycogen and fat sufficient to prevent any demand upon the protein of his tissues to supply the energy required for the performance of the work.

There is no doubt that the amount of food required by a man depends upon the muscular work which he performs. So much follows from our knowledge of the conservation of energy, but that law gives us no guidance as to the relative amounts of protein, carbohydrate, and fat which are required. To obtain evidence upon these points we must examine the diets of men whose occupations entail different amounts of manual labour.

Atwater calculated the energy value of the dietaries of civilians living under different conditions, and upon these data based his well-known standards of diet. These are given in the table on the following page, together with other dietaries for the sake of comparison.

Special importance must be attached to the dietaries of prisoners both military and civil, for in these cases it was impossible for the men to obtain extra food; work was regularly performed, and medical inspection and the weights of the men at different times showed that their health was satisfactory.

During the last two or three years special attention has been directed to the question of diet. Chittenden's [48] experiments and writings have given rise to much discussion, for he maintains that most men eat too much protein and impair their health by this extravagance. His contention is that the large amount of protein consumed overtaxes the kidneys in their work of excreting the waste products of digestion. For this he gives no evidence. On the other hand it is well known that the body is overcompensated and is able to adjust itself within certain limits to a wide range of work. This capacity is no doubt shared by the kidneys, for one kidney may for years efficiently remove the waste products which are normally discharged by two kidneys.

It is impossible here to examine fully Chittenden's experiments and views, but it may be well to emphasise again the importance of instinct and experience as guides to questions of food. Healthy

	Protein.	Fat.	Carbo-hydrates.	Calories.	Remarks.
	Grammes.	Grammes.	Grammes.		
Atwater's Standards. No work	100	...	...	2700	Definite amounts of fat and carbohydrate are not given, but they must be sufficient to make up with the protein the number of calories. The standards are for food actually eaten.
Atwater's Standards. Light work	110	...	...	3000	
Atwater's Standards. Moderate work	125	...	...	3500	
Atwater's Standards. Hard work	150	...	...	4500	
Atwater's Standards. Very hard work	175	...	...	5500	
Average food supplied gratis to four British regiments [1]	133	115	424	3369	Waste included, but not extra food bought.
British soldiers in detention undergoing sentences exceeding forty-two days without hard labour [1]	127	65	497	3272	Rations allowed.
British soldiers in detention undergoing sentences exceeding forty-two days with hard labour [1]	141	69	560	3614	Rations allowed.
Ordinary prisoners, Scotland, light work, mostly sedentary	135	35	536	3115	Food supplied.
Convicts, Scotland, "hard labour," so called	173	57	602	3707	Food supplied.
Food supplied free, seamen, Royal Navy [1]	91	48	406	2585	Seamen and boys are also allowed 4d. a day to buy the extra food required.
Food supplied free, boys, Royal Navy [1]	107	69	406	2845	
British army minimum war ration (South Africa) [1]	138	105	528	3903	
Russian army war ration (Manchuria) [1]	187	27	775	4891	
Japanese army war ration (Manchuria) [1]	158	27	840	4343	
Members of two college football teams, United States of America	225	334	633	6812	Food eaten.

[1] Third Report, 1908, Committee on Physiological Effects of Food, Training, and Clothing on the Soldier.

men and animals do not eat too much, if they perform an adequate amount of work.

The increased consumption of food which is associated with muscular work generally involves an increase of protein, carbohydrate, and fat, as shown in the dietaries already given. There is need of more protein, even although it is agreed that the destruction of that substance in the body is not increased by muscular work: there is a retention of nitrogen during muscular work, and this nitrogen appears to be stored or built up in the body as protein. Bornstein [1] found that he retained in eighteen days an amount of nitrogen which would correspond to 800 grms. of muscle. Muscles develop during work, and thus the protein of the tissues is increased.

For the supply of energy during muscular work the carbohydrates and fats are increased. These foods stuffs can replace one another, for fat is formed from carbohydrate in the body, and there is evidence to show that fat may give rise to carbohydrate. The relative amounts of these articles of food selected by different men appear to depend upon individual tastes and the comparative cost. Fat is dearer than carbohydrate, but it is a concentrated food.

The energy values of the different foods are most conveniently expressed in terms of the heat which they yield on combustion. One gramme of dry protein or of carbohydrate yields 4·1 calories, and an equal weight of fat yields 9·3 calories. The protein does not undergo complete combustion in the body; for this reason the physiological value given above is less than the physical value as determined by the calorimeter. For the supply of the energy needed during the performance of muscular work the different food substances can be substituted according to their equivalent quantities; thus 100 grammes of fat, 211 grammes of protein, and 230 grammes of carbohydrate are physiologically isodynamic. The muscles obtain energy from each kind of food, but the carbohydrates and fats are the ones most readily used. The relative quantities will depend upon the diet; carbohydrates form a large proportion of the food consumed by most working men.

A man absorbs per kilogramme of his body weight and per hour about 0·29 grm. of oxygen and discharges about 0·33 grm. of carbon dioxide, when he is at rest; directly he performs work the respiratory exchange increases, thus a walk at the rate of about three miles an hour will raise the values four or five times. If

[1] See Cohnheim, *Ergebnisse der Physiol.*, Zweiter Jahrgang, Abtheilung 1, s. 621.

the work be of an unusual kind the exchange is much greater the first time that it is performed, but by practice it may be reduced to two-thirds of its original value. This economical working of the muscles is one of the most striking results of training. The well-trained body is far more efficient than the best engine.

Influence of Muscular Work upon the Glandular Systems

It is impossible to consider this subject fully within the limits fixed for this article, but attention may be directed to two important glands, the kidney and the sweat glands.

The sweat glands are thrown into activity by muscular work, and the evaporation of the sweat cools the body and removes waste products. Figures [1] have been given to show how large an amount of water and heat may be removed from the body in this way. During work the production of heat is raised four or five times, but the increased loss of heat due to the exposure of the blood in the dilated vessels of the skin is insufficient to prevent the temperature of the body from rising to a dangerous height. The cooling of the body in such a case is effected by the evaporation of sweat and moisture from the respiratory tract. A very striking instance of the limitations and dangers incurred by a failure to sweat has been recorded by Zuntz and Tendlau ([49]). The man upon whom they made observations had no sweat glands, and directly his temperature rose to 39° on exposure to the sun or as the result of moderate work he breathed double as much air as during rest. His skin was flushed with blood, but these efforts of compensation were insufficient to prevent his temperature rising. He found that he could continue to work in summer only by frequently soaking his shirt in water; with this wet covering on his body he was able to supply a substitute for sweat.

The great loss of moisture during sweating reduces the amount of water secreted by the kidneys, unless an adequate supply of water be taken by the mouth. The urine is concentrated, and on cooling throws down a deposit of urates. After vigorous exercise albumin is frequently found in the urine. This so-called "functional albuminuria" needs further investigation on account of its

[1] Page 247.

great medical importance. The majority of the best athletes examined have passed albumin in their urine after contests in sport, such as rowing, running, and football ([50]). Is this albuminuria to be considered pathological or physiological? It is probably the expression not of disease but of disturbance in the supply of blood and oxygen to the kidneys during strenuous work. This is probably the reason why most cases of albuminuria are found among the best crews and teams; the men with the best physique and the best training are capable of the greatest exertion. During rest the albuminuria disappears.

The subject demands attention, for there is no doubt that men have been rejected for life insurance on account of this albuminuria, and many have been treated as the subjects of serious disease of the kidneys. It is difficult to imagine how much worry and misery may have been caused by the failure to recognise that albuminuria is not necessarily a sign of renal disease.

Muscular Work as a Cause of Fatigue

Fatigue is a condition which it is very difficult to define or analyse. Excessive activity of any part of the body brings about a state of increasing inefficiency. The chief characteristic of fatigue is inefficiency, and a classification of fatigue might be based upon its apparent seat of origin. Fatigue due to muscular activity alone needs consideration in this article, but it must not be thought that the condition is one in which the muscles alone are involved; it is impossible to exclude other parts of the body, for muscular activity affects all parts; the body works as a whole.

Muscular work produces fatigue, and its onset depends upon the nature of the work, its duration, and the external conditions under which it is performed. An analysis of the sensations of this fatigue shows that there is a local fatigue, a muscular soreness and discomfort due to the excessive use of one group of muscles, and a general sense of fatigue which follows a more uniform activity of the muscular system. Local fatigue may quickly manifest itself when a special movement, to which the body is not accustomed, is performed. The muscles quickly tire and respond with weaker and less orderly contractions. The causes of this condition are not well known, but it would appear that lack of sufficient nutrition, including oxygen, is one of the most important; waste pro-

ducts such as lactic acid may be formed and may injuriously affect the activity of the muscle fibres or their nerve endings. It may be, as Hough ([51]) and Hill ([52]) have suggested, that the muscular soreness experienced during work and for some hours afterwards is due to the waste products of activity, such as lactic acid.

There is another kind of muscular soreness which is not experienced at all during the time of exercise, but is felt the next day as an uncomfortable or even painful stiffness which gradually disappears during movement, but may be noticeable for two or three days. This form of soreness Hough thinks may be due to ruptures within the muscle fibres. It is difficult to obtain evidence upon this point, and it would appear more reasonable to attribute it to similar causes to those given for the first kind of muscular soreness.

The onset of fatigue, both local and general, can be delayed or largely prevented by progressive training. This may be due to the fact that the body by practice performs work more economically and adjusts more readily the circulation of the blood to meet the general and local needs of nutrition. It may be that the body acquires an immunity to its waste products or increases its capacity for oxidising or otherwise rendering them inert. The "receptive substance" between the nerve and the muscle may be an important element in muscular fatigue.

Weichardt ([53]) maintains that there is a toxin which causes fatigue, that this toxic substance is not lactic acid, and that the living body produces an antagonistic substance, an antitoxin. The injection of blood, serum, or other fluids containing the toxin is said to produce in an animal all the signs of fatigue, unless it has been previously protected by a dose of the antitoxin. These observations need confirmation, but in support of the view other arguments have been advanced. The toxicity of the urine is increased by muscular exercise and the sweat secreted during hard work is toxic, whereas that poured out by a man at rest but exposed to a heated and moist atmosphere is free from harmful substances. It is well known that an untrained man experiences the day after hard and prolonged exercise a general feeling of lassitude and disorder; this has been attributed to an auto-intoxication or poisoning by the products of the unusual muscular activity.

Ryffel has found that even after moderate exercise lactic acid can be detected in the urine and sweat, but further observations

are necessary to show the relationship of this substance to muscular fatigue.

Undue stress is frequently laid upon the capacity of the heart to perform work. This is not peculiar to the heart, a similar condition is seen in the respiratory muscles. Their activity is rhythmic, work followed by rest; they have been progressively trained from birth and work efficiently and economically. By constant practice a corresponding capacity for work can be developed in the ordinary muscles of the body. When an unusual amount of work is thrown upon the heart and the respiratory muscles, signs of fatigue are observed in them similar to those shown by other muscles.

The absence of fatigue in nerves need not be discussed here, for in the living body the nerve is a part of the nerve cell, and the nerve cells are without doubt subject to fatigue. How largely the nervous system is involved in fatigue is shown by the fact that a much greater amount of work can be performed, without the immediate experience of fatigue, when the subject is spurred on by nervous excitement. The fatigue, however, in these cases is only postponed, and the reaction is greater. The nervous excitement inhibits the sensations of fatigue, and under such conditions the body can be readily overtaxed.

Nervous impressions may diminish the sensations of fatigue; soldiers at the end of a long march step out more briskly when the band strikes up a lively tune. The interaction between the nervous and muscular systems is of the closest nature. Good mental work cannot be done after a hard day's sport, and study for a serious examination is incompatible with training for a race.

Fatigue is a protective sensation, a warning that the body needs rest. There is nothing to be gained by resisting it by the use of drugs. Work performed under such conditions is extravagant, and the price is paid later in a greater reaction and depression. The decrease in the general sensibility produced by fatigue renders a man unmindful of discomforts which under ordinary conditions would be intolerable; he can sleep profoundly and thus restore his energy.

The rational method is to prevent as far as possible the conditions which are favourable to fatigue. Progressive training enables the body to work more economically, to adjust the supply of blood to the needs of the various parts, and to strengthen the

body uniformly, so that no extra strain is thrown upon it by the early failure of any part, especially of the heart and lungs. This method has stood the test of experience, and is the only one recognised by good trainers of athletes and horses.

BIBLIOGRAPHY

[1] *Ranvier*, Arch. de physiol. norm. et path., 1874.

[2] *Haycraft*, Journal of Physiology, vol. xxxi., 1904, p. 392.

[3] *Halliburton*, Journal of Physiology, vol. viii., 1887, p. 133. Biochemistry of Muscle and Nerve, 1904.

[4] *Von Fürth*, Ergebnisse der Physiol., 1902, i., Abt. 1, s. 110.

[5] *Mellanby*, Proc. Physiol. Soc., Journ. Physiol., 1908, vol. xxxvii., p. xxxiv.

[6] *Brodie* and *Richardson*, Phil. Trans. Roy. Soc., 1899, B, vol. cxci., p. 127. *Vernon*, Journ. of Physiol., 1899, vol. xxiv., p. 239.

[7] *Leathes*, Problems in Animal Metabolism, 1906, p. 99 ; Journ. Physiol., 1904, vol. xxxi., p. ii.

[8] *Fletcher* and *Hopkins*, Journ. Physiol., 1907, vol. xxxv., p. 247.

[9] *Mellanby*, Journ. Physiol., 1908, vol. xxxvi., p. 445.

[10] *Bunge*, Zeitschr. f. physiol. Chem., 1885, Bd. ix., s. 60.

[11] *Macallum*, Journ. Physiol., 1905, vol. xxxii., p. 95.

[12] *MacMunn*, Proc. Physiol. Soc., Journ. Physiol., vol. v., 1884, p. xxiv. Phil. Trans., 1886, p. 267. Zeitschr. f. physiol. Chem., 1888, Bd. 13, s. 497.

[13] *Mörner*, Jahresber. f. Thierchem., 1897, s. 456.

[14] *Jacoby*, Ergebnisse der Physiol., 1902, i., Abt. 1, s. 213.

[15] *Robinson*, Brit. Med. Journ., 1891, vol. ii., p. 1226 ; Nineteenth Century, 1891. *Buckman*, ibid., 1894. *Mumford*, Brain, 1897, vol. xx., p. 290.

[16] *Ahlfeld*, Festschrift für Ludwig, Marburg (1890), s. 1.

[17] *Arbuthnot Lane*, Guy's Hospital Reports, vol. xliii., 1886, p. 321 ; ibid., vol. xliv., 1887, p. 359.

[18] *M'Curdy*, Amer. Journ. Physiol., 1901, vol. v., p. 95.

[19] *Tait Mackenzie*, Journ. Anat. and Physiol., 1898, vol. xxxii., p. 468.

[20] *W. G. Smith*, Proc. Physiol. Soc., Journ. Physiol., 1900, vol. xxv. ; Mind, vol. xii., N.S., No. 45.

[21] *Horsley* and *Schäfer*, Journ. Physiol., 1886, vol. vii., p. 96.

[22] *Schäfer*, Journ. Physiol., vol. vii., 1886, p. 111. *Griffiths*, ibid., vol. ix., 1888, p. 39. *Haycraft*, ibid., vol. xi., 1890, p. 352. *Fraser Harris*, ibid., vol. xvii., 1894–1895, p. 315.

[23] *Warren Lombard*, Journ. Physiol., vol. xiii., 1892, p. 1 ; vol. xiv., 1893, p. 97.

[24] *Pembrey* and *Todd*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxvii., 1908.

[25] *Henderson*, Amer. Journ. Physiol., vol. xxi., 1908, p. 126.

[26] *Zuntz* and *Schumberg*, Physiologie des Marsches, Berlin, 1901.

[27] *M'Curdy*, Amer. Journ. Physiol., 1901, vol. v., p. 95.

[28] *Bowen*, Amer. Journ. Physiol., 1904, vol. xi., p. 59.

[29] *Pembrey* and *Todd*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxvii., 1908.

[30] *Gaskell*, Journ. Physiol., vol. i., pp. 108 and 262; Journ. Anat. and Physiol., vol. xi., 1877, p. 720.

[31] *Bayliss*, Ergebnisse der Physiol., v. Jahrgang, 1906, s. 331.

[32] *Schlesinger* and *Pembrey*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxvii., 1908.

[33] *Haldane* and *Priestley*, Journ. Physiol., vol. xxxii., 1905, p. 246.

[34] *FitzGerald* and *Haldane*, Journ. Physiol., vol. xxxii., 1905, p. 486.

[35] *Haldane* and *Priestley*, Journ. Physiol., vol. xxxii., 1905, p. 225.

[36] *Geppert* and *Zuntz*, Arch. f. d. ges. Physiol. Bonn, 1888, Bd. xlii., s. 189.

[37] *Loewy*, ibid., s. 281; and 1890, Bd. xlvii., s. 601.

[38] *Pflüger*, ibid., 1868, Bd. 1, s. 61.

[39] *Pembrey* and *Cook*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxvii., 1908. *Hill* and *Flack*, Journ. Physiol., vol. xxxvii., 1908, p. 108.

[40] *Schlesinger* and *Pembrey*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxvii., 1908.

[41] *Pembrey* and *Cook*, ibid., p. xli.

[42] *Pembrey* and *Cook*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxvii., 1908, Oct. 17.

[43] *Boycott* and *Haldane*, Proc. Physiol. Soc., Journ. Physiol., vol. xxxiii., 1905–1906.

[44] *Richet*, Compt. rend. Soc. de biol., Paris, 1887, p. 482.

[45] *Pembrey* and *Nicol*, Journ. Physiol., vol. xxiii., 1898, p. 386. *Pembrey*, *Arkle*, *Bolus*, and *Lecky*, Guy's Hospital Reports, vol. lvii., 1902, p. 283. In these papers the literature of the subject is considered. *Pembrey*, Brit. Med. Journ., vol. i., 1904, Feb. 27. *Hill* and *Flack*, Journ. Physiol., vol. xxxvi., 1907–1908, p. 11.

[46] *Haldane*, Journ. Hyg., 1905, vol. v., p. 494. *Rogers*, Journ. Royal Army Medical Corps, 1908, vol. x., p. 25. *Sutton*, Journ. Path. and Bact., 1908, vol. xiii., p. 62. *Pembrey*, Guy's Hospital Reports, 1902, vol. lvii., p. 261.

[47] *Pettenkofer* and *Voit*, Zeitsch. f. Biol., Bd. ii., 1866, s. 537. See Tigerstedt Die Physiologie des Stoffwechsels, Handbuch der Physiologie des Menschen, von Nagel, Bd. i., 1906, s. 441.

[48] *Chittenden*, Physiological Economy in Nutrition, London, 1905. The Nutrition of Man, London, 1907.

[49] *Zuntz* and *Schumberg*, Physiologie des Marsches, Berlin, 1901, s. 311.

[50] *Collier*, Brit. Med. Journ., 1907, vol. i., p. 4. *Dunhill*, ibid., p. 1031.

[51] *Hough*, Amer. Journ. Physiol., 1902, vol. vii., p. 76.

[52] *Hill* and *Flack*, Brit. Med. Journ., Aug. 22nd, 1908.

[53] *Weichardt*, Arch. f. Physiol., 1905, s. 219.

SOME CHAPTERS ON THE PHYSIOLOGY OF NERVE

By N. H. ALCOCK

I. Introduction. II. The Nerves in the Living Animal. III. Fatigue. IV. Regeneration. V. The Theory of the Nervous Impulse.

I. Introduction

The physiology of the peripheral nervous system has certain peculiarities which too often deter the would-be student from the study of the subject. The experimental facts are simple and easy to understand, and have been determined with great accuracy, yet the explanation is apt to be complex and lengthy to a degree unusual even in physiology, and the task of mastering the literature and understanding the various theories of what at first sight appears far removed from any practical application is one which is too often deferred indefinitely. It is a matter for regret that this should be so, for the study of living tissues cannot be separated into watertight compartments; no one subject can be neglected without hindrance to the rest. The processes underlying the injury current of nerve are governed by the same laws that determine the secretion of the salivary glands, of the cells of the stomach or of the kidney, and it is only because so much interest has been aroused about the obvious and tangible results of the activity of these tissues that the underlying causes have for the moment been lost sight of. As soon as one reflects as to the reason why a cell of the stomach sends HCl in one direction rather than another, one comes across problems that rest on the same physico-chemical basis as in the apparently simpler case of nerve.

For those who demand an immediate practical advantage from everything they read there is one comparatively minor consideration that may perhaps appeal. The charlatan and quack, ever with us, take advantage of the prevailing neglect of electro-

physiology; it is hardly necessary to quote the instances of electropathic battery belts, the claim that nerve contracts on excitation (1), and the "records" of the electrical response in metals (3), to show that folly of a kind that one moment's reflection should dissipate finds a ready acceptance with those who consider the experimental facts of animal electricity too dull for their enlightened minds.

There is, however, one quite genuine difficulty in the study of our present subject that makes it less interesting than it will be in the future. None of the theories are in any way complete, and we come across many facts which appear to conflict with the best arranged of these explanations. All that can be done in such a case is to record these facts in the hope that later on the proper place may be found for them; the simple and easy receipt for the manufacture of hypotheses by the inclusion of favourable instances and the exclusion of everything that contradicts the theory is one that does not lead to a result on which much reliance can be placed.

Preliminary Notes

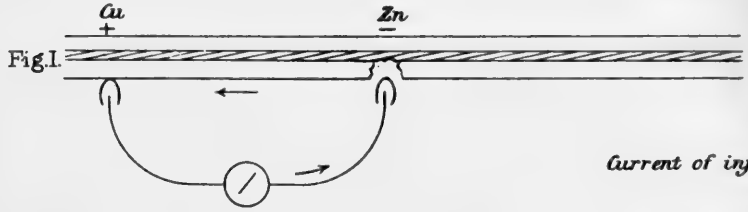
It is unnecessary to do more than briefly recapitulate the experimental facts that have been made out concerning excised medullated nerves that are still in a surviving condition, yet as they form the starting point of what follows it may not be out of place to give a short summary of the most important phenomena.

After the nerves have been excised from the body they are best kept in an approximately isotonic solution of NaCl, to which a small quantity of glucose may with advantage be added. When the effect of the excision has passed off, such nerves are isoelectric, that is, they give no current in the galvanometer, and they have apparently (except in certain known particulars) resumed the condition they were in before they were removed from the body.

Three main varieties of electrical phenomena directly connected with function can be observed in such nerves—(1) Current of injury; (2) current of action or negative variation; (3) electrotonic currents; giving to each the usual name. Excellent reasons can be given for the disuse of each of these terms, but as their significance is perfectly clear, it seems better for our present purpose to use words with which the student is already familiar

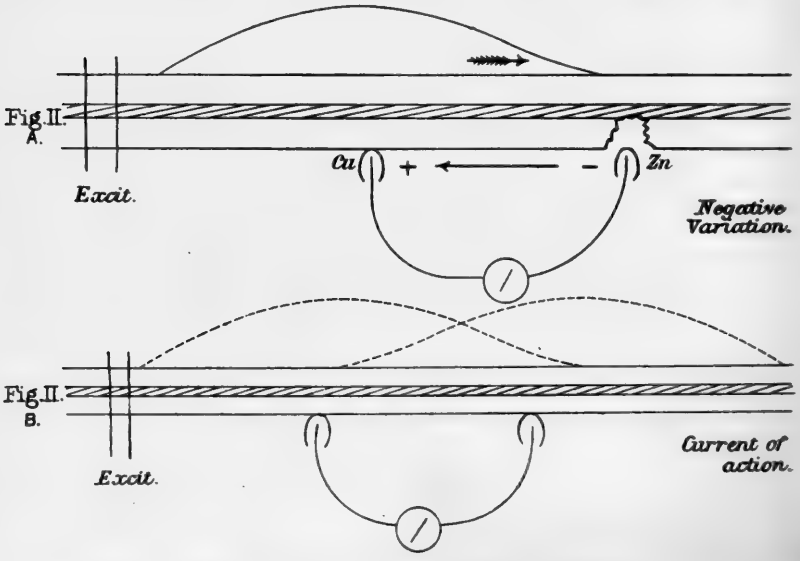
rather than introduce confusion by the employment of theoretically more perfect but unknown expressions.

The explanation of these terms is simple. If in an isoelectric nerve an injury be made at any point, that spot becomes electrically



negative (zincative [1]) to the uninjured part, and this difference of potential gives rise to the current of injury (Fig. 1).

If such an injured nerve be excited, the uninjured part also becomes electrically negative (zincative), and as this gives rise to



an opposing current to the current of injury, the latter appears to be diminished, and therefore the result is to produce a diminution or "negative variation" of the injury current (Fig. 2A).

If an uninjured nerve be excited, the normal effect is that a wave of zincativity passes down the nerve, each point becoming

[1] Like the zinc of a Daniell cell.

successively electrically negative (zincative) to the rest. This has been termed the current of action, and the negative variation is evidently only a particular case of this, namely, when the response from one spot is altered by the presence of an injury there (4), neglecting for the present certain possibilities to be considered later.

These remarks can therefore be summarised thus :—

(1) Any injured spot is electrically negative (zincative) to any uninjured.

(2) Any active spot is as a rule electrically negative (zincative) to any inactive spot.

Injury and excitation give, therefore, as a rule, an electrical response of the same sign. Whether this is the result of the same process or not is a matter that is not quite as simple as at first

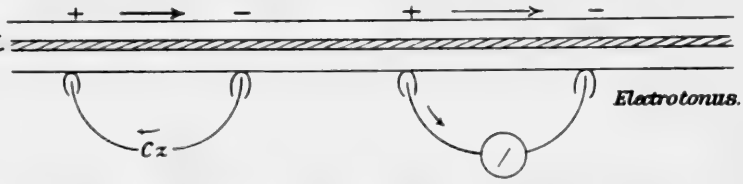


Fig. III.

sight might be supposed, though there is undoubtedly a close connection between the two responses.

There is still another phenomenon to be noted in excised medullated nerve. If a constant current be passed through one part of the nerve, the extra-polar parts of the same nerve also give a current, the electronic current (Fig. 3).

These various electric effects have been subjected to elaborate investigation and experiment, because they are the only direct unequivocal signs of nerve activity. The actual metabolism of nerve is at best very slight in amount. It is true that deprivation of oxygen for some hours paralyses a nerve (5, 6, 7), that the result of excitation gives an effect similar to that of CO_2 (8), and that experiments to be noted later give some indication of fatigue, but there is no detectable change in the reaction of nerves as a result of activity (unless certain experiments referred to later are to be interpreted in this sense), and there is no other effect such as that of heat produced or of mechanical shortening [1] that shows

[1] If a nerve is excited at one end by maximal induction shocks, and the other end examined with suitable precautions under a microscope magnifying 200 diameters, no shortening or movement of any kind can be detected. But Waller

whether a nervous impulse is passing or not, so that the electrical signs of nerve activity have assumed a greater importance than is the case in the physiology of other organs of the body. Further, these effects, occurring in such a highly specialised structure as nerve, have seemed a suitable object for the attempted explanation of many problems of general physiology. It becomes then a matter of great interest to see how far these electrical effects observed on excised nerve represent the events occurring in nerve still in the body, especially as evidence has been brought forward to show that it may be possible, under exceptional circumstances, to have a nervous impulse without the corresponding electrical change (4).

II. Nerves in the Living Animal

The first of the modern instances we shall quote is from the work of Gotch and Horsley (9). In this there is one series of experiments that bear on this question. In the cat and the monkey both the sciatic nerves and the cut end of the spinal cord gave unmistakable evidence of a negative variation which accompanied the excitation due to the reflex discharges from the nervous centres when these were excited by absinthe or (more markedly) by strychnine. Negative variations produced in this manner corresponded exactly with those produced by the electrical excitation of the cortex and other parts, and except in so far as the nerve impulse might be altered centrally by the drug (Sherrington 10), these variations represent the results of the normal excitation of the nerve fibre by the nerve cells.

Bernstein (11) in 1898 observed a similar phenomenon. If a pithed frog be lightly strychninised, the muscles of the hind legs fall into tetanus whenever any stimulus reaches the spinal cord. These tetanic contractions are more or less synchronous, and if by a modification of Bernstein's method one of the legs of the frog be connected with a myograph, and the sciatic nerve of the other be placed on electrodes, and connected with a galvanometer or electrometer, it can be easily seen that when there is a contraction of the muscles there is a negative variation in the sciatic

has shown that if strong induction shocks are passed lengthwise through a nerve (or any other moist conductor), that the heating effect of the current produces either lengthening or shortening, according as evaporation or rise of temperature predominate.

nerve. The reflex contraction can be called out by stimulating an afferent nerve by the induced current, or even by the impulses reaching the cord as a result of touching or pinching the animal. The E.M.F. of the negative variation is about ·00025 volt, as determined by the capillary electrometer (12).

It is possible to take a step further and examine the negative variation in nerves which are conducting the impulses which naturally traverse them without the complication of any disturbing agency. Two nerves have been employed for experiments of this kind, the phrenic and the vagus. Both these conduct impulses which are repeated at each act of respiration, and so it is possible to arrange the rather elaborate apparatus required with some degree of certainty of obtaining the phenomenon often enough to be readily investigated. Reid and Macdonald (13) examined the phrenic; Lewandowsky (14), Alcock and Seemann (12), and Einthoven (15) the vagus. The latter is by far the easier object to study, and allowing for the increasing delicacy of the instruments employed, the results agree very closely as far as the nervous phenomena are concerned.

Lewandowsky, using the ordinary galvanometer, found that one negative variation occurred every time the lungs were artificially blown out. Alcock and Seemann, with the capillary electrometer, observed the same phenomenon. They found in addition that a negative variation occurred at each natural inspiration, and that an effect was also observed when the air was sucked out of the lungs. Einthoven, using his string galvanometer, by far the most sensitive instrument yet invented,[1] was able to add certain very interesting details which are worthy of careful consideration.

Einthoven's results will be understood from an examination of Fig. 4. The upper line is the shadow of the "string" (a fibre

[1] This galvanometer consists of a fibre of silvered quartz, about 2·5μ in diameter, suspended in a powerful magnetic field (20,000 C.G.S. units). The fibre is illuminated by the light of the electric arc, and the shadow of the fibre, magnified 600 diameters, is thrown on a photographic plate. The instrument is thus a "moving coil" galvanometer, with the coil reduced to its simplest expression. When a current of electricity passes down the fibre, it is deflected, and 10^{-8} amperes give a measurable deflection.

The instrument therefore measures *current* not *voltage*; but if the resistance of the circuit is known, the voltage can be determined very simply by Ohm's law. In nearly all electro-physiological problems it is the E.M.F. that is of interest, as the resistance and consequently the current is varied by circumstances not bearing on the experiment.

of quartz silvered on the surface), moving up and down according to the current traversing it; the second line indicates the respiration, inspiration marking upwards. A slow wave of negative variation occurs at each inspiration (indicating that an impulse passes up the nerve at this time), a conclusion arrived at on quite other grounds by those who have observed the phenomenon of respiration.

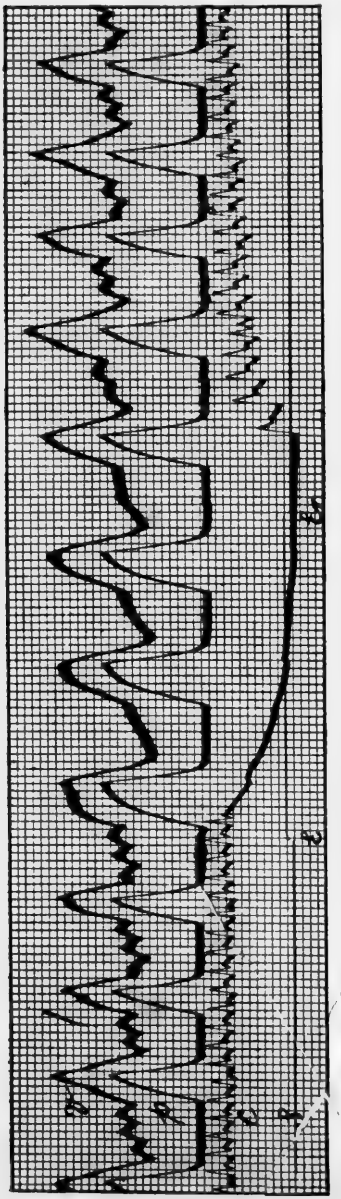


FIG. 4 (after Eintlioven).—The upper line *v* is the shadow of the string, the second line *p* the entrance and exit of air to the lungs, inspiration marking upwards, the third line *c* is a sphygmogram from the crural artery, the lowest line *s* is a signal. Between **e** and e_1 the peripheral end of the *other* vagus was excited.

There are many things of interest to be observed in studying this photograph. In the first place, the curve is a double one; superposed on the long respiratory waves are shorter ones, the result of the contractions of the heart. Secondly, to any one used to the study of the negative variations recorded by the capillary electrometer two differences are most striking—the E.M.F. of the current and the time taken by the wave. In Gotch's [16] analysis of the electrometer curve the E.M.F. of the negative variation in the sciatic of the frog is ·03 volt and the time ·01 sec.; here the E.M.F. of the respiratory curve is ·00005 volt and the duration 5 secs. The question immediately presents itself—Are these phenomena, which alike have been called "negative variation," in reality the same?

One possibility may be dismissed from the mind. As far as our present knowledge goes, these curves are not current escape or any error of the apparatus. They are abolished by ligature of the nerve, by touching the nerve with ammonia, and by "electrocution." If the peripheral end of the other vagus is stimulated, the cardiac waves disappear, as the heart is stopped, while the respiratory waves continue, as can be seen in Fig. 4. In apnœa, the cardiac continue and the others cease.

Both the E.M.F. and the time relations of these curves agree with the older observations with the electrometer. Alcock and Seeman (*loc. cit.*) give the E.M.F. of the respiratory response as ·00005 to ·0002 volts, and the time as about 4 secs.; the maximum on prolonged inflation of the lungs as ·00025 volt.

What, then, is the explanation? The differences in potential may be due (and to some extent are certainly due) to the fact that only a few of the fibres of the nerve are in action at any one time, but how is the difference in time to be accounted for? There are several possibilities. These long waves of small E.M.F. might be the algebraic sum of many short waves; and if we had the electrometer records alone to go by, these might be too slow to indicate the successive teeth of such a curve. But there is no trace of such a summation in the string galvanometer photograph, although the instrument is sensitive and quick enough to detect ·000005 volt lasting for the $\frac{1}{100}$ of a second. Further, this instrument is free from the peculiarity of the electrometer that shows the effect of equal alternate currents of short duration as a displacement of the meniscus in the direction of the sulphuric acid. The exact relation of these two phenomenon which we have called by the name of negative variation is therefore one of the problems still awaiting solution, and we have only the suggestion by Einthoven that possibly his curves are more nearly related to the electronic currents than to the short steep curves the result of single induction shocks, that Gotch has analysed in the sciatic of the frog.

Einthoven finally gives a very interesting photograph showing the variations in potential in the *uninjured* vagus as a result of the various nerve impulses passing both up and down the nerve. The exact analysis of the course is, however, so complex that we must await the result of future work before we understand the full meaning of the photograph.

III. Fatigue

The apparent absence of fatigue in nerve, which is one of the earliest phenomenon that the observer meets with and the student hears discussed, is philosophically considered a very curious property of these structures, and has both a greater importance and a closer connection with what has gone before than might at first sight be supposed. The fundamental experiments are known to every one. Medullated ([17, 18, 19]) and non-medullated ([20]) nerves can be stimulated for hours, the impulse being blocked (by cold, ether vapour, the constant current and so forth), and when the block is removed the end organ responds to an amount apparently identical with that with which the observation began. As far as this class of experiment goes, no fatigue can be detected, and even in isolated nerve, completely removed from any possibility of the natural circulation being maintained, Waller ([8]) has shown that fatigue is not found.

Various explanations could be found of this result. The most obvious, that as no fatigue can be detected there is in reality none, would be, if true, a most remarkable phenomenon. It would mean that a nervous impulse was conducted along a living structure, that connected with this was an electrical change of a measurable amount, and yet that no energy was made use of in the process, a phenomenon unlike any other occurring in the body.

The next explanation, and the one that seems the most probable, is that although there is a certain amount of fatigue, and a certain expenditure of energy, that the loss is very quickly made good, and the process of repair is so rapid [1] that even between induction shocks following one another at 500 per second (and none of the induction coils used for the first class of experiment ran at anything like this rate) there is time for the nerve to recover its initial state.

There arose at one time a curious little controversy of which a short account may not be out of place. Waller ([8]) made the suggestion that the rapid repair just referred to might be due to the medullary sheath acting as the storehouse of reserve material,

[1] Other examples of very rapid repair of tissues that admittedly show fatigue could be quoted. For example, the wing muscles of insects contract about 300 times per second, and continue in action for hours at a time, yet no one imagines that they are incapable of fatigue on this account.

and therefore that non-medullated nerve not possessing this store should prove much more easily fatiguable. Miss Sowton ([21]), using the olfactory nerve of the pike, stated that this was the case; but she omitted to exclude the possibility of the so-called "stimulation fatigue," that is, the local injury at the spot where the exciting electrodes rested. Garten ([22]), in his classic researches on the same object (of which only very brief and incidental mention can be made here), excluded this possibility, and found that true fatigue of the conducted negative variation actually occurred, recovery taking place after a suitable interval, even in excised nerve.

The objection might be made that the olfactory nerve of the pike is not comparable to mammalian nerve, and certainly in the latter "stimulation fatigue" is more easily observable than that of the propagated change ([23]), but it is probable that the difference that exists is one of degree rather than of kind. It would be interesting to try the experiments quoted in the next section on non-medullated mammalian nerve; the probability is that fatigue would be demonstrated even more readily than in the medullated variety. It is not unlikely, therefore, from these and other reasons to be presently referred to, that the structures known as sheath (including under this heading medullary sheath and neurilemma) act as stores of food material, and this does not exclude the idea of Boruttau, that the perifibrillar substance may also function in this capacity.

There is, however, a more indirect way of approaching the question that has led to very interesting results. If there is any expenditure of energy in transmitting a nerve impulse, a second impulse rapidly following the first should show some alteration. This is found to be the case.

Gotch and Burch ([16]) examined the electrical response in the sciatic of the frog, when this was excited by induction shocks. If these succeeded each other at longer interval than $\frac{1}{300}$ of a second (taking round numbers), two negative variations were observed; if the interval were less than this, only the response due to the initial stimulus appeared, and the time short enough to abolish the second response was termed by these authors the "critical interval." They found that this varied with the intensity of the exciting stimulus and with the temperature of the nerve, becoming longer as the temperature grew less. Stated differently, this "critical interval" is the "refractory period" of the nerve.

Fröhlich made a further advance, though before his results can be considered in this light it is necessary to make a very important assumption, viz. that the effect of anæsthetics (ether, chloroform, &c.) is the same as that of cold, and that the lengthening of the "critical interval" or "refractory period" due to all these agents is merely a slowing down of the processes occurring in a normal nerve in the body.

If this is granted, Fröhlich's experiments formed a very interesting example of fatigue. He took a nerve which was in a definite state of anæsthesia, and stimulated this with induction shocks which followed each other at an interval known to be a little longer than the "critical interval." The attached muscle served as the indicator. When the nerve was excited the muscle at first fell into tetanus. This is only what might be expected; the successive stimuli each gave rise to a separate impulse, and these fused at the muscle. But as the excitation continued, the tetanus very rapidly fell off, and the muscle ceased to contract, and Fröhlich's explanation is that the successive impulses fatigued the nerve, so that the refractory period became longer, the rate of stimulation was now less than the critical interval, each excitation blocked the next, and so no impulse was propagated to the muscle. Tait and Gunn ([24]) have extended these observations, using Yohimbin lactate as the anæsthetic. They find that this substance has in some respects the same action as other anæsthetics, and they are able to confirm Fröhlich's results and add some interesting details. There is little doubt, therefore, that under the action of reagents of this class nerve shows fatigue (and in all probability Waller's ([25], [26]) experiments with proto-veratrine and aconitine come under this heading), and if the preliminary assumption be accepted, it could be deduced from these observations that nerve fibres even in the body are fatiguable,[1] and only do not show this property under ordinary conditions because the processes of repair are so rapidly carried out ([27]).

IV. Regeneration of Nerve Fibres

The effects of section of a nerve are known to every student, and there is a general agreement amongst those who have experimented on the subject as to the nature of the process. This may

[1] For a different method that also leads to this conclusion, see Thörner ([28]).

be briefly summarised as consisting of the degeneration of that part of the nerve fibre which has been cut off from the appropriate nerve cell. Whether the "neurone theory" is anatomically exact or no, as far as this particular physiological problem is concerned, the degeneration exactly follows the law.

There is no such unanimity as to the events occurring subsequently. Under certain circumstances, to be considered shortly, the degenerated part of the nerve fibre is regenerated, and the particular point on which controversy has arisen is the source of the new nerve fibres.

There are three possible ways in which such fibres might arise.

I. They could grow downwards from the central end of the divided nerve, as Waller originally described in 1850.

II. They could be formed *in situ* from the cells in the peripheral portion, and then grow up towards the spinal cord.

III. They could wander in from the central end of other cut fibres, to which they originally did not belong.

Each of these possibilities must now be considered.

I. While this source of the new nerve fibres is regarded by most observers as at least the usual one, it must be remembered that there are certain conditions which must be fulfilled before regeneration can take place in this manner.

(*a*) The peripheral and central ends of the divided nerve must be brought into some sort of connection. This is usually done by apposition and suture of the two cut ends; but where there has been loss of nerve substance, and a gap is left, this can be filled by another nerve from the same individual, which is naturally the best method, or failing this, by the interposition of some other tissue. This can be either plain catgut, or a nerve from another animal, the results are about equally good in both cases (Kilvington [28]), and Marinesco ([33]) has shown that an alien nerve is absorbed as a foreign body and presents no advantages over catgut.

(*b*) The negative side of the condition is interesting. If the cut end of the peripheral part be enclosed in a rubber cap or stitched to some part of the body where nerve fibres are scarce, such as the peritoneum ([34]), no regeneration occurs at all. This is one of the arguments against the growth of the new fibres from the peripheral end, as we shall see presently.

(*c*) The portion of the spinal cord from which the nerves

originated must be intact, for if this is excised no regeneration follows (Lugaro [36]).

(*d*) In the case of the posterior nerve roots no regeneration takes place after the nerves have entered the spinal cord, and this corresponds with the anatomical fact that here the nerves lose their neurilemma. The inference is that the presence of this structure is therefore necessary in some way for the growth of new fibres.

(*e*) There must be a fresh section of both ends of the nerve, for if a cut end is sutured to an uninjured longitudinal surface, no regeneration takes place (Kilvington [28]).

If these various conditions are fulfilled, the evidence that downgrowth takes place from the central end is very good.

Ramon y Cajal and Marinesco ([33]) figure the new fibres growing downwards; these are at first seen only in the neighbourhood of the suture, and gradually grow towards the periphery. The fibres are often quaintly twisted, and the bulbous end shows curious shapes which are probably the result of amœboid movements. The new fibre seems to seek the old path by some force of chemiotactic attraction ([35]). The medullary sheath is formed first at the central end, later at the periphery, so that the former is the oldest part of the new fibre. If a second cut is made, either central to the line of suture (Langley and Anderson [35]) or peripheral to this (Halliburton), degeneration again takes place, but only in the peripheral part of the new fibres.

Finally, the embryological evidence is in favour of the central origin of the fibres, though it must be remembered that this evidence is only available by making use of the assumption that the regeneration is carried out by the same process as began the growth in the embryo. Ross Harrison ([39, 40]) has verified on various species of Rana, the original observations of His, that all the parts of the nerve fibre grow outwards from the cells of the epiblast that form the neural ridge, and that this is true not only for the axis cylinder, but also for the medullary sheath and neurilemma, in this latter particular controverting Bethe's statements, referred to in the next section. Harrison actually observed under the microscope in parts of embryos kept alive the outgrowth of new fibres from the neural crest. Each fibre had a swelling at the free end like that of a regenerating nerve, and this swelling showed amœboid movements.

There was no growth of any structure such as neurilemma from any other part of the embryonic tissue, though the conditions were sufficiently good to permit of the development of striated muscle from mesoblastic cells. Harrison further localised the cells that gave rise to the anterior and posterior nerve roots; if the back of the neural crest were cut away the latter did not develop; if His's cells were excised the anterior nerve roots did not appear.

II. Regeneration from the peripheral end.

The evidence for this view would be much more satisfactory if the third possibility to which we have referred did not exist. Briefly, there are three points to be considered :—

(*a*) The growth of new fibres when the central end of the cut nerve is no longer a possible source.

(*b*) The rapid return of sensation after section.

(*c*) Embryological and histological evidence.

(*b*) Kennedy [43] and others look on the rapid return of sensation (in a few days in some cases) as evidence of peripheral regeneration. But Head [44, 45, 46] has shown that the measurement of returning sensation is by no means as simple as was at one time supposed, and when the various explanations in any given case have been disentangled there is very little left on which to found a theory of autogenetic regeneration. Head's experiment on himself gave no support to this view, and here it was possible to make more precise observations than had hitherto been the case.

(*c*) Bethe's [47] embryological researches led him to the conclusion that before the appearance of any trace of peripheral nerve fibres a band of spindle-shaped cells can be seen in the place where the nerve is to be found. These cells were supposed to combine to make a syncytium, producing by differentiation of their protoplasm the neuro-fibrils of the nerve fibres. Braus [48], as a result of his very ingenious transplantation experiments on tadpoles, came to a somewhat similar conclusion; but as both these authors are directly opposed to Ross Harrison in their explanation of their observations, it is only possible to say that the experiments of the latter seem, with our present knowledge, the more worthy of credence.

Mott and Haliburton [34], and later Graham Kerr [49], have shown, however, that in the process of degeneration certain changes take place in the peripheral end of the nerve that simulate the

growth of new fibres. The cells of the neurilemma multiply actively. They first act as phagocytes in removing the debris of the degenerated nerve, and then elongating, form themselves into long chains of cells; but if no nerve fibres enter these chains, they never, as far as can be seen, form either medullary sheath or axis cylinder. So that although these neurilemmal cells doubtless have important nutritive and other functions (we have already referred to the suggestion that the failure of regeneration in the spinal cord is due to the absence of the neurilemma), yet by themselves these neurilemmal cells do not form new nerve fibres.

III. The third possibility, that regeneration may occur from new fibres which wander into the cut peripheral end from an alien central end, is one that gives rise to many interesting questions.

It has been known for a long time that intentional suture of nerves originally distinct leads to regeneration, but even when actual suture is not performed, growth may take place if there are any cut nerves in the vicinity, and it is occurrences of this description that invalidate much of the evidence for autogenous growth, as has been explained in the previous section.

There would appear to be degrees in the chemiotactic attraction which determines the direction of the fibres; efferent somatic fibres unite most readily with their own kind, less readily with pre-ganglionic fibres, and apparently not at all with post-ganglionic fibres ([35]). Of the various possibilities of union thus summarised there is one which has attracted special attention, as it has an immediate bearing on surgical procedure. This is the particular case in which different efferent somatic fibres are made to unite with each other. Ballance ([50]) was the first to make a practical application of the fact, although he did so under the impression that regeneration would occur from the peripheral end. He sutured part of the spinal accessory nerve to the peripheral end of the facial, and in his most successful case the patient recovered the use of the paralysed facial muscles, but with the drawback that there was a synchronous lifting of the shoulder.

Kilvington ([28]) has studied the experimental conditions under which union of this class takes place, and two of the many interesting facts he observed may be noted.

The optimum arrangement, as judged by the functional recovery of movement, is shown in Fig. 5. Here the internal and external popliteal nerves are cut across, the central end of the external

popliteal turned up out of the way, and the central end of the internal popliteal slit up lengthwise for a short distance. The peripheral ends of both nerves are then sutured to the two parts of the central internal popliteal.

It is found that regeneration takes place, and after the appropriate interval the dog has the use of his hind limb with little or no apparent defect, and such delicate co-ordinated movements as the scratch reflex are performed to all appearance as well as in the normal animal. Kilvington infers that the fibres from the internal popliteal have grown downwards into both

FIG. 5.—Optimum arrangement for restoration of function. *I.P.* Internal and *E.P.* External Popliteal nerve.

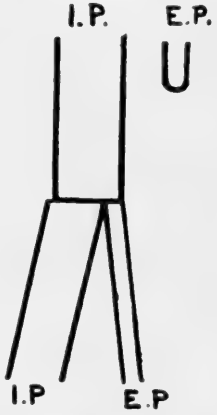


FIG. 6.—Arrangement giving "axon reflex."

internal popliteal and external popliteal. If this inference is a just one, it follows that the muscles formerly supplied by the external popliteal (and from the corresponding cells in the anterior horn of the spinal cord) are now supplied from cells that formerly supplied the internal popliteal, and through the nerve trunk the antagonistic muscles. As the co-ordination seems as good as before, the cells that have been changed over must have learned a new lesson, and this apparently applies, not only to the cells in the spinal cord, but also, as Kennedy ([43]) has shown, to the cells in the Rolandic cortex.

The earlier experiments of Langley and Anderson and Kilvington, and the later of Kilvington and Osborne, provide another fact. If the connections at the time of suture were arranged as

in Fig. 6, that is, if the central end of the internal popliteal was simultaneously sutured to both external and internal popliteal together, then when regeneration has occurred three points are noted. (Langley and Anderson observed a similar phenomenon when the central end of the crural nerve is sutured to the internal saphenous and also connects with its own muscular branch.)

(1) Co-ordination is nearly as good as in the normal animal.

(2) There are more new fibres in the two branches than in the central trunk.

(3) Excitation of, *e.g.*, the peripheral end of the regenerated external popliteal, gives a contraction of the muscles supplied by the internal popliteal; even when all connection with the spinal cord is removed by section some distance above the line of suture. This contraction is termed the axon reflex, following Langley's terminology.

Some of the new fibres in the trunk must therefore have a double peripheral ending in the branches. The inference is that either the peripheral fibres have joined together, which is a process unknown elsewhere, or else that one central fibre has branched into two at the line of suture. The latter explanation is by far the most probable. The inference is that in this case antagonistic muscles must be to some extent at least innervated from the same anterior nerve cells. It is surprising, not that co-ordination fails in the finer details, but that it exists at all under these conditions.

V. Theories of Nerve Activity

It is not possible to review, in the compass of a work of this kind, one-tenth of the literature that exists on this subject. All that can be done is to select such portions as seem worthy of consideration, not so much for their intrinsic worth as for the indication they give as to the direction in which further researches will advance.

From the physico-chemical standpoint all the phenomena of the electric currents in nerve (and in all tissues) must be due, as far as our present knowledge goes, to the movement of ions carrying charges of electricity. Current of injury, negative variation and electrotonic currents, must all ultimately have this explanation; and as no other hypothesis seems at present at all probable,

the work of the electro-physiologist has received an entirely new direction, namely, that of endeavouring to see how the laws of solutions and electrolytes can be applied to living tissues. The problem is by no means a simple one. The nature and composition of the ions has to be determined. They might be either inorganic electrolytes such as KCl, or more complex bodies such as occur in the products of digestion. They might be present in the tissues as such, or be formed by chemical action and then appear, and their distribution may be controlled by semi-permeable membranes, or by surfaces of separation which would act in a similar manner.

Before considering the modern theories of nerve action it will be convenient to note briefly the result of the micro-chemical work of Macallum ([51, 53, 54]) which has greatly influenced the theoretical view of the subject in this country.

Of these papers, two deal with the subjects with which we are now concerned, namely, the determination of (1) potassium and (2) chlorides in cells and nerve fibres.

(1) To determine the potassium ([51]) fresh nerve fibres are placed in a solution of cobalt sodium hexanitrite ($Co_2Na_3(No_2)_6$); where potassium is present, a precipitate is formed. According to Gilbert ([52]) its formula is $(Co(No_2)_2\ 3(K/Na)No_2\ nH_2O)$. The excess of the reagent is washed away with ice-cold water, and the precipitate blackened with ammonium sulphide. Macallum found a precipitate in the medullary sheath where the neuro-keratine network is supposed to exist, in Lanterman's imbrications, at the nodes of Ranvier, but not in the axis cylinder. Even at the nodes of Ranvier, where the precipitate surrounds this structure, the axis cylinder itself is free.

(2) The distribution of the chlorides ([53, 54]) was investigated by the addition to the tissues of $\frac{1}{10}$ normal $AgNo_3$ solution containing 1·5 per cent. HNo_3. The result is briefly the reverse picture of the potassium. Chlorides are absent from the medullary sheath. They are present all along the axis cylinder whenever the reagent can penetrate, either at a node of Ranvier or an injured spot. Lantermann's imbrications are an exception; K and Cl are both found there.

Taken as they stand, Macallum's researches would show that in what is presumably the active part of the nerve, namely, the axis cylinder, chlorides were present in greater amount than in either the lymph outside or in the medullary sheath, while potassium was

present in the latter but not in the axis cylinder. Macdonald has given a different explanation of these results, but it is not improbable that the original view is the more correct.

We are now in a position to consider the bearing of these observations on the theory of the nervous impulse. All the modern workers agree in supposing that the dissolved electrolytes are the cause of the electric currents, but as to the details of the process each experimenter has a different view, and the more the details are considered the less probable any given theory appears, so that a very brief account here will be sufficient.

In general, it is possible that the currents can be caused by any one of three different processes.

I. Chemical cells, of which the familiar type is the Leclanché.

II. Concentration cells, where the current is caused by the diffusion of ions with different velocities from a place of high concentration to one of lower.

III. Fluid cells, where the current is caused by the interchange of the ions of two fluids separated by a membrane.

I. The chemical-cell theories present more difficulties in the case of nerve than the other two, and in spite of the distinguished men who have been advocates on this side the general opinion is now rather adverse to this view. It is quite unlikely that there are no chemical changes in nerve. But the small amount of nerve metabolism, the difficulty of showing any change in this metabolism as a result of activity, and the apparent absence of any heat produced, are all observations which tell against the probability that chemical activity is directly concerned with the nervous impulse.

One series of observations, however, can be taken as supporting the chemical view, namely, those on the temperature coefficient. It has been observed that the rate of change of a physical process is less altered by variations in temperature than that of a chemical one—in other words, that the temperature coefficient given by the equation $\frac{\text{velocity at } (T^{\circ}+10)}{\text{velocity at } T^{c}}$, is usually less than 1·2 in the former case, more than this in the latter.

Maxwell (55) has for this reason carefully measured the velocity of the nervous impulse at different temperatures. He took the pedal nerve of the giant slug (Ariolimax Columbianus) as the object, and although the observations are not easy even in this

comparatively favourable object, it is probable that Maxwell's mean value of 1·78 is sufficiently near the truth, and Keith Lucas [56] as a result of observations by a different method on the frog gives a mean value of 1·79.

This is definitely higher than the usual physical value of 1·2, and might be taken as indicating a chemical basis of nerve conduction if one could be certain (which is very far from being the case) that a tissue which contains loose combinations of electrolytes with proteins would not have a similar coefficient. At any rate Keith Lucas shows that the value 1·78 to 2·01 is very nearly the same for conduction in both nerve and muscle, and markedly different from that of 3·26 to 3·6 for the refractory period in both tissues [57, 58], so that the underlying processes are probably different in the two cases.

Maxwell makes the suggestion that if nervous impulse is a chemical process it is probably not a direct oxidation, as if it were the coefficient would be higher. This would agree with the absence of heat produced. But we can hardly pursue the subject further in the present state of our knowledge, though it presents interesting problems that further work may solve.

II. *Concentration Cells.*—Macdonald [59] has adopted this theory of the causation of the nervous phenomena, and as he has based his views on a long series of ingenious experiments, they merit at least a careful examination, even if his conclusions are not accepted in every detail. Adopting the same plan as before, and separating experimental facts from the inferences therefrom, Macdonald's work may be summarised as follows :—

(1) The specific resistance of nerve (sciatic of cat) is 180 ohms, approximately equal to ·3 per cent. NaCl.

(2) When a nerve is placed for a short time in a dilute solution of electrolytes, the injury current is increased ; in a strong solution it is diminished. In the particular case of chlorides this alteration follows the " concentration law," namely—

$$E_\omega = E_a \times \log \frac{1}{n}$$

where E_ω = the final E.M.F. after immersion.
E_a = the initial E.M.F. before immersion.
n = the concentration of the solution in gram-molecules per litre multiplied by the dissociation coefficient.

(3) The inference is drawn from these and other considera-

tions that a nerve fibre has a structure consisting of a "core" containing a concentrated solution of electrolytes, a semi-permeable membrane outside this, and outside the membrane a "sheath" containing dilute electrolytes.

(4) From the concentration law $E_\omega = E_a \times \log \frac{1}{n}$ a calculation can be made of the concentration of electrolytes in the core. For when $n = 1$, then as $\log 1 = 0$, $E_\omega = 0$, therefore a solution of $\frac{m}{1}$ (dissociated) MCl would cause the injury current to vanish, and would presumably be equal in E.M.F. to the solution of the electrolytes in the axis cylinder. If these consist of KCl, this concentration is nearly 10 per cent.

(5) The conductivity of this solution in the axis cylinder can also be calculated, if this conductivity of the whole nerve is known, if the relative amounts of axis cylinder, sheath, and connection tissue are estimated, and if the conductivity of the sheath be supposed to be the same as that of the solution in which the nerve is placed for a short time. Macdonald gives the value from these data as equal to 2·5 per cent. KCl very approximately.[1]

(6) Under the microscope the axis cylinder of a living tissue is clear and transparent.[2] At the injured end granules are seen, and these stain with neutral red. These red-stained granules gradually appear further and further down the nerve, and the rate of appearance varies as the concentration of the fluid bathing the fibres, being $\cdot 17 \times 10^{-5}$ cm. per second for $\frac{m}{10}$ NaCl, $\cdot 30 \times 10^{-5}$ for $\frac{m}{20}$ NaCl. Macdonald infers that this process gives a graphic representation of the diffusion of the ions causing the injury current. Toluidine blue gives a rather different appearance which may represent the action current.

(7) Macdonald agrees with Macallum in his picture of the distribution of chlorides in the axis cylinder, but disagrees as to the distribution of potassium. He declares that while potassium

[1] Some unpublished experiments indicate that this value may require revision. The strength of solution in which the sciatic nerves of the cat remain unaltered in weight is 1·16 per cent. NaCl (60).

[2] All authors agree with this. If the fibre is fixed different appearances are seen; that usually accepted as the best shows longitudinal fibrils in a clear or granular matrix. Ashworth (61), examining the giant nerve cells and fibres of Halla parthenopeia, where these appearances are very distinct, finds quite definite fibrils, arising from the nerve cell and continued into the nerve fibre. If the nerves in the animal resemble those in the frog, this observation supports the usual view.

is invisible under ordinary circumstances, the black precipitate is invariably obtained in the axis cylinder at every injured spot. Both neutral red and toluidine blue are readily precipitable by KCl, and the granules stained by these dyes are probably caused by the diffusion of this electrolyte.

(8) The theory deduced from these observations is that the axis cylinder is surrounded by an impervious wall except at Ranvier's nodes, and is filled with a colloidal solution with potassium chlorides adsorbed on the surface of the colloid molecules. As the salt is attached in this manner it is supposed to be masked, so that it does not give the potassium reaction, and does not exert osmotic pressure, but can still conduct electricity. Injury (and to a less extent excitation) causes these colloid molecules to aggregate and become larger ([62]). Their surface is therefore diminished, and the electrolytes are set free into simple aqueous solution. From the nature of the precipitates by Macallum's methods the electrolyte is inferred to be KCl, and the neutral red and toluidine blue precipitates confirm this. The concentration of salt is from the "concentration law" about 10 per cent. This theory is therefore a purely physical one, and has a close relationship to the theory propounded by Sutherland ([63]). Both these theories give an intelligible explanation of what has always been a difficulty, namely, the peculiar rate of transmission of the nervous impulse ([64, 65]).[1]

While this Macdonald-Sutherland hypothesis would explain the observations just referred to, there are still many difficulties to be faced, some of which are of a formidable character. Potassium chloride is supposed to be masked in such a manner that it exerts no osmotic pressure, yet that the ions can move so as to conduct electricity. It is supposed to be present as KCl, yet Cl appears at once on the use of $AgNO_3$, while the K is masked and only appears when there is an injury—a return by a back door to the "alteration-theory" that had been abandoned. The rate of diffusion of the +K ion is ·00066, of the −Cl ion is ·00069,

[1] The most recent determinations ([65]) give the rate at 30 metres per second in the frog's nerves at ordinary temperatures, 65 metres per second at 35° C. Helmholtz gave 33 metres per second for human nerve (which would make this process in man at 36° occur at the same rate as in the frog at 15° C.) But as Tigerstedt points out, the arm of this subject was cooled by a casing of plaster of Paris, and so this value is too low. Waller gives 50 metres per second; Alcock as the mean of forty experiments on man gave 66 metres per second.

so that to produce a current in the right direction diffusion must be supposed to be faster down the nerve than into the electrodes. Finally, as the difference in velocity of the two ions is so small, and as the E.M.F. is the *difference* of the diffusion into electrodes and nerve, a very high concentration is needed—according to the "concentration law" equal to 10 per cent. KCl—yet the chemical analysis of the tissue (as far as the observations go) shows that even if all the K and Cl be supposed to be present in the axis cylinder and none elsewhere, there is not enough to give a concentration of more than ·5 per cent. at the outside.

III. The theories based on fluid cells are at first sight more promising, especially as it has not yet been possible to give exact details which can be put to the test of direct experiment.

The view of Brunings (66), perhaps the best instance of this theory, is that animal electricity in general, and nerve in particular, is an example of a "diosmotic cell." This is an arrangement by which two fluids, which may be of the same osmotic pressure but differ in composition, are separated by a membrane, which is impermeable to both fluids as a whole, but permeable to at least the kation of the fluid lying within the cell. Such an arrangement would give a current on fracture of the membrane, would not give heat externally, would show the same osmotic phenomenon as a nerve, and does not require a greater concentration of electrolytes than is met with elsewhere in the body.[1] The electrolytes are supposed to be "preformed"; they might be adsorbed on the surface of protein molecules or not.

Alcock (64) has published some results on the electrical conductivity of nerve before and after chloroform and ether anæsthesia which bear on the question, if the assumption is made that these agents produce a maximum injury. As both drugs cause an electrical effect of the same sign as the injury current and of the same order of magnitude this is not an unreasonable hypothesis. The result is that in nerve there is no alteration of conductivity (within 2 per cent.), while there is a marked diminution in the polarisation.[2] The inference from this is that chloroform does

[1] Alcock and Lynch (60) give the figures for chlorine in nerve fibres. Some unpublished results on the potassium content support the view given above, but the experiments are still too few in number to justify the pronouncement of a final opinion.

[2] Waller (67) had previously observed the alteration in polarisation. His results do not contradict those of Alcock, as Roaf and Alderson (69) suppose.

not in nerve set free electrolytes,[1] and if the preliminary assumption be granted, that there are none set free by an injury. This is quite consonant with the theory just stated, but presents some difficulty to the concentration cell theory. Macdonald's invocation of "pseudo polarisation," and his supposition that the electrolytes in nerve are free to conduct electricity but not to exert osmotic pressure, is an explanation that seems to require a further experimental basis before it can be unreservedly accepted.

It might be supposed that the location and properties of the membrane or surface of separation which divides the fluids would present some difficulties. Ostwald (70) originally showed that such a membrane could exist, and that it might be permeable to either kations or anions, but not to both. In the case of nerve the membrane would have to be permeable to kations alone, as stated above. Alcock's (64) further observations on the action of chloroform showed that while the results on nerve could be taken either way, the experiments on frog's skin required for their explanation the presence of such membranes situated just below the outer surface, and that no simple diffusion process would be sufficient. So that as far as the membrane is concerned both the "concentration cell" and the "diosmotic" theories have some experimental justification.

Here the subject must be left as far as the present occasion is concerned. For the future we may hope that further experiment will enable us to decide between the present series of conflicting hypotheses.

Although we have considered the matter solely from the standpoint of nerve, it is admitted that the same laws govern the life of every cell in the body, and the inquiry is really a fundamental one into the properties of living matter. To any one who takes an interest in anything beyond the routine work of examinations such inquiries cannot fail to be of the greatest importance, and it is only in physiology that it is necessary to defend the acquisition of knowledge for its own sake.

[1] Moore and Roaf (68) and Roaf and Alderson (69) have advocated the contrary view as far as the action of $CHCl_3$ is concerned, but the discussion is too elaborate to be continued in this place.

BIBLIOGRAPHY

[1] *J. C. Bose*, Comparative Electrophysiology, London, 1907.

[2] *A. D. Waller*, Proc. Physiol. Soc., J. Physiol., 37, xviii.

[3] *J. C. Bose*, Response in the Living and Non-Living, London, 1902.

[4] *F. Gotch*, J. Physiol., 28, p. 32.

[5] *H. von Baeyer*, Verworn's Zeitschrift, Bd. 2, H. 1, p. 169.

[6] *F. W. Fröhlich*, Verworn's Zeitschrift, Bd. 3, H. 1, p. 75.

[7] *K. H. Baas*, Pfluger's Archiv., Bd. 103, p. 276.

[8] *A. D. Waller*, Lectures on Animal Electricity, vol. i.

[9] *F. Gotch* and *v. Horsley*, Phil. Trans. Roy. Soc., 182, 1891, p. 514.

[10] *C. S. Sherrington*, Integrative Action of the Central Nervous System, New York, 1906.

[11] *Bernstein*, Pfluger's Archiv., Bd. 73, s. 376, 1898.

[12] *N. H. Alcock* and *J. Seemann*, Pfluger's Archiv., Bd. 108, s. 426.

[13] *W. Reid* and *J. S. Macdonald*, J. Physiol., 23, p. 100.

[14] *M. Lewandowsky*, Pflüger's Archiv., Bd. 73, p. 288; and Inaug. Dissert. Halle a. S., 1898.

[15] *W. Einthoven*, Pflüger's Archiv., Bd. 124, s. 246.

[16] *F. Gotch* and *G. J. Burch*, J. Physiol., 24, p. 410, 1889.

[17] *Bernstein*, Pfluger's Archiv., Bd. 15, p. 289.

[18] *Wedenski*, Medisch. Zentralbl., 1884, p. 64.

[19] *Bowditch*, Du Bois Reymond's Archiv., 1890, p. 489.

[20] *Brodie* and *Halliburton*, J. Physiol., 28, p. 181, 1892.

[21] *S. C. M. Sowton*, Proc. Roy. Soc., vol. 66, p. 379.

[22] *S. Garten*, Beitrage zur Physiol. der Marklosen Nerven, Jena, 1903.

[23] *N. H. Alcock*, Proc. Roy. Soc., 1904, vol. 73, p. 166; 1906, vol. 77, p. 267; 1906, vol. 78, p. 159.

[24] *J. Tait* and *Gunn*, Quart. Journ. Exper. Physiol., i. p. 1.

[25] *A. D. Waller*, Proc. Physiol. Soc., J. Physiol., 25, p. i., and 36, p. xxx.

[26] *A. D. Waller*, Proc. Physiol. Soc., J. Physiol., 36, xxx.

[27] *E. Pfluger*, Pfluger's Archiv., Bd. 122, p. 593.

[28] *B. Kilvington*, British Medical Journal, 1905, i. p. 935; 1905, ii. p. 625; 1907, i. p. 988; 1908, i. p. 1414.

[29] *W. Thörner*, Verworn's Zeitschrift, Bd. 8, H. 5, p. 530.

[32] *Kilvington* and *Osborne*, J. Physiol., 34, p. 267.

[33] *Marinesco*, J. f. Psychiat. u. Neurologie, vii. p. 141.

[34] *Halliburton*, *Mott*, and *Edmunds*, Proc. Roy. Soc., B. 78, p. 259, 1906.

[35] *Langley* and *Anderson*, J. Physiol., 30, p. 439.

[36] *Lugaro*, Neurol. Zentralblatt, 25, p. 786.

[39] *Harrison*, *Ross*, Archiv. f. Mikros. Anat. u. Entw., 57, 1901.

[40] *Harrison*, *Ross*, Sitzungs b. d. N. Gesell. f. Nat. u. Heilk., 1904.

[42] *Ballance* and *Stewart*, The Healing of Nerves, 1902.

[43] *R. Kennedy*, Phil. Trans., B. 188, 1897, p. 257; Brit. Med. Journ., 1904, ii. p. 729.

[44] *Head*, *Rivers*, and *Sherren*, Brain, 28, p. 99, 1905.

[45] *Head* and *Sherren*, Brain, 28, p. 116, 1905.

[46] *Head* and *Thompson*, Brain, 29, p. 537, 1906.
[47] *Bethe*, Allg. Anat. u. Physiol. der Nervensystems, 1903.
[48] *Braus*, Anat. Anzeiger, 26, p. 433, 1905.
[49] *Kerr*, *Graham*, Roy. Soc. Edin. Trans., vol. 41, 1905, p. 121.
[50] *Ballance* and *Stewart*, Brit. Med. Journ., 1903, May 2.
[51] *A. Macallum*, J. Physiol., 32, p. 95.
[52] *Gilbert*, Inaug. Dissert., Tubingen, 1898.
[53] *Macallum* and *Menten*, Proc. Roy. Soc., B. 77, p. 165, 1906.
[54] *A. Macallum*, Proc. Roy. Soc., 76, p. 217.
[55] *Maxwell*, J. Biol. Chemistry, iii. 1907, p. 358.
[56] *Keith Lucas*, J. Physiol., vol. 37, 1908, p. 112.
[57] *Bazett*, J. Physiol., 36, p. 414, 1908.
[58] *Woolley*, J. Physiol., 37, p. 122, 1908.
[59] *J. S. Macdonald*, Proc. Roy. Soc., 67, p. 315, 1900, and p. 325, *l.c.* Thompson-Yates Lab. Reports, 4, p. 2, 1902. *J. S. Macdonald* and *S. C. M. Sowton*, ibid., Feb. 5, 1903. *J. S. Macdonald*, Proc. Physiol. Soc., J. Physiol., Dec. 17, 1904 ; March 18, 1905. Proc. Roy. Soc., 76 B., p. 322. Proc. Physiol. Soc., J. Physiol., June 17, 1905. Proc. Roy. Soc., 79, p. 12, 1906.
[60] *N. H. Alcock* and *G. Roche Lynch*, J. Physiol., 36, p. 93.
[61] *J. H. Ashworth*, Proc. Roy. Soc., B., vol. 80, p. 463.
[62] *J. S. Macdonald*, Science Progress, vol. 2, p. 482.
[63] *W. Sutherland*, Am. Journal Physiol., 1906, vol. 17, pp. 266, 297.
[64] *N. H. Alcock*, Proc. Roy. Soc., 1903, vol. 72, p. 414.
[65] *von Miram*, Engelmann's Archiv., 1906, p. 533.
[66] *W. Brunings*, Pfluger's Archiv., Bd. 100, p. 367.
[67] *A. D. Waller*, Proc. Physiol. Soc., J. Physiol., 38, p. vi.
[68] *B. Moore* and *H. E. Roaf*, Proc. Roy. Soc., vol. 73, 1904, p. 382 ; B., vol. 77, 1906, p. 86 ; Deutsch. Med. Wochensch., 33, p. 1568 ; Zentralb. Physiol., 21, p. 477 ; Arch. Intern. Physiol., 5, p. 68.
[69] *H. E. Roaf* and *E. Alderson*, Biochem. Journal, vol. ii. p. 412.
[70] *Ostwald*, Zeitsch. f. Physik. Chemie, vol. 6, 1890.

RECENT RESEARCHES ON CORTICAL LOCALISATION AND ON THE FUNCTIONS OF THE CEREBRUM

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Introduction

The experimental study of the functions of the cerebrum, after a period of activity lasting through three decades, reached its acme in an important research (Sherrington and Grünbaum), which resulted in the belated recognition of the histological investigation of Bevan Lewis and Henry Clarke (1878) on the cortical localisation of the motor area of the brain. Of late years the histological has largely replaced the experimental method, and the study of cortical localisation, although still in its infancy, may now fairly claim to be regarded as a branch of exact science.

Owing to the far-reaching importance of the controversy regarding the neurone theory, the majority of the numerous recent publications on the anatomy and histology of the nervous system deal with the finer histology of nerve cells and fibres. Of 711 contributions, for example, which appeared during the years 1905 and 1906, and which were critically abstracted and reviewed by Edinger and Wallenberg in their last report, over 300 papers were concerned with this subject, and few of the remainder were of direct physiological significance. It is not the purpose of this article to deal with purely histological investigations which have no immediate bearing on cortical localisation, and therefore no reference will be made to such contributions beyond the remark that, of those by English writers, the papers of John Turner are especially worthy of attention.

During the past eight years numerous publications have appeared on the subject of cortical localisation by the histological method. In these several contributions the mode of evolution and the functional significance of the different cell layers of the cortex cerebri have been considered from both the ontogenetic

and the phylogenetic aspects; and the whole cortex cerebri in many orders of mammals (including man) has been mapped out into various histologically different regions.

Of these regions, experimental or histo-pathological proof of the functions of the precisely-defined psychomotor and visuo-sensory areas is complete. In the case of the prefrontal region, which is the latest evolved, the most variable, and the most complexly constructed portion of the human cerebreum, histo-pathological evidence of its functional significance has been derived from the examination of cases of mental disease, which method constitutes an advance on the time-honoured study of cases of gross lesion of the brain.

Finally, with regard to the localisation of the language centres, important papers by Marie and by Monakow, and a lengthy volume by Moutier, have been published; and the existence of Broca's speech area has thereby been seriously threatened if not rendered entirely doubtful. Articles on the psychological experiences connected with the different parts of speech, on the language mechanism and its psycho-physiology with regard to the functions of the cerebrum, and on the subject of sense-deprivation, have also been recently published.

In the course of the present article, the lamination of the cortex cerebri and the functional significance of its several layers will first be considered. The subject of cortical localisation by means of the histological method will then be detailed. This description will be followed by remarks on the mode of evolution of the cerebral functions. The higher functions of the human brain will afterwards be dealt with, and in connection with this matter the psycho-physiology of the language mechanism will be discussed. The subject of sense-deprivation will next receive attention, as a preliminary to the consideration of the recent researches on aphasia. The article will be concluded by references to certain matters of interest with regard to the functions of the cerebrum, and to a number of recent publications of importance, which could not be conveniently included in the general text.

Lamination of the Cortex Cerebri

Since the year 1872, when Meynert published a description of the structure of the cortex cerebri which, from the general aspect,

has required little modification, numerous classifications of the various layers of which it is composed have appeared.

The various subdivisions which have been made by the several authors, owing to the different methods of preparation which have been employed, to the different aspects from which the subject has been studied, and to the different regions of the cortex cerebri which have been examined, have resulted in the employment of different numerals to designate the same or similar layers; and thereby much confusion has resulted. This will be avoided during the following description by the employment of such terms as clearly indicate the cell layers which are under reference.

Whilst from the aspect of cell form, few if any of the published descriptions equal in elaboration, and in probable accuracy, the account given by Cajal in the numerous papers he has produced as the result of a systematic employment of various modifications of the method of Golgi, his classification is at present of histological rather than of physiological interest.

Another and more recent classification, that of Brodmann (1906), is more immediately useful, and, in consequence of the elaborate and prolonged investigations of the author on the subject of cortical localisation, deserves reference here. Brodmann divides the cortex cerebri into the following layers :—

(1) A zonal layer, without cells (the equivalent of the tangential layer of Krause).

(2) A layer composed of the "molecular" and "small pyramidal" layers of other writers.

(3) A layer of medium and large pyramidal cells.

(4) An internal granular or stellate layer.

(5) A layer of ganglionic or deep pyramidal cells.

(6) A layer of deep spindle-shaped or polymorphous cells.

For the purposes, however, of this article, which deals with the subject from the functional rather than the structural aspect, the description has been adopted which was published by the present writer in 1900, and which is based on the mode of development of the several laminæ of the cortex cerebri. This classification, which has been adopted, amongst others, by Mott and by Watson, is as follows :—

(1) The superficial layer of nerve fibres or "molecular" layer (*outer fibre lamina*). (Average prefrontal depth, ·30054 mm.)

(2) The layer of small, medium, and large pyramidal cells (*outer cell lamina*). (Average prefrontal depth, ·83116 mm.)

(3) The layer of granules (*middle cell lamina*). (Average prefrontal depth, ·22883 mm.)

(4) The inner layer of nerve fibres or "inner line of Baillarger," containing large and frequently solitary cells (*inner fibre lamina*). (Average prefrontal depth, ·23032 mm.)

(5) The layer of polymorphic cells (*inner cell lamina*). (Average prefrontal depth, ·30979 mm.)

This five-layered type, though subject in different regions to structural modifications which probably possess in all cases a functional significance, is common to the whole cortex cerebri, with the exception of the hippocampus and the pyriform lobe, which parts belong to the archipallic, in contradistinction to neopallic cortex (Elliott Smith). In the psychomotor area, for example, the Betz cells lie in the inner fibre lamina, and the middle cell lamina is reduced in depth almost to vanishing point. Again, in the visuo-sensory area, the middle cell lamina is hypertrophied and duplicated by the interposition of a special fibre layer, the "line of Gennari."

The mode of development of this five-layered type of cortex will now be briefly described.

In the fœtus of four months lamination has not begun, and the cortex consists solely of a superficial indifferent layer and of a deeper layer of undifferentiated neuroblasts. The average depth of the former is 0·154665 mm., and of the latter 0·67758 mm., a total of 0·832245 mm., which is less than half the normal adult general average depth of 1·90064 mm.

For simplicity of exposition, the process of development will be first described in the case of each separate layer, and the results will then be summarised.

Primary Cell Laminæ of the Cortex

Lamina 2, Pyramidal Layer, Outer Cell Layer.—The pyramidal layer is the last cell layer of the cortex to develop during the process of lamination. In a fœtus of six months this layer is separable from the subjacent middle cell layer owing to the less differentiated condition of its cell elements, and it is at this period only one-fourth of the depth to which it attains in the adult. At

birth and in early infancy it is still little more than one-half of the adult depth.

Lamina 3, *Granule Layer, Middle Cell Layer.*—The granule layer develops in the sixth month of fœtal life, and at this period it is separable from the superjacent outer cell or pyramidal layer owing to the more differentiated condition of its cell elements. At this period it is already one-half of the adult depth, and by the time of birth it has attained to a depth which is nearly three-fourths of this.

Lamina 5, *Polymorphic Layer, Inner Cell Layer.*—The polymorphic layer is the first cell layer to appear, and it is separated off from the rest of the partially differentiated neuroblasts of the cortex by the development of the fourth or inner fibre lamina at the sixth month of fœtal life. The polymorphic layer is already, at the period referred to, about three-fourths of the adult depth, and it undergoes a slow further development until after birth. In a child of six weeks it has attained a depth which is within 18 per cent. of the adult normal.

Primary Fibre Laminæ of the Cortex

Lamina 1, *Superficial Layer, Outer Fibre Layer.*—At the fourth month of fœtal life the cortex consists of this layer and of a deeper undifferentiated mass of neuroblasts. The layer under description is already about one-half of the adult depth, and it remains unchanged until the development of lamination in the sixth month. At birth, however, it has attained to a depth which is about two-thirds of the adult normal. It is probable that its further development to the normal adult depth occurs in association with that of the subjacent second, pyramidal, or outer cell layer.

Lamina 4, *Inner Fibre Layer, Inner Line of Baillarger.*—This layer appears in the sixth month of fœtal life, and almost at once attains to nearly the normal adult depth. The cleavage of the partially differentiated neuroblasts of the cortex into an upper and a lower portion by the development of this layer is the most striking feature of the process of lamination. In view of what will be stated later concerning the functions carried on by the inner cell layer, this cleavage of the neuroblasts is an occurrence of the greatest significance.

Summary.—The *inner cell layer*, therefore, appears before the others, in consequence of a cleavage of the undifferentiated neuroblasts into an upper and a lower portion, and it is almost at once of a depth which is about 75 per cent. of the adult normal. It remains at almost a stationary depth until after birth. Its depth in a child of six weeks is 82 per cent. of the adult normal.

The *middle cell layer* is differentiated next in order, and is almost at once about one-half of the normal adult depth. It gradually increases in thickness, and at birth it has attained to a depth which is 75 per cent. of the adult normal.

The *outer cell layer* is the last layer of the cortex to be differentiated, and at this time it is only one-fourth of the normal adult depth. It gradually increases in thickness, and in an infant of six weeks it has attained to a depth which is about 60 per cent. of the adult normal.

In the adult human cerebrum, as will at once be seen from the measurements given on page 287, the outer cell lamina or pyramidal layer, in spite of its late evolution, becomes the prominent layer of the cortex, and in depth is greater than the depth of the combined layers 3, 4, and 5, which lie below it. The functional significance of the facts mentioned in this description will be referred to later.

The above account of the mode of evolution of the cortex cerebri has recently been confirmed by G. A. Watson from the phylogenetic aspect. This writer, whilst hitherto paying especial attention to the insectivora, has carefully studied the cortex cerebri of many orders of mammals. He adopts the above classification of the cortical layers, but, for reasons which he details, employs a slightly different terminology, grouping the first and second laminæ together under the term "supra-granular," and the fourth and fifth together under the term "infra-granular." He remarks:—

"Regarded from the developmental aspect—ontogenetic and phylogenetic—the facts adduced support the thesis that the mammalian cerebral cortex (neopallium) is built up primarily on an infra-granular basis, *i.e.* the infra-granular portion is the earliest to appear in the process of development, very quickly reaches maturity, and in the adult, especially if average size of component nerve cell is taken into consideration, presents remarkably little difference in absolute depth in one of the lowest mammals and in the highest.

"The granular layer may be said to be the next addition to the

cortex. Ontogenetically it appears shortly after the infra-granular portion of the cortex, and it reaches its maximum development in depth and definiteness in the projection spheres of the cerebrum. The last layer of the cortex to appear ontogenetically is the supra-granular (pyramidal). It is the slowest of all the layers to reach maturity. It is scarcely existent at all in certain regions in some of, if not all, the lowest mammals, and even at its best in the latter it reaches but a slight absolute depth as compared with its depth in practically every region of the neopallium in the human subject."

The above description of the mode of development of the cortex cerebri is illustrated in the following figure, which indicates, in graphic form, the five primary cell and fibre laminæ of the cortex of fœtuses of four and six months, a new-born child, a normal human adult, and a mole. It will be at once seen that the cortex of the human adult differs from that of the insectivore chiefly in the degree of development of the second, pyramidal, or outer cell lamina. In spite of the human brain being one of the largest and that of the mole one of the smallest in the mammalian phylum, the actual average depths of the granular and infra-granular portions of the cortex (laminæ 3, 4, and 5) are very similar in the two.

It may here be remarked that Brodmann, in the course of his prolonged investigations into the structure of the cerebral cortex of the mammalia, has incidentally and independently (1906) made similar observations to those of Watson. He states that, during the ascent of the mammalian series, his layer 3, which is substantially the outer cell lamina or pyramidal layer of the writer and the supra-granular layer of Watson, increases in depth, whilst his layer 6, which is equivalent to the inner cell lamina 5 of the writer and the lower part of the infra-granular region of Watson, on the whole diminishes in depth. Brodmann also makes certain generalisations regarding the variability of the individual layers of the cortex cerebri, which, though they confirm the individual observations of several other writers, are worthy of reference here owing to the wide field covered by the investigations of this author. He remarks that his layer 4 (granule layer of other writers) is the most variable; that his layers 3 and 5 (medium and large pyramids, and infra-granular pyramidal-shaped cells) exhibit the greatest histological differentiation; and that his layer 6 (polymorphic layer or inner cell lamina of the writer) exhibits the greatest variation in breadth. He further remarks that the psychomotor and striate (visuo-sensory) areas of the cortex cerebri are most highly developed in primates.

Certain facts regarding the lamination, the period and the mode of its evolution, and the functional significance of certain special regions of the human cortex cerebri, will now be briefly detailed,

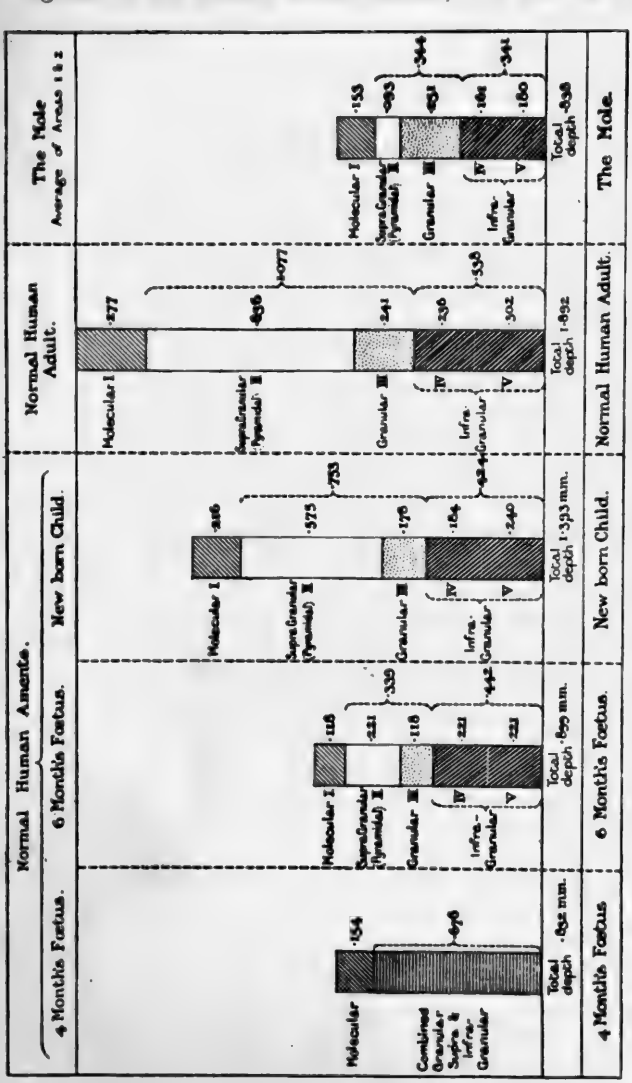

FIG. 1 (G. A. Watson, 1907).—Illustrates approximately the relative depths of the cerebral cortical layers in normal human aments (four and six months' fœtus and new-born child), the normal human adult, and the Mole. The micrometic measurements in the first four cases are taken from "The Histological Basis of Amentia and Dementia" (*Archives of Neurology*, vol. ii. 1903) by J. Shaw Bolton: those of the cortex of the Mole are also by Dr. Bolton. Supra-granular (pyramidal) layer left blank; infra-granular (iv. and v.) shaded darkly.

Note.—The infra-granular cortex in the six months' fœtus and new-born child were practically of the same depth in the specimens measured, viz. ·442 to ·424. In the figure the darkly-shaded part (infra-granular cortex) in the third column is therefore represented somewhat too deep.

as a preliminary to the consideration of the functional significance of the several primary laminæ of the cortex cerebri.

The Visuo-sensory Area.—The lamination in this region is

specialised from the five-layered type already referred to, and consists of the following layers :—

1. The superficial layer of nerve fibres (*outer fibre lamina*).
2. The layer of pyramidal cells (*outer cell lamina*).
3. The middle layer of nerve fibres, containing solitary cells of Meynert (*middle cell lamina*):
   - 3*a*. The outer layer of granules.
   - 3*b*. The middle layer of nerve fibres or "line of Gennari" containing solitary cells of Meynert.
   - 3*c*. The inner layer of granules.
4. The inner layer of nerve fibres or "inner line of Baillarger," containing solitary cells of Meynert (*inner fibre lamina*).
5. The layer of polymorphic cells (*inner cell lamina*).

The specialisation of the visuo-sensory cortex consists, therefore, in essentials, in a duplication of the third primary lamina of the cortex, and in the interposition, between the double layer, of a layer composed of nerve fibres. Of this triple layer, layer 3*a* is an additional feature; layer 3*b* is an exaggeration of a thin fibre band, the "outer line of Baillarger," which in the adult cortex lies between the second and third primary laminæ, but is only visible in sections prepared to show nerve fibres; and layer 3*c* is the original third primary lamina increased in depth.

In congenital or long-standing blindness the depth of layer 3*b* is decreased by nearly 50 per cent., and that of layer 3*a* is decreased by more than 10 per cent., owing to atrophy of the optic radiations. The other layers of the cortex are unchanged in depth by the existence of blindness.

These facts prove that the cortical region under consideration is the projection centre for visual impressions or the visuo-sensory area.

The cortex in this region rapidly attains to mature development. The second, pyramidal, or outer cell lamina thus develops much earlier than is the case in the visuo-psychic and prefrontal regions. For example, in infants of one and three months respectively, its depth is already 84 per cent. of the adult normal. A further important fact is that in the normal adult this cell layer of the visuo-sensory area is only about five-ninths of its depth in the visuo-psychic and prefrontal regions of the cerebral cortex.

The Visuo-psychic Region.—At the periphery of the visuo-sensory area, where this passes in each direction into the neighbouring cortex, termed by the writer "visuo-psychic" (which word has since been adopted by Campbell and by Mott), an abrupt change

in lamination takes place, layer 3*b*, the line of Gennari, suddenly ceasing, and layers 3*a* and 3*c*, the two layers of granules, running into one and becoming layer 3 of the visuo-psychic region, which is thus of the ordinary five-layered type.

Congenital or long-standing blindness causes no modification of the lamination of the visuo-psychic region, which fact proves that this region possesses no "visuo-sensory" functions.

The cortex of this region reaches maturity later than the visuo-sensory, but earlier than the prefrontal. The second, pyramidal, or outer cell layer in infants of one and three months is respectively nearly two-thirds and more than three-quarters of the normal adult depth. This layer reaches to practically the same adult depth as in the prefrontal region. In cases of mental disease this layer does not vary in depth according to the degree of dementia existing in the patients, though a small and practically constant decrease in depth, which may be due either to subdevelopment or to retrogression, is evident in such cases.

The Prefrontal Region.—The cortex of this region is late in reaching maturity. As has been stated, the pyramidal or outer cell lamina is the last layer of the cortex to develop. It is visible owing to the undifferentiated condition of its constituent neuroblasts in a fœtus of six months, and is at this time only one-quarter of the normal adult depth. In infants at birth and at the age of six weeks it is still less than two-thirds of the normal adult depth.

It is the only cell layer of the cortex cerebri which varies measurably in depth in "normal" brains.

In cases of mental disease it is under-developed to different degrees, not only in idiots and imbeciles, in the severer grades of which its depth is only two-thirds of the adult normal, but also, and here to a lesser extent, in chronic and recurrent lunatics without dementia. The degree of its retrogression in demented patients varies directly, and to an equally marked degree as its subdevelopment in the case of amentia, with the amount of dementia existing in the respective cases.

Of these three regions of the cortex, therefore, the visuo-sensory area first reaches maturity. Though highly specialised, the cortex of this area is, however, not well developed, as the outer cell lamina or pyramidal layer remains at but five-ninths of

the maximum adult depth. The visuo-psychic cortex attains to maturity later, but then becomes of the maximum adult depth. The prefrontal cortex is the last to reach maturity. The outer cell lamina in this region varies in its degree of development according to the mental capacity of the individual and in its degree of retrogression according to the amount of mental decadence which exists. Further, it varies in measurable depth in "normal" individuals.

All these variations regarding the degree of development occur in the pyramidal or outer cell layer, which is the last lamina to be evolved, and the most important feature of the human adult cortex cerebri.

The inner cell lamina or polymorphic layer of the cortex, which is the first to be evolved, is, on the other hand, in all the three regions referred to above, of extremely constant *average* depth. A very slight decrease in the average depth of this layer occurs, in the prefrontal region, in cases of mild cerebral and mental degeneracy (high-grade amentia), and in cases of chronic insanity with moderate dementia. A considerable decrease, on the other hand, exists, also in the prefrontal region, in more marked aments (whether normal fœtuses and infants, or idiots and imbeciles) and in gross dements who are unable to carry on the ordinary animal functions, such as attending to their own wants, &c.

Functions of the Different Cell Laminæ of the Cortex Cerebri

As has been stated, the cerebral cortex consists of three primary cell laminæ (layers 2, 3, and 5), and of two primary fibre laminæ (layers 1 and 4). The evidence above adduced regarding the ontogenetic and phylogenetic development of these laminæ enables certain definite conclusions to be drawn with regard to their functional significance.

The outer cell lamina (2, pyramidal), to which may be added the outer fibre lamina (1), is the prominent feature of the human cortex, and constitutes a "higher level" basis for the carrying on of the cerebral functions. It is the last cell layer of the cortex to be evolved and the first to undergo retrogression. In the visuo-sensory area (projection sphere) the outer cell lamina rapidly attains maturity, but is then only about five-ninths of its depth

in the visuo-psychic and prefrontal regions of the cerebral cortex. In the visuo-psychic region this layer develops earlier than in the prefrontal region, but later than in the visuo-sensory area, and eventually attains to practically the same adult depth as in the former. In this region it is of practically constant adult depth, and does not vary in measurable depth according to the mental capacity of the individual. In the prefrontal region the outer cell lamina develops later than in the other regions referred to It is the only cell layer of the cortex cerebri which varies definitely in measurable depth in "normal" brains. It is under-developed to different degrees according to the mental capacity of the individual in persons exhibiting various grades of mental subevolution; and it undergoes degrees of retrogression which correspond to the amount of dementia existing in cases which permanently suffer from diminution or loss of their mental powers.

The second, pyramidal, or outer cell lamina of the human cerebral cortex, therefore, subserves the "psychic" or associational functions of the cerebrum. These functions are pre-eminent in the prefrontal region (centre of higher association); *they are less important in the visuo-psychic region* (region of lower association); *and they are of least importance in the visuo-sensory region* (projection sphere). *These three regions are therefore of different grades in the hierarchy of cerebral function.*

The results obtained by Watson during his histological investigation of the cerebral cortex of the mammalia supply the complement from the phylogenetic aspect to the above (ontogenetic) conclusions. Watson finds that in the insectivora the pyramidal or outer cell layer is in a rudimentary condition, though the lower layers of the cortex approximate in depth to that of these layers in the normal human adult. Further, the pyramidal or outer cell layer is better developed in the rodents than in the insectivores; it is again better developed in the ungulates and in the carnivores than in the rodents; and it is strikingly more developed in the primates than in the carnivores.

He therefore functionally correlates this layer with the educability and general intelligence which appear in an increasing degree during the ascent of the mammalian scale.

Watson remarks:—

"The supra-granular (pyramidal) layer—which is, relatively to the infra-granular cortex, so poorly developed at birth—is slow in reaching maturity, and is, even at its best, in certain lower mammals,

such as the insectivora, only of an insignificant absolute depth—subserves the higher associations, the capacity for which is shown by the educability of the animal. It has therefore to do with all those activities which it is obvious that the animal has acquired (or perfected) by individual experience, and with all the possible modifications of behaviour which may arise in relation to some novel situation, hence with what is usually described as indicating intelligent as apart from instinctive acts, the former being not merely accompanied but controlled by consciousness (Lloyd Morgan)."

The middle cell lamina (3, granule) is developed after the fifth, polymorphic, or inner cell lamina, and before the second, pyramidal, or outer cell lamina. In the prefrontal region of a fœtus of six months it has just become differentiated, by commencing specialisation of its constituent cells, from the superjacent second or outer cell lamina, and it is already one-half of the normal adult depth. In a child at birth it has become three-fourths of the normal adult depth.

In the visuo-sensory area the optic radiations end in the midst of a hypertrophied and duplicated third or granule layer. The duplication is due to the interposition in the midst of the hypertrophied third or granule layer of a well-marked fibre band, the line of Gennari, which fibre band, as has already been stated, is a hypertrophy of the outer of the two horizontal interradiary fibre plexuses of the adult cortex, namely, the " outer line of Baillarger." In old-standing or congenital optic atrophy, the outer (and additional) of the granule layers is decreased in thickness by more than 10 per cent., and the line of Gennari is decreased in thickness by nearly 50 per cent.

As has been pointed out by Watson, a hypertrophied third, granule, or middle cell lamina appears to be characteristic of the projection areas of the cerebrum. In the case of the visuo-sensory area (visual projection sphere), the third or granule layer first becomes definitely duplicated in the order primates, though slight indications of duplication occur in the higher carnivores.

The third, granule, or middle cell lamina, therefore, primarily subserves the reception or immediate transformation of afferent impressions, whether these arrive directly from the lower sensory neurones or indirectly through other regions of the cerebrum.

The fifth, polymorphic, or inner cell lamina is the first cell lamina of the cortex cerebri to be differentiated during the process of

lamination. In the prefrontal region of a fœtus of six months it is separated off from the rest of the cortex by the fourth or inner fibre lamina, and is already within 29 per cent. of the normal adult depth. In a child of six weeks it has advanced to within 18 per cent. of the normal adult depth.

It is of extremely constant average adult depth.

A very slight decrease in the depth of this layer exists in cases of high-grade amentia and of chronic insanity with moderate dementia. A considerable decrease, on the other hand, exists in more marked aments (whether fœtuses and infants, or idiots and imbeciles), and in gross dements who are unable to carry on the ordinary animal functions, such as attending to their own wants, &c.

The fifth, polymorphic, or inner cell lamina of the human cerebrum, therefore, in association with the fourth or inner fibre layer, subserves the lower voluntary and instinctive activities of the animal economy, and thus forms a lower level basis for the carrying on of cerebral function.

Final proof of the last statement has, from the phylogenetic aspect, been afforded by the researches of Watson, who has shown that the " infra-granular " region contains the important cell layers of the lower mammalia, and is very little inferior in depth (see Fig. 1, page 291) to the normal adult human depth of the conjoined fourth and fifth laminæ.

Watson's conclusions on this question are as follows :—

" The infra-granular portion of the cortex (iv. and v.) (omitting the constituent cells which possess motor or analogous functions) is concerned especially with the associations necessary for the performance of the instinctive activities, that is, all those which are innate and require for their fulfilment no experience or education. These form the basis of many complex actions necessary for the preservation of the individual and the species, such as the seeking appropriate shelter and protection, the hunting for food—each after his own kind —and the quest of the opposite sex. Although these acts may be accompanied by consciousness, there is no evidence to show that this is 'focal' or that essentially they are controlled by consciousness (Lloyd Morgan). It is believed that lower mammals have provided in the infra-granular cortex (which is relatively so fully matured at birth in them as well as in man, and which in the adult, even in animals low down in the mammalian scale, reaches such a great degree of

absolute development) a sufficient cerebral cortical mechanism for the performance of these lower associations. The actions which are the outcome of such associations are often complex, and as an instance of the class included under this heading the tunnelling of the mole may be mentioned. Such more or less stereotyped actions may show signs of improvement in their performance, firstly, as the result of perfection by use of an inherited mechanism, and secondly, as the result of the intermingling of activities for which it is concluded that the supra-granular layer is responsible. In the latter case, however, the actions would merge into those which are more properly described as habitual intelligent, or into the class of 'incomplete instincts' (Lloyd Morgan), or 'mixed instincts' (Romanes)."

Watson finally remarks, on the subject of the functions of the "supra-granular" (outer cell layer) and "infra-granular" (inner fibre layer and inner cell layer) :—

"In practical animal behaviour the two sets of processes are probably more or less constantly interwoven, the higher activities (supra-granular layer) coming to the aid of the lower as far as the capability of the animal allows. In the case of the lower mammals (*e.g.* insectivora) the limits of this capability are comparatively soon reached, and correspondingly these mammals possess a relatively poor supra-granular layer. Many of these lower mammals have adopted a safe mode of life, others have resorted to fecundity. With these, which may, for present purposes, be termed extraneous aids to survival, their essentially instinctive activities have been relatively sufficient to ensure their continued existence. There has, therefore, in these mammals, been little necessity for the development of a supra-granular layer, the infra-granular portion of the pallium providing most of the necessary cortical physical basis required for practical behaviour.

"The infra-granular layers, with the reservation to which reference has been made, thus constitute the earlier developed and more fundamental associational system of the cerebral cortex; the supra-granular layer, a higher and accessory system superadded, and of any considerable functional importance only in certain regions in lower mammals, such as the insectivora."

Before the question of cortical localisation receives attention, an important communication by Mott (1904), on the progressive evolution of the structure and functions of the visual cortex in mammalia, calls for reference, as a prominent feature of the article is the consideration paid to the cell lamination of the visuo-sensory and visuo-psychic regions. The paper deals with the subject from not only

the histological but also the clinico-anatomical and experimental aspects, and contains a mass of interesting information. The author describes the visual cortex of the insectivora, rodents, marsupials, ungulates, carnivora, lemurs, and primates. He arrives at the following conclusions :—

"There is a correlation of structure and function as exhibited by a progressive complexity of cell lamination of the visual cortex in mammalia from the insectivora to primates. The more the animal depends on vision as a directive faculty in its preservation the more complex is the structure.

"The transition of uniocular panoramic to perfect binocular stereoscopic vision shows successive stages in the number of direct fibres until, in the primates, there is semidecussation and, as far as my observations go, this may be correlated with a progressive development in the layer of higher associational pyramidal cells lying above the layer of granules.

"The progressive evolution of vision as a directive faculty is simultaneous with a motor adaptation, especially related to the mode of feeding and defence rather than to a particular species.

"Carnivorous animals, especially cats, therefore, have their eyes set forward, abundant direct fibres, and good binocular vision, to enable them to seize their rapidly moving prey with their teeth or paw.

"Better motor adaptation, as Sherrington has independently suggested from his flicker observations, then is probably the essential cause of the direct path of the optic fibres and binocular vision.

"It is, however, in the primates that we have semidecussation of the optic fibres, a macula lutea, eye movements in all directions independent of head movements. Convergence and perfect binocular stereoscopic vision associated with the hand, which, in the apes, becomes the principal executive agent in the procuring of food, defence, and flight. Visual images are now always associated with impressions of the exploring hand, and the ideas of form, substance, extension, and qualities of objects are the complex of the visual and tactile kinæsthetic images, and capable of endless variations. This we may connect with the appearance in the zoological series of an occipital lobe, a line of Gennari visible to the naked eye, a deep layer of pyramids with a double layer of granules in the visuo-sensory striate area. But even more important than this is the appearance of a definite associational zone in which there is a much greater depth of pyramidal cells, the third layer of which is characterised by very large pyramids serving as higher complex association neurones between the visual cortex and the auditory and tactile motor areas. As we

rise in the scale of primates this associational zone increases with the more perfect specialisation of the fore-limbs for manipulation and the erect posture, and this we may correlate with the increase in area of the associational or visuo-psychic zone, the increasing development of the parietal lobe, and the pushing back and infolding of the striate visuo-sensory cortex, so that in the highest types of man it comes to occupy the infolded calcarine region of the mesial surface, although some lower types still preserve the anthropoidal character. It is probable that the same causes give rise to the shifting forward of the anterior motor eye centres."

In this connection reference may be made to a paper by Wilfred Harris. This writer discusses the question of binocular and stereoscopic vision in man and other vertebrates, with regard to the decussation of the optic nerves, ocular movements, and the pupil light reflex.

Cortical Localisation by means of the Histological Method

The researches of Flechsig on the development of the human brain by a study of the process of myelination are so well known to neurologists that any description of them may seem superfluous.

The conclusions at which he arrived are, however, of fundamental importance, and form the origin, if not entirely the basis, of our present knowledge of cortical localisation by histological methods. Again, his generalisations in the gross have successfully passed through a storm of discussion and dissent which is almost unsurpassed in the history of research. Lastly, even at the present time, except by neurologists, the researches of Flechsig are by no means as generally understood and appreciated as they merit. A short description of the main features of the investigations of this writer is therefore perhaps not entirely out of place as an introduction to the subject under consideration.

By studying the exact period of myelination of different parts of the cerebrum in the human fœtus and infant, Flechsig was enabled to divide the cortex cerebri into the two great classes of "sensory centres" and "centres of association." The former myelinate earlier than the latter, and possess a well-marked system of fibres of projection. The latter myelinate later and are rich in long systems of fibres of association. The difference is really one of degree only, as Flechsig does not deny that fibres of projection

exist in the association centres, and that association systems exist in the sensory spheres.

In the whole cerebrum he described in 1898 no less than forty separate myelogenetic fields which develop at different periods. In 1901 he reduced these to thirty-six, and in 1903 he made no alteration in the number although he stated that later investigation might eventually cause him to do so.

Of the *sensory spheres* he describes four, namely, for (1) bodily sensibility; (2) visual; (3) auditory; and (4) olfactory and gustatory sensations. (1) has eight separate myelogenetic fields, and each of the others has three each.

Of the *centres of association* he originally described four, namely, the frontal, the parietal, the temporal, and the insular. Later he combined the temporal and parietal centres into one, the great posterior centre of association. In 1900, however, owing to his discovery of a centre of projection in the gyrus subangularis, he again separated these centres.

In Fig. 2 these *sensory spheres* and *centres of association* are indicated.

In the temporal and parietal centres of association there exist, according to Flechsig, peripheral zones, which develop earlier, and central zones, which develop later; the former adjoin the sensory centres, and are united to them by numerous arcuate fibres.

In the frontal centre of association similar zones exist, but their disposition is much more complex.

The insular centre of association, and also that in the precuneus, consist of peripheral zones only. Flechsig is of opinion that the peripheral zones may be intermediate types between the central territories of association and the sensory projection spheres.

Hence, of the centres of association, the *frontal* exhibits the greatest complexity, the *temporal* and *parietal* are intermediate in structure, and the *insular* and that in the *precuneus* are the least complex of the types.

Flechsig's views on the functions of the central territories of the areas of association are as follows: "The central territories of the zones of association (especially the middle of the angular gyrus, the third temporal convolution, and the anterior half of the second frontal convolution) are apparently the nodal points of the long systems of association, whilst the peripheral zones only feebly show these characteristics.

"The central territories are terminal territories; they are essentially characteristic of the human brain. Isolated destruction of these is never accompanied by phenomena pointing to disturbance

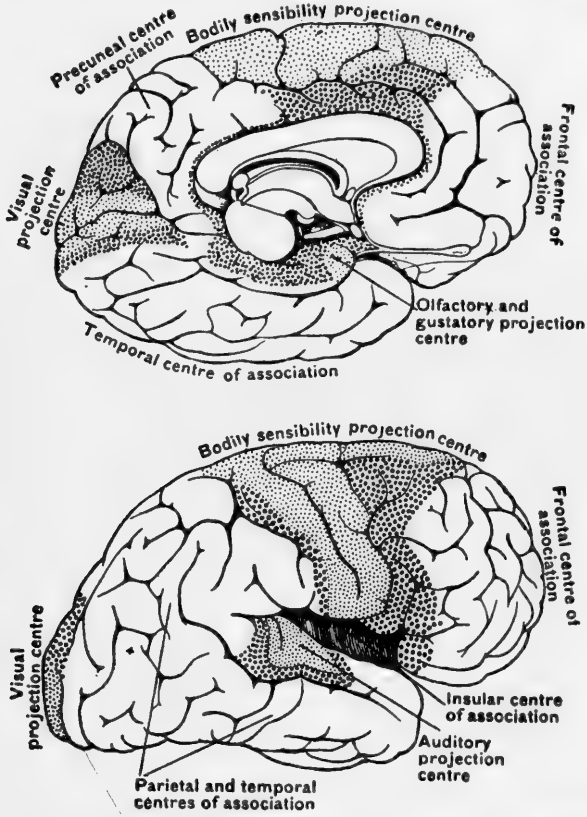

FIG. 2 (after Flechsig).—In these diagrams the "centres of projection" and "centres of association" are mapped out according to Flechsig. The small dots are placed in the chief focus of each centre of projection. Around these chief foci are the regions to which a smaller number of fibres of projection pass; these are indicated by larger dots. These figures, which represent the different cortical spheres indicated by Flechsig as the result of his embryological studies, should be compared with Figs. 3 and 4, and 5 and 6, which illustrate the various areas into which the adult cerebral cortex has been subdivided by Campbell and Brodmann respectively.

of motion or sensation. Motor phenomena, which occasionally accompany lesions of these territories, must be interpreted as *actions à distance.*

"The central territories of the zones of association are in more

or less direct relationship, each with several sensorial zones, some with all.

"After their bilateral removal intelligence is affected, and especially is association of ideas interrupted. These central territories are thus probably of great importance for the exercise of intellectual activity, for the formation of mental images composed of several sensory qualities, for the accomplishment of arts, such as the naming of objects, speaking, &c. These functions are especially interfered with in affections of the posterior centres of association. Clinical observation establishes this fact, and thus justifies the legitimacy of our division of the cerebral cortex into sensory centres (centres of projection) and centres of association." (*Archiv de Neurologie*, ii., 1900, pp. 337–338.)

The views of Flechsig were severely criticised by Hitzig, who, however, is disposed to admit their general truth in a less positive form; and by Vogt, who directly contradicted many of Flechsig's conclusions, and especially the thesis of the constancy and regularity of myelination of the different systems of fibres. He is inclined to look upon the majority of either early or late myelinated fibres as projection fibres, and he regards the method of Flechsig, though not valueless, as inferior to the more recent methods of Campbell and Brodmann and himself, namely, the study of the cell and fibre architecture of the adult cerebrum. Monakow, in his criticism, drew attention to the small proportion which the projection fibres form of the total mass of cortical fibres of any of the convolutions, and he thinks that it is not possible, however roughly it be done, to define the regions which are poor in these fibres and those which are abundantly supplied with them. Sachs, whilst admitting that the sense centres are sharply defined off at an early period from the rest of the cortex, considered it impossible to prove later, when myelination has advanced, that medullated projection fibres do not pass to the centres of association. Bianchi also has for many years strongly combated the generalisations of Flechsig. He is not satisfied that myelination of the various bundles of cortical fibres follows a constant law or occurs in a regular sequence. He denies that the phenomena of anatomical evolution need necessarily presuppose the existence of functional activity of corresponding grade. He remarks, for example, that there may be complete myelination of the supposed centre for reading in the brain of an imbecile who has never learned

to read. He is of the opinion that the only region of the brain which can be regarded as purely associational in function is the prefrontal area, which is generally acknowledged to possess no fibres of projection; and, excluding the language zone, he considers that the whole post- and infra-Rolandic portion of the cortex cerebri is perceptive in function. "One can symbolise the cerebral mantle as a state with a representative system—a parliament and government. The mantellar parliament would be constituted by the perceptive zones. . . . The central government would be represented by the frontal lobes." (Textbook, 1906, p. 172.) Bianchi, in other words, denies that the post- and infra-Rolandic parts of the cerebrum can be subdivided into areas of projection and zones of association.

As a general statement it may be remarked that the conclusions of Flechsig, in their essential features, have been widely accepted, and that, whilst the projection areas, as has been already pointed out, probably occupy neither the identical position nor the same extent of cortex in the adult brain that they do in the fœtus and infant, it may be assumed that a great parieto-temporal centre of association exists posteriorly, and a more complex prefrontal centre of association anteriorly, the insular and precuneal centres being less complex in type, and probably of less importance, than either of the former.

After this introduction to the question in its more general aspects, the subject of cortical localisation by histological methods will now be considered in detail.

The first important paper on cortical localisation was that of Bevan Lewis and Henry Clarke, published in 1878, on the cortical localisation of the motor area of the brain. This communication, which localised the motor area in front of the furrow of Rolando, attracted little attention owing to the fact that the conclusions contained in it were opposed to the results of the numerous physiological experiments which, during the last two decades of the nineteenth century, largely monopolised the field of inquiry into the functions of the cerebrum. The observations of Lewis and Clarke have, however, at last obtained complete if belated recognition in consequence of the experimental work of Sherrington and Grünbaum, recently confirmed by Oscar Vogt, and the histological researches of Campbell and of Brodmann. It is an interesting and in many respects a fortunate fact that the experi-

mental method, which was responsible for the non-recognition of an important contribution to our knowledge, was also the method which first supplied evidence of its truth.

With the exception of the elaborate cell and lamination studies of Hammarberg, which were published posthumously in 1895, and of a paper by Schlapp in 1898 on the cortex of the ape, no contributions of direct interest appeared until the year 1900, when the present writer communicated his paper on the exact histological localisation of the visual area of the human cerebral cortex.

In this paper the exact limits of the human "visuo-sensory area" were mapped out in six hemispheres derived from persons with normal vision and from cases of long-standing and congenital blindness, and the surrounding zone of cortex, the lamination of which was unaffected by the absence of vision, was described under the term "visuo-psychic."

The limits given to the former area indicated the approximate truth of the opinion at this time held by Henschen and supported by the embryological researches of Flechsig and the clinico-pathological investigations of Seguin, Vialet, and others; and their correctness has since been confirmed by Campbell, Brodmann, Elliot Smith, and many other investigators.

Since this paper was published, numerous contributions have appeared on the subject of cortical localisation by the histological method.

Of these the chief are by Brodmann (1902–1907), Campbell (1905), W. Kolmer (1901), Hermanides and Köppen (1903), Köppen and Lowenstein (1905), Elliott Smith (1904–1907), O. Vogt (1906), Mott (1907), G. A. Watson (1907), and Mott and Kelley (1908).

In these papers the whole cortex in many orders of mammals has been mapped out into various histologically different regions, but, except in the case of the psychomotor and visuo-sensory areas, experimental or histo-pathological *proof* of the function of these regions is not yet complete.

The most elaborate of these researches are those of Brodmann and of Campbell. These authors have independently mapped out into histologically different areas the whole human cortex cerebri, as well as the cortex cerebri of many orders of mammals. Owing

to the great importance of the subject, which, however, it must be remarked, is still in its infancy, the human maps of these investigators are reproduced here as Figs. 3, 4, 5, and 6.

As might be expected in the case of such elaborate and totally independent investigations, and in view of the great difficulties involved in the cutting up, blocking, sectioning, orientating, and reproducing in diagram form of the cortex of entire human hemispheres, the maps given by Brodmann and by Campbell differ considerably in detail from one another.

They agree with one another, on the other hand, much more than either of them resembles the maps of Flechsig (see Fig. 2). It must not be forgotten, however, that the diagrams of Flechsig indicate the projection areas of the fœtus, which there is reason to suppose differ considerably in distribution from those existing in the adult. This difference is due to the increased development of the later evolved associational spheres in the latter, which affects both the position and the relative size of the earlier evolved projection spheres. For example, Flechsig's area for bodily sensibility is both pre- and post-Rolandic, although he states that the majority of the projection fibres pass behind the central fissure. In the adult it is at least probable that this projection area is entirely post-Rolandic; and it is known that the psychomotor area is pre-Rolandic. At the period when the latter area was considered to be both pre- and post-Rolandic, and to be sensorimotor in function, its supposed distribution closely resembled the fœtal bodily sensibility area of Flechsig; and the two were regarded as identical. The maps of Brodmann and of Campbell must not therefore be regarded as impugning the general accuracy of the diagrams of Flechsig with regard to the projection areas of the fœtus.

It may be remarked that in only two regions are the maps of Brodmann and of Campbell in complete accord, namely, in the psychomotor or Betz cell area (4 of Brodmann and "precentral" of Campbell), and the visuo-sensory area (17 of Brodmann and "visuo-sensory" of Campbell). The former of these is the area mapped out by Lewis and Clarke (1878), and the latter is that mapped out by the writer (1900). The extent of the visuo-psychic region (18 of Brodmann), which was described by the present writer as surrounding the visuo-sensory area, but was not more closely defined owing to its somewhat indefinite limits,

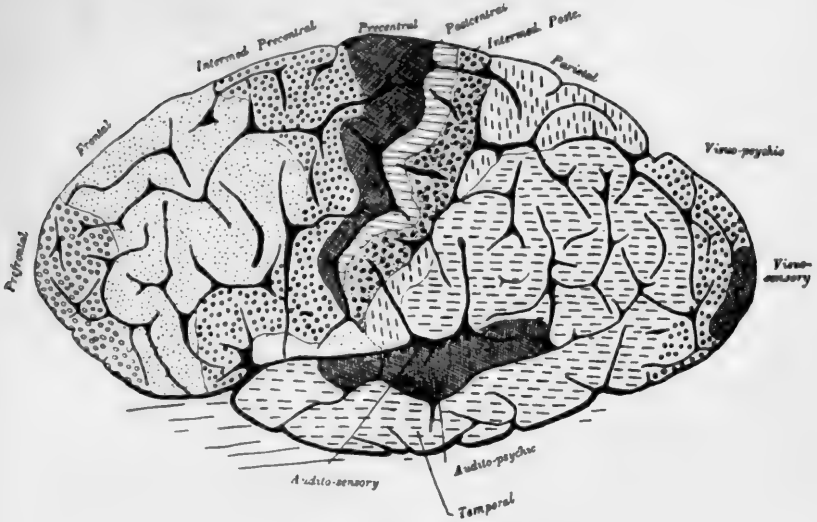

FIG. 3 (Campbell, 1905).

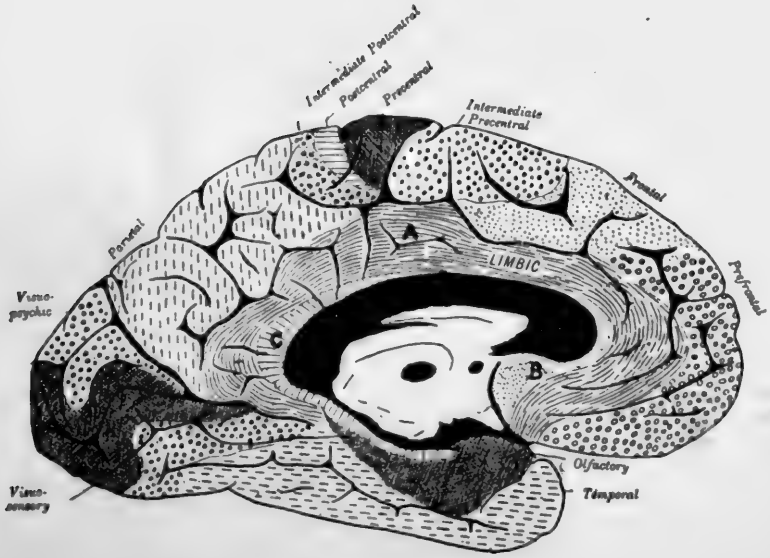

FIG. 4 (Campbell, 1905).

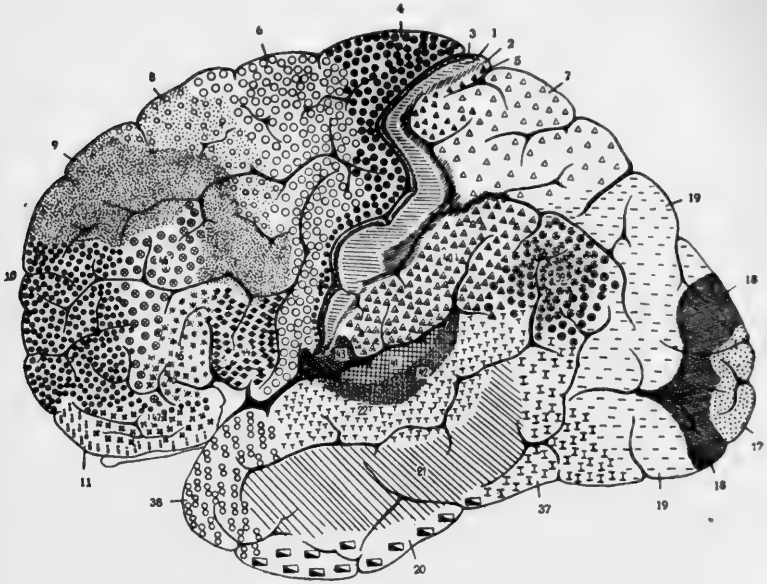

FIG. 5 (Brodmann, 1902–1907).

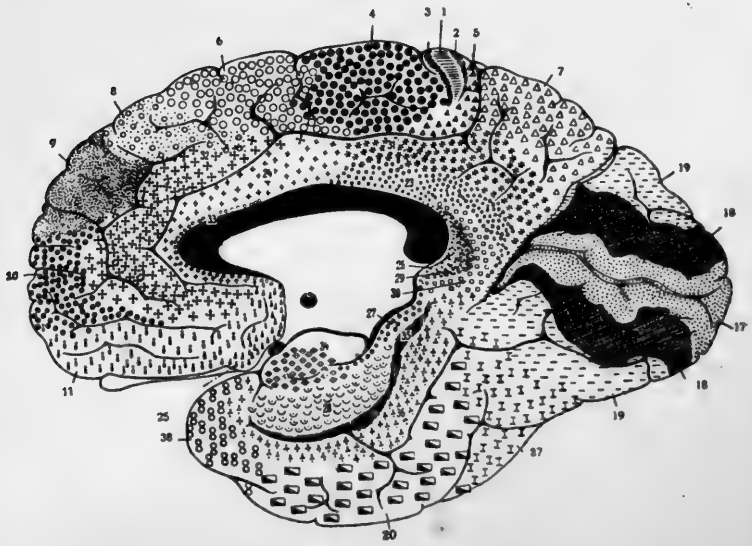

FIG. 6 (Brodmann, 1902–1907).

is given so differently by Brodmann and by Campbell that it might appear that no advance had been made on his original description. A careful study of the maps of Brodmann and of Campbell in the light of the writer's special knowledge of the histological characters of several portions of the cortex cerebri has, however, convinced him that the more elaborately detailed map of the former of these investigators is the more correct. In support of this statement he would refer to the recent paper of Gordon Holmes on the histology of the post-central gyrus, in which the findings of Brodmann are confirmed.

The writer is, however, of the opinion that, whilst further histological research will undoubtedly enable certain other projection areas to be as precisely defined as have been the psychomotor and visuo-sensory areas (even if Brodmann's findings in those respects should not be confirmed in their entirety), the exact differentiation of the remainder and greater portion of the grey mantle into equally precise areas will be attended with great difficulty owing to the probability that considerable differences exist in the case of different individuals. He nevertheless regards such precise differentiation as possible, and considers that light will in the future be thrown on the histo-pathology of amentia or cerebral sub-evolution by this means. For example, in the six occipital regions mapped out by the writer in the paper already referred to, the shape and apparent extent of the visuo-sensory area exhibit considerable individual differences quite apart from the questions of age and blindness. As such differences exist in a projection area, it is probable that more marked variations will occur in the case of the later specialised areas of different brains. Though fissuration and histological differentiation do not run hand in hand, the researches of Karplus on the fissuration of the human cerebrum with regard to family likeness are worthy of mention in this connection.

Beyond a relatively gross subdivision of the cerebral cortex into different areas, it is unlikely that the histological method will be of assistance, as cerebral function, even when relatively low in grade, consists of associational processes which involve many related regions of the cortex. Further, as is shown especially by the study of sense deprivation, the maimed brains of patients suffering from this disability are capable, to a remarkable extent, of replacing the normal methods of association by dis-

similar, though related, modes which in many instances fulfil their purpose in an admirable manner.

Hence, the histological investigation of a given cerebrum is probably capable of affording a rough criterion of the anatomical basis which subserves, not the actual grade of functional activity, but *the possible limits of educability of the organ.* It may be remarked that this mode of viewing the subject disposes of the chief objection urged by Bianchi against the doctrine of Flechsig.

It may therefore be stated that the exact limits of the psychomotor or Betz cell area, and of the visuo-sensory area, are known beyond doubt, and that their functions have been proved by experimental or histo-pathological methods. As regards the less certainly defined visuo-psychic region, the associational, in contradistinction to receptive, function of this area has been developmentally proved by facts stated earlier in this article. These from a different aspect, that of the evolution of cortical lamination, confirm the doctrine of Flechsig with regard to centres of association and of projection. A similar statement may be made with regard to the well-known, but as yet not precisely defined, prefrontal region of the cortex cerebri (10 of Brodmann). Further, anatomical evidence points to the post-central gyrus or some part of it as the projection area for bodily sensibility, and the recent experiments of Oskar Vogt, who states that ablation of this gyrus in the monkey is followed by ataxy without palsy, have finally proved the truth of this view. There are anatomical grounds for considering that the projection spheres for hearing and for olfactory and gustatory sensations are more or less correctly located, but experimental or histo-pathological proof in these cases is not yet available. With regard to the numerous other areas mapped out by Brodmann and by Campbell, there is little doubt that future research will enable both their exact or variable limits to be determined, and their functions to be finally proved.

It is thus possible to make the broad statement that the human cerebral cortex, excluding for the moment the frontal lobes, is histologically differentiable into areas of projection connected with the various senses, each of which areas possesses a zone of cortex connected with or surrounding it, and into further areas which occupy the remainder of the cortex. Reasoning by homology on the truths known with regard to the visuo-sensory and visuo-psychic regions, it is possible to state that the areas of projection

are chiefly concerned with the reception of afferent impressions of various kinds, and that the cortex in relation to each of these is especially concerned with associational functions or psychic processes hall-marked by their several sensory areas. It may further be provisionally stated that a large part of the remainder of the cortex under consideration may probably be regarded as the physical basis of language (not *words*, but word-groupings), *i.e.* a mechanism for the symbolic integration of the various more or less complex products of cerebral association. This question will be considered later in connection with the subject of the higher functions of the human cerebrum.

As regards the frontal lobes, but two regions call for especial remark here, namely, the psychomotor area and the prefrontal region.

With regard to the psychomotor area ("precentral" of Campbell, 4 of Brodmann), it is hardly necessary at the present time to indicate the various reasons which prove that this area is associational and not sensory in function, and that, in addition, it possesses a direct efferent connection with the motor groups of lower neurones.

The cerebral cortex may, in fact, be regarded as a complex sensori-motor mechanism. Of this the non-frontal portion consists of sensory areas (centres of projection) and of zones of association of various types and grades of complexity. The frontal lobes, on the other hand, contain the efferent portion of the mechanism. The psychomotor area may be regarded as the lowest grade of this, and as concerned on the one hand with the integration and on the other with the efferent transmission of the motor expression of the associationally elaborated results of sensorial stimulation.

The prefrontal region (10 of Brodmann) is the most complex of the zones of association of Flechsig. It is the last portion of the cortex to be evolved and the first to undergo retrogression. The outer cell lamina or pyramidal layer of this region varies directly in depth according to the mental power of the individual, in the case of fœtuses and infants, idiots and imbeciles, and chronic and recurrent lunatics without dementia. In cases of dementia, degrees of retrogression occur which vary directly with the existing grade of dementia. Finally this layer of the cortex is the only layer which varies measurably in depth in normal individuals. On

these grounds alone it is possible to assign to the prefrontal cortex the highest and latest evolved functions of voluntary attention and inhibition, and of selection and co-ordination of the various individually complex processes of cerebral association. The prefrontal portion of the cortex is thus concerned in the performance of the highest grades of cerebral function, and also bears to the psychomotor area a similar relationship (though in the converse direction as regards action) to that borne by the posterior regions of association to the centres of projection.

To endeavour to indicate the functions of the cortex of the intermediate portion of the frontal lobes would in the present state of knowledge be to enter the realm of conjecture. It may, however, be remarked that part of this associational zone undoubtedly contains the physical basis of the motor aspect of the mechanism of language, which is the instrument for the symbolic integration of the various more or less complex processes of cerebral association. Until the recent publication of the investigations of Marie and of Monakow, Broca's area was generally regarded, by neurologists at least, as the region concerned with one portion of this mechanism, namely, the "speech centre." Now, however, as will be indicated later, a much broader view must be taken of the complex mechanism of language, which possesses multifarious associational connections with probably the whole cerebrum. The mechanism of language must in fact be regarded, not merely as a series of cortical centres, one or more of which may be blotted out without more than local interference with the mental functions, but as the absolutely essential factor to the adequate performance of these.

With reference to the respective functions of the two greatest centres of association, a large body of neurologists, notably Bastian, Hughlings Jackson, Mott, Schäfer, and Flechsig himself, are of opinion that gross mental disabilities are more likely to occur in lesions of the posterior centre than of the anterior, whilst Wundt, Hitzig, Ferrier, Bianchi, &c., hold the opposite view.

From the purely neurological aspect, especially when considering the different varieties of "aphasia," the former view had undoubtedly much in its favour. For example, until quite recently, cases of Wernicke's (sensory) aphasia were generally considered to exhibit gross mental disability, whilst cases of Broca's (motor) aphasia were supposed to be free from this symptom. The

latter opinion is, however, disputed *in toto* by Marie, who has been confirmed in his observations by numerous recent writers.

Premising, however, that the posterior centres of association were concerned with processes of lower association alone, general mental disability would still be evident in cases of gross lesion of the hinder part of the hemispheres, as the patient would under these circumstances be unable in many cases to produce satisfactory evidence of general mental soundness. In many other cases, also, such an entire disturbance of perceptive and ideational processes as occurs, would be not unlikely to cause too great a strain on the higher associational functions, and to directly result in the development of symptoms of true mental alienation. This is the result which actually ensues in many cases of sense deprivation. It is further rendered probable by the fact that no less than one in every 280 of the general population is at the present time suffering from mental alienation, and that the proportion of potential psychopaths is very much greater. That this explanation is correct is finally shown by the fact that the latest developed and most complex portion of the human cerebrum, namely, the prefrontal area, is, as has already been indicated, the region which is especially affected in the subjects of mental disease.

Though it is not necessary to describe in detail the differences in degree of development and in structure which exist between the cerebrum of man and those of the anthropoid primates, it is desirable, in this connection, to indicate here briefly the chief of these. It consists, as may be seen by a study of the various publications already indicated, in the immense development of the anterior and posterior zones of association which has occurred in the human brain. Concurrently with this increase in the extent of the great zones of association there has developed in man the power of abstract thought and the employment for this purpose of highly complex articulate and written language. As the centres of lower association in the anthropoid primates differ from those of man in extent and complexity, so do the precepts of the former differ from the highly complex lower psychic units of the latter. Equally does the rudimentary prefrontal region of the anthropoid primates, which imperfectly marshals the relatively simple lower psychic units of these animals, differ from the notable and still developing prefrontal lobe of man, the capacity of which, for co-ordinating the infinitely complex lower psychic units, which

are compounded in the human mind, into harmonious series of concepts by means of voluntary attention and selection, is only limited by the degree of functional development of this lobe in any particular individual of the race. The lower associational centres of man, which represent the physical basis of the content of mind, are thus co-ordinate in development with the centre of higher association and co-ordination, which represents the physical basis of the capacity to voluntarily group into a harmonious and connected sequence the higher psychic units of the mind.

Passing now from the highest to one of the lowest orders of mammals, namely, the insectivora, one may obtain histological evidence of equal importance with regard to the functions of the cerebrum. Watson, in his recent paper, has mapped out the minute brains of certain members of this order into histologically different regions. Certain of these areas he regards as centres of projection, and another, on the dorsal and mesial aspect, he designates "motor" from its histological structure. The remainder of the cortex, from the embryonic appearance of the cells contained in it, he designates "undifferentiated." The conclusions of Watson with regard to his investigation are best expressed in his own words :—

"It seems necessary to assume that animals like the mole are possessed of some means of simple sensory association, otherwise it is probable that the animal's waking life would tend to be one of almost continuous sensory confusion. Such association is called up by the stimulation of one or other or more than one special sense, and passes more or less directly to a motor or efferent result. This appears to be the lowest grade of conscious neopallial association—*i.e.* of psychic function—and it doubtless persists in mammals much higher in the scale than the insectivora, and possibly in the highest, though obscured in them by the development of a higher grade or grades. It is not likely to exist as a random passing to and fro of impulses from this sensory area to that, but to lie in some fusion zone. Careful examination of the cortex of animals like the mole has failed to reveal any attempt at the development of a 'psychic' zone in direct relation to any of the sensory projection spheres. The writer does not consider that on histological grounds one is justified in drawing close analogies between the areas he has termed 'undifferentiated' in the mole, &c., and the areas of cortex surrounding the projection spheres in certain higher mammals. From the histo-

logical aspect, therefore, the assumption that animals like the mole possess any special areas of association, however small, appears to be unjustified, and there is also, in view of the following remarks, some reason for believing that such areas are in them physiologically unnecessary, in spite of the probable requirement by these animals of some physical basis for simple sensory association.

"Dr. Bolton has suggested to the writer that in the mole and similar animals the fusion zone for simple sensory impressions, *i.e.* lowest grade of conscious association, lies in the area which has been designated 'motor.' Taking the mole, for example, the areas mapped out as kinæsthetic, fifth sensory, visual, &c., are simple sensory reception spheres for the respective senses, whilst area 1" (motor) "is the psychic equivalent of all these, and at the same time efferent. Area 1" (motor) "would thus receive impulses from each or all of the sensory projection spheres and turn them into motor equivalents. It is a general area of simple sensory association with the origin of the efferent (motor) tracts included. This is as far as such an animal as the mole has got in the direction of higher association. The structure of the cortex, however, even of this area, especially if regarded as being of an associational type, is of a relatively elementary nature.

"The above suggestion does away with the apparent anomaly of the relatively great extent of area 1" (motor) "if this be looked upon as nothing more than a 'Betz cell' region. It also coincides with the fact that this area ranks with the best developed portion of the cortex as regards supra-granular (pyramidal) layer which mammals such as the mole possess, poor though this is.

"The writer's views have been founded upon a study of the cortex cerebri, not only in adult mammals but also in fœtal and young animals. He concludes that in the cerebral cortex of many—and probably of all—adult lower mammals there are areas, considerable in extent, which throughout life advance little—as regards complexity of their component nerve cells—beyond their condition in the fœtal or very young animal. It is therefore on histological grounds presumed that such areas are of comparatively little functional value to the animal.

"He also considers it proved, as the result of the investigations of Bolton and himself, that the structure of the neopallium is founded upon an infra-granular basis. Further, it is suggested that in the earliest attempts at evolution of structure which come to be of any considerable functional value, the neopallium follows the plan of cortical architecture long previously in the phylogenetic scale laid down in the hippocampus, which plan in the latter situation has become fixed, and, as a plan, permanent. The earliest and lowest grade of

neopallial representation is thus, as regards structure, a repetition of the hippocampal type—granular and infra-granular cortex. By the accrescence of a supra-granular layer of varying degrees of depth and complexity of its component nerve cells, different grades of representation may be reached, and are reached to some extent in the same animal, even if this occupies a lowly place in the mammalian phylum, and to a greater extent the higher is the position in the scale to which the animal belongs."

To summarise and correlate the mass of histological data which bears on mammalian cortical localisation from the aspect of cerebral function would be beyond the scope of this article. Many of the observations of the several authors differ greatly in detail, as is naturally to be expected in the case of a subject still in its infancy, and some are contradictory. Further, the greater part of the published work deals with histological observations rather than with physiological deductions. It is thus not yet possible to properly correlate the results of the various investigations which deal with animal behaviour under different conditions, and the deductions which may be drawn from them with regard to the psychic processes which take place in the different members of the various natural orders, with the histological data which have hitherto been obtained with regard to the cerebra of the mammalia.

Evolution of Cerebral Function

The following broad statements, with regard to the mode of evolution of cerebral function, are, however, possible, if they be regarded in the light of a partially proved provisional hypothesis.

The term "neopallium" has been introduced by Elliott Smith to designate the cortex cerebri which is peculiar to mammals, and which consists of a variable area intercalated between the pyriform lobe and the hippocampus. This term is employed in contradistinction to the "archipallium" of the lower vertebrates. The neopallium increases in amount with the ascent of the mammalian scale, and in man constitutes almost the whole of the cortex cerebri.

The functions of the neopallium are the reception of sensorial stimuli, the conservation of associative memory, the performance of the higher psychic processes, and the evolution of the com-

plicated motor phenomena, which depend on these, and which serve as the sole objective indications of the performance of psychic processes.

The neopallium is thus the highest sensori-motor ganglion of the mammalia.

The archipallium is built on a basis which consists primarily of but two cell laminæ, which are homologous with the middle (granule) and inner (polymorphous) cell laminæ of the neopallium (Turner, Watson). The neopallium is characterised by the additional development of an outer (pyramidal) cell lamina, which serves as the physical basis of "psychic" in contradistinction to "instinctive" processes. This cell lamina is barely present in the neopallium of the lowest mammalia, and increases in depth with the ascent of the mammalian scale (Brodmann, Watson). It is earliest and also least developed in the projection areas, and is later developed and more highly evolved in the regions concerned with associational functions. The human brain is characterised by the evolution of a prefrontal region of notable size, and of great complexity of histological structure (Flechsig, Bolton, Turner, Watson). The outer cell lamina of this region varies measurably in depth in normal individuals, and in its degrees of evolution and retrogression varies in depth according to the mental capacity of the subjects of mental sub-evolution and dissolution.

In the earlier evolution of the neopallium, certain projection zones of simple structure exist, together with a rudimentary "motor" area, the function of which is to fuse the products of the projection areas and turn them into motor equivalents. The remainder of the cortex is embryonic in structure (Watson), and is probably latent as regards functional activity.

During the ascent of the mammalian scale, the projection and motor areas increase in complexity of structure (Brodmann, Elliott Smith, Mott, &c.), and advance in functional activity. Until, however, the carnivora are reached (Campbell), there is no indication of the development of histologically differentiable associational zones around or near the centres of projection. It is probable that, in agreement with the relatively embryonic structure of the rest of the cortex, the functional activity of this is largely latent.

By the primates are reached, well-developed and histologically differentiable zones of association exist in the neighbourhood of the projection areas, and similarly developed cortex exists in front

of the psychomotor area. The remainder of the cortex has largely ceased to present embryonic features.

The cerebrum of the higher primates is thus characterised by the evolution of regions of associational cortex, posteriorly between the projection areas, and anteriorly in front of the psychomotor area. The former is probably concerned with the higher elaboration of the "sensorial," and the latter with that of the "motor" aspect of the cerebral functions.

In man the area of cortex devoted to associational functions is enormously enlarged posteriorly, and is still more increased anteriorly by the evolution of a notable prefrontal lobe. Concurrently with this increase in the zones of association, language has been evolved, from both "sensorial" and "motor" aspects, as a complex mechanism for the symbolic integration of the various more or less individually complex products of cerebral association; and the higher psychic functions, of voluntary attention and inhibition, and of voluntary selection and co-ordination into orderly sequence of the processes of lower cerebral association, have been developed.

The Higher Functions of the Human Cerebrum

The further consideration of the functions of the cerebrum, namely, the description, or attempted description, of those functions which are peculiar to man, necessitates the passing of the border-line between physiology and psychology. Hitherto the subject of aphasia has been regarded as a branch of the former science, and has fallen under the purview of the neurologist. Recent investigations, in particular those of Marie, have, however, shown that a wider view must be taken of the relationship of language to the psychic functions, and of the influence on these of the disabilities which are described under the term "aphasia."

As a preliminary to the further consideration of the functions of the cerebrum and to the description of these investigations, it is therefore necessary, for the benefit of such readers as are not versed in psychological terminology, to introduce here certain general observations and definitions.

As has already been remarked, the cerebrum should be regarded as a great sensori-motor ganglion, the only objective indications

of the functions of which are derived from the various motor exhibitions which are presented by its possessor.

In the lower animals these are of two kinds, evidences of feeling or emotion, and evidences of intelligent (instinctive or acquired) activity; and either of these may be partly indicated by means of articulatory exhibitions.

The same evidences of cerebral activity are presented by man, in whom, however, the indications of emotion are more numerous and complex, and the evidences of psychomotor activity are infinitely more elaborate. The latter, apart from the ordinary motor indications of intelligence, consist of gestures and of spoken and written language.

Any discussion of the theory of the emotions would be out of place in this article, but it may be indicated in passing that they are probably evolved from the lower or instinctive plane of motor exhibition. This is suggested by the common observation that very young infants "make faces" indicative of various emotions under the influence of gastro-intestinal irritation, long before they present evidence of intelligent motor activity, and still longer before they are able to articulate a word. Further, objective indications of probably experienced emotions become well-developed in infants at a time when the ordinary motor indications of intelligence are still highly inco-ordinate.

Of the indications of human psychic activity, the most important, namely, *language*, will now be considered.

The elements on which cerebral activity is based are the various sensory impressions which arrive at the cortex and which are conserved there as sensori-memorial images. These elements form the raw material of the psychic processes and are spoken of as *sensations*. To be understood, sensations require localisation in space and reference to the objects from which they arise. The cerebral process involved in the preliminary fusion of sensations is spoken of as *perception*. For example, the sound of a clock ticking results in the localisation of the sensation in a certain direction and to a particular object, the clock. Not only, however, does the process of perception involve the fusion of direct sensations, but it also necessitates the awakening and fusion with these of sensori-memorial images of former sensations. In the act of identifying an object, *e.g.* a locomotive, the various sensations arising from it awaken a variable number of sensori-memorial

images. Again, the sound of the word "horse" awakens certain sensori-memorial images, which may be of any type, from the written word "horse" to the last horse we have seen.

The presentation of a sensation, therefore, results in a cerebral process which evolves the psychic product termed a *percept*. This cerebral process necessarily varies on each occasion on which it occurs. The word "microscope," for example, heard at different times, evokes numerous related but dissimilar sensori-memorial images.

Perception, therefore, is a cerebral process which is similar in nature but differs in detail on each occasion on which it occurs. It is thus incorrect to speak of a cerebral centre for percepts, which are psychic products that, except by accident, need never be identical even if the arousing sensation is the same.

It may be remarked that perception can hardly be described as the act of naming objects, for it is as often the reverse, namely, the act of applying one or more sensori-memorial images to a name; or the identifying of a sensation with a sensori-memorial image. The last corresponds to the crude perceptions of animals: the others to perceptions involving the employment of the symbolic mechanism of language.

The next grade of complexity of cerebral processes which is rendered possible by the aid of language is the formation of a *concept* or general notion, *e.g.* the evolution of a general name such as animal, man, building. The psychic product is termed a concept, and the process of conception involves the revivification of numerous sensori-memorial images which present common points of similarity.

The cerebral process involved becomes still more complex for the evolution of such "abstract concepts" as heaviness, beauty, religion.

It is at once evident that the process of conception, whether it takes the form of generalisation from a series of sensori-memorial images to a general name, or of revivification of a series of sensori-memorial images in order that the meaning of a general name may be interpreted, is a very complex one; and necessarily differs in detail, in spite of a general similarity in nature, on each occasion on which it occurs. It is thus incorrect to speak of a cerebral centre for concepts.

A physical basis for the several words which symbolise the

variable cerebral processes termed conception undoubtedly exists in the cortex cerebri. Common or abstract names, however, are not concepts, but are merely symbols which enable former active processes of conception to be recorded, and future acts of conception to be evolved.

Proper, common, and abstract nouns may thus be compared in function to the algebraic symbols employed by mathematicians, whilst sensori-memorial images and crude sensations may be compared to the numerals of arithmetic.

Language is, however, an infinitely more complex symbolic system than is that employed by mathematicians; and its "numerals," *i.e.* its sensori-memorial images and crude sensations, are innumerable.

As will be indicated later, the complete performance of the respective psychic processes, with the resulting reintegration of the particular percepts or concepts of which words are symbolic, does not necessarily occur during the mechanical employment of the language mechanism. Rowland, in fact, in her investigation of the psychological experiences connected with the different parts of speech, distinguishes three stages of meaning—(1) A feeling of familiarity with the word; (2) a feeling that she would know how to use it; and (3) the unrolling of the images. The paper of this author, which includes a valuable bibliography, is well worthy of study in this connection.

The cerebrum possesses an almost infinite capacity for the development of symbolic systems. New languages may be acquired, and as if on the principle of "the more the merrier," with each new acquisition the process of further acquirement appears to become easier. The numerous skilled psychomotor performances which only compare with language in variety and complexity, *e.g.* music, painting, sculpture, &c., may also be indicated as allied in nature to, though lower in grade than, the symbolic systems of language and mathematics.

The language mechanism, like the routine systems and "red tape" of every-day life, whilst a good servant, tends to become a bad master, unless the cerebral processes necessary for the elucidation of the meaning of the words employed are continually being voluntarily performed. It is thus especially necessary, during the voluntary employment of written or spoken language for the evolution and reproduction of the highest psychic products, *e.g.*

abstract thought, to continually revert to concrete examples. Many results of the higher reasoning processes would in fact be quite unintelligible to the reader in the absence of concrete illustration, and, what is even more important, the author himself would not infrequently find a tortoise successful in its race with a hare. Philosophic disputes have as a rule depended largely on questions of definition, or on the employment of the same words under slightly different connotations. Forms of words are worse than useless unless their exact meaning is appreciated, and many discussions and disputes have arisen owing to the critic holding strictly to these, and thereby rendering it difficult or impossible for their originator to make his intentions quite clear and intelligible.

The necessarily imperfect employment of the language mechanism, owing to the occasional impossibility of satisfactorily discovering a form of words in which to clearly express the exact meaning of the writer or speaker, is in fact one of the most fruitful sources of disputation. It is not intended to imply by this remark that such a person *knows* what he wishes to express. He is aware that the phrases he employs do *not* express what he desires, and at times his uncompleted cerebral processes may reach their goal through the suggestion by another individual of a suitable form of words.

On the other hand, from the purely didactic aspect, a speaker occasionally finds his only safe refuge in generalities which are capable of varied interpretation. Many a sermon is acceptable to, and is approved by, a congregation, which would be up in arms if the preacher produced concrete illustrations of his meaning, *e.g.* his views with regard to certain political questions, &c.

The nature and mode of employment of the symbolic mechanism of language will now be briefly discussed.

The whole of the higher intellectual processes are dependent on, and develop *pari passu* with, the evolution of language. Till of recent years the majority of, and even now many, individuals depend on the sense of hearing for the acquisition of the greater portion of their (human) psychic content, though persons who read and write perhaps gain an equal amount by means of the sense of sight, and the more intellectual members of the race probably acquire the greater part by means of the latter sense. It may, however, be remarked that in some normal intelligent reading-

and-writing individuals visual association, and in others auditory association, is the more natural method of acquisition.

Language, therefore, as the instrument of thought, or even as its compeer, for the higher refinements of thought depend so entirely on, and draw so much of their inspiration from, the possession of a highly elaborate vocabulary, is of fundamental importance for the performance of the higher, as of the less complex, psychic functions.

Language, according to the type of sensorial or sensori-motor avenues through which it is acquired and stored, and by means of which it is employed, possesses four chief physical bases in the cerebral cortex, namely, the auditory, visual, cheirographic, and articulatory. For the sake of simplicity no attempt is made to separate the kinæsthetic from the purely motor divisions of the latter two, though, in fact, it may be regarded as certain that these are differently located. The kinæsthetic divisions, are, however, those which are at present under reference. All these "word-centres" naturally lie in or near the auditory, visual, and general sensory projection spheres of the cortex, as words merely constitute one variety of sensorial impression. It might therefore be supposed that loss of any one of the four afferent avenues to these physical bases of language would not, owing to the commissural connections between the several spheres, be of serious import, apart from the non-reception of sensations through the absent channel. That such a view is incorrect can, however, readily be demonstrated. The spheres referred to, with their commissural connections and their afferent and efferent projection systems, merely form a convenient mechanism for the mechanical acquisition and reproduction of language, which would be meaningless unless during the employment of its mechanism there occurred an active associational participation on the part of practically the whole mantle of the cerebrum.

A word, *per se*, represents merely an auditory or visual sensation, or a cheirographic or articulatory kinæsthetic impression, unless it is employed as a symbol on which to integrate the percept or concept which it signifies; and for this the cerebral mechanisms or associational systems connecting the different projection and sensori-memorial regions of the cortex are needed.

Further, both these developed percepts and concepts, and also the associational processes involved in their formation, differ

not fundamentally but in detail on every occasion on which they are evolved or employed.

Words may arise into consciousness through any of the four language spheres. When, however, they are voluntarily and silently reproduced, *i.e.* thought of, words are invariably awakened through the articulatory word-centre under normal conditions. Further, this reproduction requires a muscular effort, and cannot take place without a definite articulatory attempt, usually, but not necessarily accompanied by a slight expiration. Again, words cannot be voluntarily repeated in thought by means of the cheirographic centre if the hand is not actually moved, unless such hand-movements are replaced by slight movements of the head, or even of the lower jaw or the eyes, through the agency of their respective motor spheres. Such observations as have just been indicated are valuable because they render it probable that the important factors in the reproduction are not the muscular movements but the sensorial impulses derived from these; otherwise there is no reason why such muscular movements should not be imagined without any attempt at their actual performance. If words should spontaneously arise in the visual or the auditory word-centre, the condition is so abnormal as to constitute a hallucination, which the subject may or may not be able to distinguish from a true visual or auditory sensation. A homologous phenomenon to such a hallucination may be observed during the stimulation of the psychomotor area of a monkey which has recovered from anæsthesia. Such an animal regards the movement, say of the arm, with great surprise, and at once performs a voluntary and opposite movement, exactly as if the limb had been moved by an external agency.

There is thus reason to consider that words invariably arise into consciousness by sensorial or sensori-memorial, and not by psychomotor, means; and the observation that normally they are voluntarily awakened by the preliminary aid of the psychomotor area is of significance with regard to the thesis that the frontal lobes are concerned with psychic function from the higher associational and also the motor aspect, and the remainder of the cerebrum from the sensorial, sensori-memorial, and lower associational.

However they arise into consciousness, words naturally possess very different symbolic values. Articles, pronouns, prepositions, conjunctions, interjections, and the simpler adjectives,

adverbs and verbs, when thought of alone (articulatory word-centre), as a rule arouse little beyond their respective visual or auditory word-images, which, in themselves, are meaningless. Adjectives, adverbs, verbs, and abstract nouns, when thought of alone (articulatory word-centre), arouse first their respective visual or auditory word-images. These, however, are meaningless until by complex processes of association they are defined and illustrated through the sensori-memorial spheres attached to the various sensory or projection areas. Common or proper nouns, when thought of alone (articulatory word-centre), may first arouse their visual or auditory word-images, but they frequently at once awaken a whole series of processes of association, and thereby determine the reproduction of sensori-memorial images attached to one or more of the several sensory or projection areas. It may be remarked that any such series of processes of association differs in detail on each occasion on which it is evolved. For example, the mental processes induced by the word "cat," whether this be thought of (articulatory sphere) or be heard or seen (auditory or visual sphere), are different, not fundamentally but in detail, on each occasion on which they are aroused. This ever-varying perceptive content is consequent on the revivification of, and the modification of the complex relations of, the numerous existing sensori-memorial images, of which the word is symbolic, which are constantly taking place under the influence of even apparently unrelated afferent impressions.

Hence, the auditory, visual, cheirographic, and articulatory word-centres merely signify the cortical regions in which lie the physical bases of mental algebraic symbols. These, unless they serve as inciting agents from which spread, in different directions throughout the cerebrum, complex impulses of association, signify no more than unmeaning sounds, shapes, and musculo-kinæsthetic sensations.

Language is produced by the suitable co-ordination of the verbal content of the auditory and articulatory word-centres. It is originally acquired by imitation under the influence of auditory sensations, and in educated persons language is more highly evolved owing to education of the visual and cheirographic spheres. When, however, it has once been acquired, language (*i.e.* functional activity of the several word-centres with their commissural systems) is not necessarily employed as the instrument of thought, although it has been primarily evolved for this purpose.

Examples are common in which the mechanism of language is employed in a purely mechanical manner. Imbeciles can at times learn by rote long paragraphs, of the meaning of which they are ignorant. Children learn a large portion of their lessons in this way. Adults, even, may learn the Lord's Prayer backwards, or sentences in an unknown foreign tongue. Direct evidence of the purely mechanical nature of these performances is often afforded by the inability of the subjects to complete their feat, if they are stopped during its course, unless they start again at the commencement. Occasionally quite remarkable examples of mechanical memory and of mechanical employment of the word-centres are met with. From the former aspect may be mentioned the reproduction of long verbal or musical compositions after a single reading or hearing, and from the latter the performances of "calculating boys." An interesting article on the latter subject has recently been published by F. D. Mitchell.

Examples of this mode of employment of the language mechanism may be readily drawn from every-day life. Many word-complexes, which are frequently repeated, *e.g.* daily prayers, are often gone through in a purely mechanical manner, whilst the individual reproducing them is perhaps thinking of something else. Again, it is appreciated by few that language, as normally employed, is very largely a purely reflex, or, at any rate, automatic function; and that the significance of what is spoken is but feebly appreciated by the speaker. In the majority of persons the word-vocabulary which is in common use is very limited, and the phrase vocabulary is both extremely limited, remarkably stereotyped, and in many instances quite automatically employed. In educated, and particularly in "well brought up" persons, on the other hand, the word and phrase vocabularies, though equally stereotyped, are much more extensive in range.

The voluntary employment of the language mechanism is attended by greater executive difficulties than is the reflexly induced and automatically performed mode which has just been indicated; and it is at times involuntarily incited, to the detriment of the performer, by emotional disturbances. For example, nervous persons, when in the presence of their real or imaginary, social or intellectual, superiors, speak haltingly and from a limited vocabulary owing to the attempt to converse, not automatically, but to order. On the other hand, in the voluntary employment

of written or spoken language for the evolution and reproduction of the highest psychic products, *e.g.* the production of an abstruse thesis, the language mechanism is made use of solely for the purpose for which it has been evolved, namely, as the instrument, and the important assistant, of thought.

During the above observations an endeavour has been made to indicate that language, though so commonly employed in a largely automatic manner, and with but a feeble appreciation of its signification, is nevertheless in essence a symbolic mechanism for the integration of sensori-memorial images, and, though more complex, is analogous, as an instrument, to the symbolic system employed by mathematicians.

By its use it is the servant, and the necessary servant, of thought; by its abuse it becomes the compeer, or even the supplanter, of thought.

It is evident from the above considerations that any gross structural or functional derangement of the language mechanism must necessarily seriously impede, or even in certain cases prevent, the adequate performance of those complex processes of association which serve as the physical basis of the psychic functions.

Apart from its general bearing on the higher functions of the cerebrum, this discussion of the language mechanism has served a further purpose, namely, the paving of the way to a clear understanding of the far-reaching importance of the investigations of Marie on the subject of aphasia.

With the latter object in view, another allied subject will now be considered, namely, the gross modifications of cerebral function which are the necessary consequences of congenital or acquired deprivation of the senses of hearing and sight. In cases of sense deprivation, the structural and functional maiming of the cerebrum concerns one or more of its earliest developed, most stable, and functionally lowest parts, namely, the centres of projection. Such lesions consequently present a simpler problem for study, in spite of their far-reaching influence on the functions of the cerebrum, than do the variable and often diffuse lesions which produce the complex symptomatology of aphasia.

The senses of sight and hearing, especially the latter in uneducated individuals, are so necessary to, and play such an important part in, both the evolution and the conservation of the

normal functions of the cerebrum, that deprivation of one or both of these senses in congenital or early cases grossly modifies, and in adult cases necessitates an entire readjustment of, the associational processes which constitute the physical basis of the psychic functions.

In cases of deafness or blindness in which the deprivation is congenital or is acquired in early life, the psychic functions are either very imperfectly evolved, or are performed in an entirely abnormal manner. In early or congenital deafness, the complex mechanism for the reception, storage, and reproduction of language, or the symbolic representation of the results of sensorial excitation and of psychic association, is incapable of evolution, unless the patients are laboriously educated through other avenues of sensation. It is hardly necessary to add that mutism is a necessary consequence of this disability, though a considerable development of lip-language can often be induced by education. Such patients, in fact, unless educated by special methods, would necessarily possess mental functions relatively little removed from those of the lower primates. On the other hand, the congenital or early blind can obtain a large and important part of their mental content by means of the sense of hearing, just as do ordinary uneducated (*i.e.* non-reading and non-writing) individuals. That the former can supplement their methods for the acquisition and communication of information by means of the deaf and dumb alphabet, &c., and the latter by means of the tactile motor sense, does not affect the fundamental difference between them, which is based on the fact that a highly important part of the mental content is normally (in the uneducated) acquired by means of the sense of hearing and not by that of sight.

In such cases deafness is therefore a more serious deprivation than blindness, as, for the evolution of the functional activity of the cerebrum, an entirely new development of associational spheres, to replace those normally employed for auditory and spoken language, has to be acquired. In the case of congenital or early acquired blindness, on the other hand, the complex sphere of language, with all its psychic components, can be employed in a perfectly normal manner, and almost exactly as it is brought into use in the case of persons who neither read nor write.

Deprivation of sight or hearing, when occurring later in life, results, in the educated, in relatively less cerebral disability, and

probably an approximately equal amount in the case of either of these senses. In the uneducated, loss of hearing produces greater cerebral disability than does loss of sight.

In all cases of acquired deafness or blindness, however, the following results ensue. On the one hand, the patient suffers a permanent loss of one or both of the important avenues of special sensation, and on the other, all kinds and degrees of structural and functional impairment develop in the cerebrum in consequence of the deprivation. Not only does secondary atrophy of the particular afferent fibres to the cerebrum result, but the complex associational relations between the special projection area or areas and the rest of the cerebrum are seriously affected. The special sensori-memorial images dependent on the lost sense or senses pass more and more into the sphere of the permanently subconscious. The physical bases for the evolution of even the most elementary (already experienced) percepts require readjustment to the altered conditions. Finally, the mechanism for the development of new and the correction and continuation of already experienced percepts, which normally involves the majority of, if not all, the projection or sensory areas of the cerebrum, together with their related memorial spheres, becomes imperfect or "maimed."

In all these types, therefore, both sensory and also extensive and grave associational deprivations exist; and the cerebrum, as a machine, is maimed not only in its most stable and earliest acquired regions, namely, in one or more centres of projection or sensory areas, but also throughout its intricate, later evolved, and more important (from the psychic aspect) systems of lower association.

Sense deprivation is, however, followed, in all, or nearly all, early and congenital cases, and in many acquired cases, by still more serious disturbances of the psychic functions than those already indicated. In the former, imperfect evolution of the higher functions of mind is usual if not invariable; and in both types dissolution of the centre of higher association, with consequent dementia, is of common occurrence. In congenital cases involution of the centre of higher association, with resulting dementia, is eventually incited by the stress of prolonged sense deprivation and the consequent abnormal modes of psychic association which result. In other words, the abnormally working psychic machine sooner or later breaks down.

In persons who acquire sense deprivation later in life, the mental stress involved on the one hand in the sense disability, and on the other in the more or less unsuccessful attempts to revive the related memories which tend to pass more and more into the permanently subconscious, or to replace the absence of these memories by the integration of percepts and concepts on an unusual sensori-memorial basis, often, or perhaps invariably, results in the development of irritability, or depression, or general emotional instability. In rare cases like one cited by Clouston, partial removal of the sense deprivation by operation (for cataract) may result in a return to normal psychic life. In the case, however, of individuals who possess higher cortical neurones of deficient durability, insanity followed by dementia ensues.

It may finally be stated that cases of congenital or early acquired deafness are more liable to imperfect mental development, with which is associated mutism, than are cases of congenital or early acquired blindness.

Further, both in the cases in which the sense deprivation is congenital or acquired early in life, and in those in which it is acquired after adult life has been reached, cerebral involution is more likely to occur in the case of the deaf than in that of the blind. This statement is supported by a series of cases which were recently published by the writer, for, of the ten in the series, three were deaf and dumb, two were deaf, four were almost or totally deaf and blind, and only one, a well-marked high-grade ament, who had been certified for thirty-seven years, was blind.

Recent Researches on Aphasia

The description of the language mechanism and the evidence of its fundamental importance to the performance of the psychic functions—especially that derived from the study of cases of sense deprivation—have been given at considerable length. Whilst the primary object of the writer has been the elucidation of the manner in which the higher functions of the cerebrum are performed, he has at the same time endeavoured to so present the subject of language as to prepare the reader, not merely for the appreciation of the gist of the recent researches on aphasia, but for the acceptance of their results as truths of great importance.

The statements, that our views of aphasia require entire re-

vision, and that the time-honoured localisation of the motor speech centre in the cortex of the posterior portion of the third frontal gyrus (the speech area of Broca) is incorrect, are of so revolutionary a nature that the reader may well require more evidence of their truth than is afforded by the papers even of so renowned a neurologist as Pierre Marie. Such evidence as can be derived from the psycho-physiological study of the subject of language, and from the results of recent research on cortical localisation and cerebral function, the writer has endeavoured to produce.

Before indicating the views of Marie, it is desirable to refer shortly to the theory of aphasia, advanced almost simultaneously by Monakow in 1906. This investigator throws doubt on the accepted localisation of the speech centre, and expresses the opinion that aphasic disorders are caused less by destruction of certain special regions of the cerebrum than by local losses of functional continuity between the various centres which together constitute the language mechanism. To this disturbance of functional continuity he applies the term *diaschisis*. He indicates that local affection of a connecting tract of fibres may cause temporary suspension of the functions of one part of the mechanism by removing from this the stimulus to action which normally proceeds from another part. On the other hand, relatively independent parts of the mechanism may pass into a state of abnormal activity from lack of the controlling impulses which normally proceed to them from other portions. Disturbances of local function may thus arise in consequence of lesions situated in different parts of the brain.

This theory is propounded by Monakow to explain the frequent discrepancies which exist between the clinical symptomatology and the anatomical lesions of cases of aphasia.

He points out that many cases of aphasia occur in which search for the expected lesion gives a negative result; that a still larger number of cases recover although the lesion persists and even becomes more extensive; and that aphasic disorders often persist in cases in which the lesion is found to be situated beyond the limits of the speech area. He further remarks that "sensory aphasia" may occur with lesion of Broca's gyrus, and "motor aphasia" with lesion of the zone of Wernicke; and that at times the symptomatology varies greatly in cases in which the situation and relations of the lesion are practically identical.

The views of Monakow may thus be regarded as affording a plausible explanation of the contrary and negative evidence, with regard to the localisation of the speech-centre, which has been published ever since the time of Charcot.

The articles of Pierre Marie, the first of which was published some months earlier than the paper of Monakow, treat the subject of aphasia in a more radical manner.

Marie, as the result of a study of the subject during a period of ten years at the hospital at Bicêtre, has expressed the opinion that the whole of the accepted doctrines regarding aphasia require reconsideration.

He distinguishes in the orthodox manner between "motor aphasia" or the aphasia of Broca, "sensory aphasia" or the aphasia of Wernicke, and "anarthria" or the subcortical motor aphasia of Déjérine.

In the first of these conditions the patient is usually described as being unable to speak, although he understands what is said to him, and as a rule retains his intellectual powers unimpaired. In the second the patient is regarded as being able to speak in a more or less intelligible manner, but to have more or less marked impairment of intelligence. In the third, the only disability which exists is loss or affection of the power of articulate speech.

In order to explain the views of Marie it is unnecessary to consider in detail the various more or less complicated types of symptomatology, which occur in cases of aphasia, and which are readily classed under one or other of the aphasias of Broca and of Wernicke. For such a description the reader is referred to the various classical publications.

As the result of his investigations Marie considers that only one form of true aphasia exists, namely, that of Wernicke, and that the so-called "aphasia of Broca" is the "aphasia of Wernicke" + "anarthria." He considers that Broca's gyrus is not concerned with the function of speech, that the "area of Wernicke," namely, the supra-marginal and angular gyri, and the hinder portions of the first and second temporo-sphenoidal gyri, is the site of the lesion which causes true aphasia, and that a lesion of the lenticular zone is the cause of anarthria.

Marie thus limits the lesion of aphasia to the region of the cerebrum which has till of late been regarded as the seat of the visual and auditory word-centres.

Further, and this is the most important part of the doctrine, Marie urges that in true aphasia intellectual impairment is invariably present. "C'est qu'il y a chez les aphasiques quelque chose de bien plus important et de bien plus grave que la perte du sens des mots; il y a une *diminution très marquée dans la capacité intellectuelle* en général." He considers that the notion of intellectual impairment should dominate the doctrine of aphasia.

He affirms that in all cases of the aphasias both of Broca and of Wernicke there is a greater or lesser amount of difficulty in the understanding of spoken language, and that evidence of definite diminution of the intellectual powers can invariably be obtained if the patients are properly studied. For this purpose he gives his subjects complicated instructions. Instead, for example, of telling the patient to cough, spit, put out his tongue, or shut his eyes, he gives certain instructions of which the following two are very commonly employed. "Of three pieces of paper of unequal size which are placed on this table, you will give me the largest, you will crumple up the medium one and throw it on the ground, as to the least you will put it in your pocket." . . . "You will stand up, you will go and tap three times on the window with your finger, then you will return before this table, you will walk round your chair, and you will sit down." He points out that, on superficial observation, aphasics may appear to possess normal intelligence, but that careful investigation readily enables their defective mental powers to be determined. He gives, as an illustration, a description of the blunders made by an aphasic who, prior to the onset of his infirmity, had been a really good cook, when he was provided with the necessary ingredients and instructed to prepare an "œuf sur le plat" or fried egg. His account of the incident is as follows:—

"Un de mes malades, atteint depuis des années d'une aphasie d'intensité moyenne qui ne l'empêche d'ailleurs pas de se mêler à la vie commune, est un cuisinier, un bon cuisinier qui, sans aucun doute, savait bien son métier. Je lui demandai un jour de me faire un 'œuf sur le plat.' Nous nous rendimes donc tous à la cuisine, avec la surveillante qui devait remplir les fonctions d'expert. Là, devant le fourneau, on remit au malade les ingrédients necessaires: un plat, un œuf, du beurre, du poivre et du sel et on l'engagea à exercer ses talents. Cet homme hésite un

moment, puis commet les solécismes suivants, qui nous sont au fur et à mesure signalés par notre surveillante, passablement scandalisée de voir un cuisinier se tirer aussi mal d'une épreuve qui, pour une simple ménagère, n'eût été qu'un jeu : il commence par casser son œuf de façon fort maladroite et le vide dans le plat sans aucune précaution pour éviter de crever le jaune, puis il met du beurre dans le plat, par-dessus l'œuf, saupoudre de sel et de poivre et met le tout au four. C'était là une faute capitale et la surveillante nous fit remarquer qu'il avait fait l'inverse de ce qui devait être fait, le beurre devant être chauffé au préalable et l'œuf jeté dedans. Inutile d'ajouter que le plat n'était absolument pas présentable, ce qui, d'ailleurs, ne parut pas émouvoir outre mesure notre malade. Ici encore il est bien évident qu'il ne s'agissait pas d'un trouble du langage, mais d'une déchéance intellectuelle."

Further, Marie denies that aphasics are able to express their meaning, in the absence of speech, by means of descriptive mimicry. For example, he states that he has never yet come across a patient who was able in this way to indicate his occupation when asked to do so.

He thus considers aphasia to be essentially characterised by an impairment of the intellectual powers, and he therefore regards the "area of Wernicke" as an intellectual and not a sensory centre. His views are consequently in accord with the more recent results of the study of cortical localisation, for the area of Wernicke is a zone of association and not an area of projection. The visual and auditory word-centres naturally lie in either the "sensory" or the "psychic" zones devoted to vision and hearing respectively, for there is no essential difference between the cortical projection of, and the conservation of the image of, a word, and of any other cause of sensorial stimulation. Marie, in fact, though he attributes word-deafness to defective comprehension and denies the existence of this as a pure symptom, admits the existence of word-blindness as a fairly pure symptom, associates it with hemianopsia, and locates its lesion in the general visual centres. In this connection the attention of the reader may be usefully drawn to the observations already made on the psycho-physiology of the language mechanism in educated and uneducated persons. Language is learned through the sense of hearing, and it is only by education that it is further learned by the sense of sight. Word

vision is thus an additional acquisition superadded to the mechanism of language, which under normal circumstances can carry on its functions in the absence of the capacity to read and write. It is therefore only to be expected that word-blindness should be found clinically to be fairly common as a pure symptom, and should be less intimately associated with the general functions of the cerebrum than word-deafness, which disability necessarily seriously maims the normal, and earliest developed, mechanism for the acquisition and reproduction of articulate speech.

It may be added that Marie does not deny the existence of pure motor aphasia, but he terms this "anarthria," and locates its lesion in the lenticular zone, namely, "in the lenticular nucleus, in its neighbourhood, in the anterior part and the genu of the internal capsule, or, may be, in the external capsule." That such a lesion may cause the subcortical motor aphasia of Déjérine is of course generally recognised, but Marie goes further and denies that pure motor aphasia can also occur in consequence of a lesion in Broca's gyrus.

It is impossible to summarise here the pathological evidence which is produced by Marie in support of his contention, but the general scope of his inquiry may be indicated.

He states that an examination of the original specimens of Broca clearly shows that they do not afford adequate support to his localisation of the speech-centre in the posterior portion of the third frontal gyrus. He remarks that when Broca enunciated his doctrine in 1861 he was thirty-seven years of age, and was not yet a professor; and that Bouillaud was sixty-nine years of age, and had been professor of clinical medicine at la Charité for thirty years. He then suggests that Broca's views gained acceptance owing to the still dominant influence of Bouillaud, who even in 1825 had localised the faculty of articulate speech in the frontal lobes, which localisation Bouillaud regarded as confirmatory in this respect of the phrenological doctrines of Gall. Marie then traces the crystallisation of Broca's views into the form of a dogma to the experimental investigations of Fritsch and Hitzig, of Ferrier and Yeo, &c.

With regard to his own researches, Marie states that his doctrine of aphasia is based on the systematic examination, during a period of ten years, of nearly a hundred cases of aphasia, which included more than fifty autopsies.

He adopts a twofold line of argument to prove that "la troisième circonvolution frontale gauche ne joue aucun rôle spécial dans la fonction du langage" (p. 243). On the one hand he shows that cases exist, in right-handed individuals, in which local destruction of the posterior part of the third frontal convolution is not followed by aphasia. One of Marie's figures in illustration of such a case is reproduced opposite (Fig. 7).

On the other hand he shows that characteristic examples of the aphasia of Broca occur in which the third left frontal convolution is absolutely intact. In Fig. 8 is reproduced an illustration of such a case.

The patient was a beautiful example of the aphasia of Broca. The gyrus of Broca is intact. The "aphasia of Broca" which was presented by the patient is here attributed to a lesion R-R1, which is the cause of the anarthria, and to a lesion R1-R11, which has given rise to the aphasia.

The views of Marie, which in his first paper were indicated and illustrated, rather than supported by the complete evidence on which they are based, have naturally re-aroused interest in a subject which of late years has been taught in dogmatic form rather than investigated. One of his earliest critics was Déjérine, who bitterly opposed his doctrines with regard to both sensory and motor aphasia, and endeavoured to demonstrate that they are in complete opposition to the facts derived from clinical observation. Marie, in a subsequent article, replied in a masterly and restrained manner to the vehement criticisms of Déjérine, and, in a third, published an essay on the genesis and mode of evolution of the doctrine of Broca.

In September 1907 an important discussion took place at the International Congress at Amsterdam, and many of the leading neurologists in the world expressed their views on aphasia. It is a significant fact that the speakers as a whole appeared to lay stress on the absence of definite knowledge regarding the exact lesions which produce the different types of symptomatology grouped under the term "aphasia," rather than to discuss any particular types of lesion.

The chief evidence on which the views of Marie are based has recently been published by his pupil Moutier in a bulky volume entitled *L'Aphasie de Broca*. In this work the whole question of aphasia is elaborately and fully discussed. After a historical

FIG. 7.

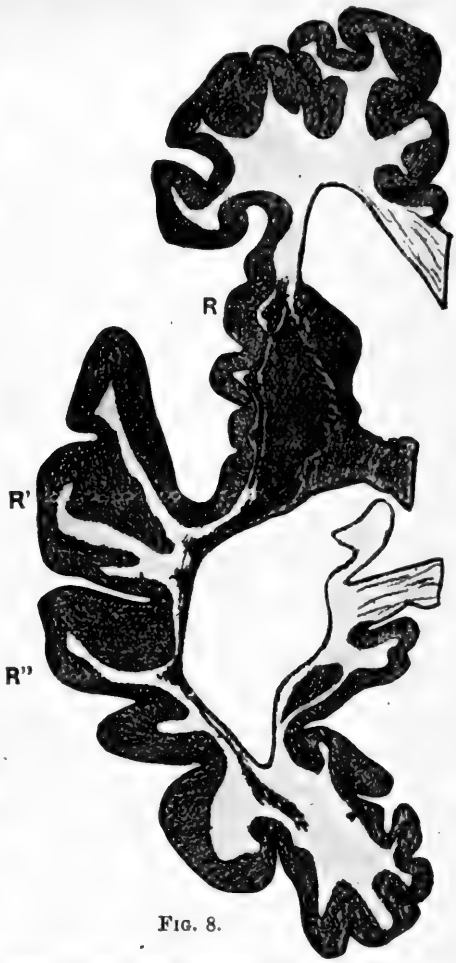

FIG. 8.

FIG. 7 (Marie, 1906).—Horizontal section of the left hemisphere of Ber. . .
The third frontal convolution is almost entirely destroyed by a softening. This patient showed neither any sign of Aphasia nor any anarthric trouble.

FIG. 8 (Marie, 1906).—Horizontal section of the left hemisphere of Per. . . .
The softening met with here is the type of *deep softening* of form B. It is indicated by the black line which, from R to R', occupies the external capsule and the base of the white substance of the convolutions of the insula. At R' the line of softening bifurcates and extends forward and inward towards the internal capsule; posteriorly the softening crosses the temporo-parietal isthmus, and passes into the white substance of the temporo-occipital lobe R'', where it occupies the neighbourhood of the external wall of the occipital horn of the lateral ventricle, and follows its contour closely; it leaves this wall quite at the back of it and ends in the white substance of the occipital lobe.

This patient was one of the finest cases of the Aphasia of Broca that I have had the opportunity of observing. Here the Aphasia of Broca had been set up, owing to the lesion R R' which had caused Anarthria, and to the lesion R' R'' which had caused Aphasia.

description of the genesis and mode of evolution of the doctrine of Broca, the following table (p. 96) is introduced—

Relevé total des cas avec autopsie (1861–1906) . . .		304
Observations inutilisables		201
1. Insuffisantes	26	
2. Lésions trop étendues	175	
Restent 103 observations avec destruction localisée :		
1. Favorables a la 3e frontale (ou tenues pour telles) . . .		19
(*a*) Lésion corticale	8	
(*b*) Lésion sous-corticale	11	
2. Contraires a la 3e frontale		84
(A) Il y a aphasie. Le pied de F3 est intact . . .	57	
(B) Il n'y a pas d'aphasie. Le pied de F3 est détruit .	27	
(*a*) Par traumatisme	4	
(*b*) Par tumeur	14	
(*c*) Par ramollissement.	5	
(*d*) Des deux côtés	2	
(*e*) Chirurgicalement chez un droitier . . .	2	

In this table the author summarises all the cases, recorded up to 1906, in which the results of post-mortem examination are stated. It will be noted by the reader that, of the 304 recorded cases, but 103 possess the necessary details or exhibit sufficiently circumscribed lesions, for their utilisation as evidence for or against the doctrine of Broca. Of these 103 cases but 19 are in favour of, and no less than 84 are against, the localisation of the speech-centre in the posterior part of the third frontal convolution.

The subject of aphasia is considered in detail from both anatomical and clinical aspects. A complete bibliography from 1861 to 1907 is inserted. According to their relative importance, more or less lengthy details regarding the cases recorded in the several publications are inserted in a convenient form for reference. Half the volume is devoted to a description of the personal observations of the author. The methods employed for the clinical examination of aphasics are described, and detailed records of 44 cases are inserted. The book contains 175 illustrations, many of which are full-page plates.

The bearing of the views of Marie on the subject of cortical localisation will now be considered.

It must at once be confessed that the doctrines of Marie are destructive rather than constructive from the aspect of cortical

localisation. On the other hand, from the aspect of cerebral function, they are throughout constructive in tendency. From both points of view, however, they are in accord with the results of recent histological and psycho-physiological research.

From the aspect of cortical localisation, Broca's speech-centre is disrated by Marie. This is a conclusion for which modern histological investigations have already prepared the way. On referring to the maps of Brodmann and of Campbell, the reader will see that both these observers indicate a histological type of cortex ("intermediate precentral" of Campbell, and 44 of Brodmann) in the posterior third of the inferior frontal convolution, which differs from that of the psychomotor area. Campbell, in fact, whose monograph appeared before the publication of the papers of Marie, protested against the assumption that a lesion of the area of Broca is the essential factor in the production of motor aphasia on the ground that this region is histologically undifferentiable from, and is included in, his "intermediate precentral" area. He cites two cases of destruction of Broca's area in which permanent motor aphasia existed. In a third case, however, in which the area of destruction is even more extensive, the patient, though twelve years previously he had suffered from complete but transitory aphasia, exhibited no speech defect whatever during the whole of this period and right up to the time of his death.

The more detailed map of Brodmann, it is true, indicates a special histological type (No. 44) in Broca's area, but this type does not possess "motor" characteristics, and is indeed separated from the psychomotor or Betz-cell region (No. 4) by an area (No. 6) which, though less in extent, is similar in distribution to the "intermediate precentral" area of Campbell. If, as Campbell suggests, this last area is "specially designed for the control of skilled movements of an associated kind," his argument *re* motor aphasia is strengthened by the exclusion from this "intermediate precentral" region, by Brodmann, of Broca's area.

The views of Marie will now be considered with regard to their bearing on our knowledge of the functions of the cerebrum. Marie states that the essential feature of aphasia is the existence of intellectual impairment, although the patient may appear, from the aspect of every-day life, to possess normal mental faculties. To put this opinion into other words, Marie in effect states that

the sufferer from aphasia is sane, but at the same time suffers from intellectual disability.

As has been remarked earlier in this article, the prefrontal region (No. 10 of Brodmann) is the highest zone of association, and insanity depends on sub-evolution or dissolution of this region. In the case of sub-evolution the patient may be permanently idiotic or imbecile, permanently or temporarily insane, or liable to the onset of insanity: in the case of dissolution, according to its degree, the patient suffers from a corresponding grade of permanent dementia.

On the other hand, it has been stated that the post- and infra-Rolandic regions of the cerebrum contain the sensory projection spheres and the various zones of association subserving the complex associational processes which occur with regard to the projection spheres individually and collectively. A gross lesion situated in the "area of Wernicke," *i.e.* in the very midst of this region of association, must therefore seriously interfere with the performance of the cerebral functions of lower association, namely, with the evolution of percepts of various types and grades of complexity.

Further, according to the distribution and depth of the lesion almost any grade and type of psycho-sensorial disability may be expected. The greater its proximity to the visual or auditory projection spheres, the greater must be the likelihood of relatively pure word blindness or deafness. For reasons already stated, the former of these disabilities can only occur in persons who have learned to read and write, and it is the more likely to exist in a pure form. The latter can occur in either educated or uneducated individuals, and in either case is unlikely to exist in a pure form (see pp. 334–5).

On the other hand, a lesion, and especially a superficial one, located away from the projection spheres, would be expected to cause disabilities with regard to the more complicated processes of lower association, with resulting intellectual impairment.

As will have been gathered from the remarks on the function of language, the complex mechanism which serves as its physical basis must necessarily be co-extensive in distribution with the projection spheres, and the whole region of lower association. The visual and auditory word-centres lie in or near the visual and auditory projection spheres, as words seen and heard are merely

one variety of sensorial impression. On the other hand, the more or less complex cerebral processes which are needed for the evolution of the percept symbolised by a certain word may involve the cortex in and near each of the several projection spheres. For example, the word "mouse" at once sets on foot processes of association which pass to every projection sphere with the solitary exception of the gustatory, and even this may be reached in a person who has eaten a fried mouse in the hope of thereby recovering from an attack of whooping cough.

We may note a word, *i.e.* receive the sensorial impression produced by it; we may go a step further and recognise it as understandable; but it is only when, by active, though not necessarily voluntary, processes of cerebral association, numerous sensori-memorial images of different orders have thereby been aroused into the field of consciousness, that the word acquires meaning. These processes of association are of widespread distribution, and differ in detail, though they are similar in their general tendency, on each occasion on which they occur. In the normal brain these processes of association are directed and controlled, and suitable sensori-memorial neurone complexes are accepted, whilst undesirable are rejected, by means of the centre of higher association. In dreamy states they follow certain natural laws, and their course depends solely on the existing state, as regards excitability, of the various associated groups of neurones. In the maimed brain of an aphasic, whether it be functioning in a controlled or in an involuntary manner, such processes of association are necessarily imperfectly and inadequately performed.

The fairly common, rather than very occasional, determination of an "area of Wernicke," and therefore of "aphasia" as a special symptomatology, like the determination of other special symptomatologies through local cerebral lesions, depends, in fact, on the distribution, and consequent liability to occlusion, of certain branches of the cerebral arteries. Had the arterial supply of the cerebrum been evolved in a different manner, it is conceivable that "aphasia," as it occurs, would be unknown, for lesions due, *e.g.* to tumours, traumatism, &c., would not have sufficed for its complete identification and description.

"Aphasia," however, exists, as a complex of varying types of symptomatology; and the study of these by Marie has produced

a mass of evidence which confirms the correctness of the observations with regard to cortical localisation and cerebral function which have been recorded during recent years. These observations are difficult to correlate with—in fact, they are in many respects opposed to—the hitherto current doctrines with regard to aphasia; but they have received confirmation and derived illumination from the researches of Marie.

The attention of the reader will finally be drawn to certain matters of interest with regard to the functions of the cerebrum, and to a number of recent publications, the consideration of which could not be conveniently introduced into the general text of this article without interference with its continuity.

The first subject which will be briefly indicated is termed "alteration of personality." This may be conveniently defined as a mental state in which the higher cerebral functions are exercised, not over psychic processes founded on such recently acquired time-related portions of the content of mind as constitute the normal personality, but over psychic processes founded on complex and time-related portions of the subconscious content of mind, which exhibit such abnormal prominence as to entirely replace for the time those recent experiences on which normal cerebral activity depends. In such cases not only one, but several such time-related portions of former experience, may separately and at different times acquire abnormal prominence, and thereby give rise to the phenomena of multiple personality. In the normal individual, on the other hand, the recent time-related personality cannot be voluntarily subordinated, and all that is possible in this direction is the occurrence of some degree of associational elaboration of former sensori-memorial images, which is always imperfect and often incorrect. To test the truth of this statement, the reader needs only to endeavour to recall, in a time-related manner, the events of yesterday.

This "alteration of personality" or switching on of a former period of cerebral activity, with temporary obliteration of later experience, is common in hysteria, epilepsy, and hypnotic states. The phenomenon is of importance in that it proves that, whilst the exercise of the cerebral functions is an active process which derives its pabulum from both the past and the present, *the whole of the psychic life is* nevertheless *recorded in the cerebrum in a*

time-related manner. Thus, in certain pathological states of the cerebrum, not only may the clock of cerebral activity be put back, but the subject may reproduce in exact detail lengthy portions of former experience, and, stranger still, may start an entirely new time-related psychic life from the point of former experience to which he has returned. He may then, as if nothing had happened, return to the normal point of cerebral activity and recommence his ordinary time-related psychic life, with complete obliteration, as far as his conscious knowledge is concerned, of the experiences he has passed through whilst in the abnormal psychic state. It is possible, then, for a person to live two or more psychic lives, of which only one is normal, and in his normal waking state to be entirely unaware of the existence, apart from periods of time for which he cannot account, of his other, or numerous, "sub-egos." Interesting cases of "multiple personality" which might seem incredible had they not been studied and recorded by competent and entirely trustworthy observers, have recently been published by Morton Prince and by Albert Wilson. Three less important cases have also been published by Lemaitre.

Such cases differ somewhat from good examples of systematised delusional insanity, which are, however, of interest in this connection. In the latter the personality is altered, but this alteration is due, in the developed state, to the permanently abnormal prominence of certain time-related portions of what should be part of the subconscious content of mind. These particular time-related experiences serve as a basis on which develops a continually increasing aggregation of abnormal psychic units. In other words, in place of the normal gradually changing personality, a certain former personality remains as a permanent basis on which is built up a continually increasing abnormal psychic edifice. In such cases, when they become "chronic," it is probable that the greater part of the available psychic content consists of symbolic verbal groupings which have become relatively stable through frequent repetition; and that the processes of cerebral association required for the reintegration of the former percepts and concepts which these verbal groupings symbolise, and for the revival of old sensori-memorial images, are markedly reduced. These symbolic verbal groupings continue throughout the life of the sufferer to entirely dominate what would otherwise be relatively normal processes of *immediate* cerebral activity, and in this, in effect though greater

in degree, resemble the "opinions" of many of the one-idea-ed "cranks" in the outside world.

It may be remarked that these various abnormal types of cerebral activity are at present chiefly of academic interest, apart from their obvious bearing on criminology. Our knowledge of the psycho-physiology of the brain is still in its infancy, and though it is at any rate certain that in such cases the cerebrum is not functioning in a normal manner during the phases of "alteration of personality," not only is no satisfactory explanation yet forthcoming, but it is even difficult to be certain in the complicated cases which of the several phases represents the "normal." It is probable, however, that the subject will receive illumination when our present crude acquaintance with mental disease is replaced by the scientific knowledge which will undoubtedly follow its systematic study.

Though the more difficult question of the time-related recording of psychic experience in the cerebrum, and of the influence of this on the normal processes of cerebral association, is at present an obscure one, the simpler problem of the manner in which the immediate functions of the cerebrum are performed derives much illumination from the study of insanity. It would be an unwarrantable digression to discuss here the various abnormal types of *immediate cerebral activity* which are met with during the clinical investigation of mental disease. One or two examples may, however, with advantage be introduced for illustrative purposes.

In certain cases classed under the symptomatological group of "mania," the centre of higher association is in functional abeyance, and the cerebrum acts as an uncontrolled sensori-psychomotor machine. Instead of, as normally happens, but a small selected number of the ever-entering stream of afferent impressions being noticed, almost every visual and auditory stimulus in the neighbourhood of the patient is accepted. Processes of cerebral association incited by these occur pell-mell, and find motor expression in emotional disturbance, rapid movements, and a riotous display of words. It is impossible to obtain more than the momentary attention of the sufferer. This condition of uncontrolled sensori-psychomotor activity may last for many weeks, after which the patient becomes, at any rate for the time, sane. Such patients usually exhibit numerous signs of physical and

mental degeneracy; but all grades exist, from individuals who may be regarded, in their normal condition, as "sane," to others, of greater cerebral degeneracy, who are never really so. In such cases the cerebrum, as regards its lower complexes, is "racing"; and, in the more degenerate types, objective signs of generally aberrent and sub-normal cerebral activity are permanently in evidence.

On the other hand, cases are common in which, from toxæmia of the cortical neurones and consequent pathological conditions of these elements, all grades and types of temporary or permanent maiming of the processes of cerebral association are existent. Such patients exhibit what is described as "mental confusion." The earliest evolved and most stable parts, *i.e.* the projection spheres, are the least affected, and hence the patients are able to receive sensory impressions in a more or less normal manner. The later evolved zones of lower association (and especially the latest evolved centre of higher association) are, however, more seriously affected, and hence the patients make frequent mistakes with regard to the identifying of sensations, suffer from hallucinations, and may exhibit any type and grade of defective comprehension and any symptom of "aphasia." In such cases the cerebrum is temporarily or permanently maimed owing to lesion of its constituent elements.

Though examples of abnormal cerebral activity of the *immediate* type might be multiplied to any extent, those given above will suffice to indicate that our knowledge of the higher functions of the cerebrum, though still in its early stages, does not depend solely on histological, neuro-pathological, and experimental data, but may derive illumination and illustration from the study of mental disease.

A number of recent papers of interest will now be referred to.

The mechanism and localisation of the psychic processes has formed the subject of a recent paper by Jendrassik. This writer denies the existence of an "association centre," on the ground that the connections between memory images are not actual paths but occur through a "tuning" of associated images, with the result that if one of these is evoked the images in harmony with it are also aroused into consciousness. His theoretical discussion is rather unsatisfactory, but the deduction may be readily drawn that he considers association to be a process, and the psychic products, which are evolved as results

of this, to have no fixed cerebral centres. His opinion thus approximates to the views enunciated during the course of this article.

Bianchi, on the other hand, considers that the cerebrum, apart from the frontal lobes, is the seat of centres for percepts, and that a centre for concepts exists in the prefrontal region. He argues that both percepts and concepts exist apart from words, though the evidence he adduces is chiefly or entirely in favour of the existence of words in the absence of percepts and concepts. He severely criticises the doctrine of Flechsig, chiefly on the ground that the phenomena of anatomical evolution do not correspond with those of the development of functional activity. For example, he remarks that the supposed centre for reading in an imbecile may be completely myelinated although the subject may never have learned to read. He states that histological evidence is not in favour of the areas of projection possessing a simpler structure than the regions of association. He discusses the complex nature of the processes of association which are necessary for the synthesis of a perception. He thus regards the portion of the cortex which is now differentiated into areas of projection or sensory areas and into posterior regions of association, as a series of perceptive zones; and he is of the opinion that the only regions of the brain which can be regarded as associational are the prefrontal lobes, which are generally admitted to contain no projection fibres. He regards these lobes as the region of cerebral executive government, and considers that here the elaborated products of the perceptive zones, or mantellar parliament, are fused together.

Instead of three anatomical grades in the hierarchy of cerebral function, namely, areas of projection, regions of lower association, and a region of higher association, Bianchi thus recognises but two, zones of perception and a centre for concepts. Further, he regards percepts and concepts as entities with an anatomical basis apart from that for words. His opinion thus differs from the views elaborated during the course of this article, namely, that percepts and concepts are merely psychological generalisations signifying the results of processes of cerebral association which differ in detail, though they possess an underlying general similarity, on each occasion on which they occur. Bianchi regards words, not as symbols for the integration of processes of cerebral association without which they are meaningless, but as means for the communication of already existing percepts and concepts. Language, in the opinion of Bianchi, is thus merely a mechanism for the expression of thought, and not, as is the view of the writer, a symbolic instrument without which it is impossible for the psychic functions to be adequately performed.

Mills and Weisenburg have published a paper in which, after collating the clinical evidence in favour of the localisation of the higher psychic functions in the prefrontal lobe, they describe an interesting case of left prefrontal tumour. The patient, a physician, was affected with regard to his higher psychic functions, his judgment and powers of comparison, his grasp of work, his disposition, &c.

Shepherd Ivory Franz has published a series of observations on the effect of experimental lesions of the frontal lobes in monkeys and cats. He finds that when these lobes are destroyed recently formed habits are lost; and he indicates his reasons for concluding that the results are not due to shock. Unilateral lesions are followed merely by a slowing of motor impulses. He concludes that the frontal lobes appear to be concerned in the performance of normal and daily associational processes, and that by means of them we are able to learn and to form habits.

Mills and Weisenburg have recently produced clinical and pathological evidence indicating that the cortical areas for the representation of movements, of sensibility, and of stereognosis are distinct from one another and are each divided into several sub-areas.

Oskar Vogt has published an interesting article on the functional significance of the pre- and post-central gyri. He confirms from the experimental aspect the researches of Sherrington and Grünbaum with regard to the pre-Rolandic position of the excitable motor areas. He shows that the anterior limits of the excitable limb areas correspond accurately to those of Brodmann's pre-central type (No. 4); and that the centres for movements of the head and eyes and for mastication correspond with the still more anterior histologically differentiated area of Brodmann (No. 6). In certain of the lower apes he has found that the excitable region does not extend as far back as the fissure of Rolando, and that the motor type of cortex in these has the same posterior limits. Further, by a study of the effects of destructive lesions in eleven lower apes, he concludes that palsy without ataxy follows destruction of the pre-central gyrus, and that considerable ataxy but no palsy results from destruction of the post-central gyrus.

Eugen Wehrli, in a paper dealing with lesions of the occipital region, denies that these afford proof of the exact cortical localisation of the visual area; and he is not disposed to regard local differences of histological structure as evidence in favour of the localisation of the visual area in a special region of the cortex. This paper well illustrates the critical attitude still held by many writers with regard to the recent researches on cortical localisation, and indicates that

the most elaborately detailed investigations, even when repeatedly confirmed, may still fail to gain general acceptance.

The last investigation which will be referred to is not of direct physiological interest, but is nevertheless worthy of mention owing to its bearing on the subject of heredity. J. P. Karplus has recently published a work which deals with the fissuration of the human cerebrum from the aspect of family likeness. He has examined in a series of cases the cerebra of two or more members of a family, and also the brains of several members of families in the ape, dog, rat, and goat.

He draws interesting conclusions with regard to the family likeness of the pattern of the fissures. He further finds that, whilst in the monkey the two hemispheres resemble one another, in man the original bilateral symmetry of fissuration is lost, and the sulci of the individual hemispheres possess a family permanence.

Whilst it is true that the convolutional pattern of the brain does not run hand in hand with, and in fact bears little relationship to, the various histologically differentiated areas into which the cerebral cortex has been divided, the truth that the former is susceptible to the impress of heredity is at least suggestive with regard to the possibility of this in the case of the latter.

BIBLIOGRAPHY

L. Bianchi, On the Teaching of Flechsig with regard to the Perceptive and the Associative Zones. Internat. Med. Congress of Madrid, 1903. Textbook of Psychiatry, translated by J. H. Macdonald, 1906.

J. S. Bolton, The exact Histological Localisation of the Visual Area of the Human Cerebral Cortex. Phil. Trans., vol. 193, 1900. The Histological Basis of Amentia and Dementia. Archives of Neurol., vol. ii., 1903. The Functions of the Frontal Lobes. Brain, 1903. Amentia and Dementia: a Clinico-Pathological Study. Journ. Ment. Sci., 1905–8, chiefly April 1905, April 1906, and April and July 1908.

K. Brodmann, Beiträge zur histologischen Lokalisation der Grosshirnrinde. Journ. für Psychol. und Neurol. Mitteilung I. Die Regio Rolandica. Bd. 2, 1902–3. Mitteilung II. Der Calcarinatypus. Bd. 2, 1903. Mitteilung III. Die Rindenfelder der niederen Affen. Bd. 4, 1905. Mitteilung IV. Der Riesenpyramidentypus und sein Verhalten zu den Furchen bei den Karnivoren. Bd. 4, 1905. Mitteilung V. Über den allgemeinen Bauplan des Cortex pallii bei den Mammaliern und zwei homologe Rindenfelder im besonderen. Zugleich ein Beitrag zur Furchenlehre. Bd. 6, 1906. Mitteilung VI. Die Cortex gliederung des Menschen. Bd. 10, 1907.

A. W. Campbell, Histological Studies on the Localisation of Cerebral Function. Cambridge, 1905.

J. Déjerine, L'aphasie sensorielle. Sa localisation et sa physiologie pathologique. La Presse médicale, 11 Juillet 1906. L'aphasie motrice. Sa localisation et sa physiologie pathologique. La Presse médicale, 18 Juillet 1906.

L. Edinger und *A. Wallenberg*, Bericht ueber die Leistungen auf dem gebiete der anatomie des centralnervensystems. Dritter Bericht, 1905 und 1906.

S. I. Franz, On the Functions of the Cerebrum. The Frontal Lobes. Arch. of Psychology, March 1907.

W. Harris, Binocular and Stereoscopic Vision in Man and other Vertebrates with regard to Decussation of Optic Nerves, Ocular Movements and Pupil Light Reflex. Brain, cv., 1904.

Hermanides und *Köppen*, Über die Furchen und über den Bau der Grosshirnrinde bei den Lissencephalen, insbesondere über die Lokalisation des motorischen Zentrums und der Sehregion. Arch. f. Psychiatr., 37, 1903.

Gordon Holmes, A Note on the Condition of the Post-Central Cortex in Tabes Dorsalis. Rev. of Neurol. and Psychiat., vol. vi., No. 1, 1908.

Ernst Jendrassik, The Mechanism and Localisation of the Psychical Processes. Neurol. Centralb., xxvi., 1907, pp. 194 and 254.

J. P. Karplus, Zur Kenntnis der variabilität und vererbung am zentralnervensystem des menschen und einiger säugetiere. Wien, 1907.

W. Kolmer, Beitrag zur Kenntniss der "motorischen" Hirnrindregion. Arch. f. mikr. Anat. u. Entwgesch., 57, 1901.

Köppen und *Lowenstein*, Studien über den Zellenbau der Grosshirnrinde bei den Ungulaten und Karnivoren und über die Bedeutung einiger Furchen. Monatsch. f. Psychiat. u. Neurolog., 18, 1905.

A. Lemaitre, Trois cas de dissociation mentale. Arch. de Psychol., 1907, p. 252.

Bevan Lewis and *Henry Clarke*, The Cortical Localisation of the Motor Area of the Brain. Proc. Roy. Soc., No. 185, 1878.

Pierre Marie, Revision de la question de l'aphasie. La Semaine médicale, 1906, 23 Mai, 17 Octobre, and 28 Novembre.

Mills and *Weisenburg*, Localisation of the Higher Psychic Functions. Journ. Am. Med. Assoc., Feb. 1906. The Subdivision of the Representation of Cutaneous and Muscular Sensibility and of Stereognosis in the Cerebral Cortex. Journ. of Nerv. and Ment. Dis., Oct. 1906, p. 617.

F. D. Mitchell, Mathematical Prodigies. Am. Journ. of Psychol., Jan. 1907.

Von Monakow, Aphasia and Diaschisis. Neurol. Centralb., Nov. 16, 1906, p. 1026.

F. W. Mott, The Progressive Evolution of the Structure and Functions of the Visual Cortex in Mammalia. (Bowman Lecture, 1904.) Arch. of Neurol., vol. iii., 1907.

Mott and *Halliburton*, Localisation of Function in the Lemur's Brain. Proc. Roy. Soc., 1907, B. vol. 80, p. 136.

Mott and *Kelley*, Complete Survey of the Cell Lamination of the Cerebral Cortex of the Lemur. Proc. Roy. Soc., 1908, B. vol. 80, p. 488.

F. Moutier, L'aphasie de Broca. Paris, 1908.

Morton Prince, The Dissociation of a Personality : a Biographical Study in Abnormal Psychology. New York, London, and Bombay, 1906.

Eleanor H. Rowland, The Psychological Experiences connected with the different Parts of Speech. The Psychological Review, Monograph Supplement, January 1907.

Elliott Smith, The Morphology of the Occipital Region of the Cerebral Hemispheres in Man and the Apes. Anat. Anz., 24, 1904. Studies in the Morphology of the Human Brain, with Special Reference to the Egyptians. No. 1, The Occipital Region. Records of the Egyptian Gov. School of Med. 2, 1904. A New Topographical Survey of the Human Cerebral Cortex. Journ. of Anat. and Phys., 41, 1907.

John Turner, A Study of the Minute Structure of the Olfactory Lobe and Cornu Ammonis. Brain, 1906, p. 57. The Structure of Grey Matter. Brain, 1907, p. 426.

O. Vogt, Über strukturelle Hirncentra, mit besonderer Berücksichtigung der strukturellen Felder des Cortex pallii. Verhandl. der anatom. Gesellsch., 1906, p. 74. Der Wert der myelogenetischen Felder der Grosshirnrinde. Anat. Anz., 29, 1906.

G. A. Watson, The Mammalian Cerebral Cortex, with Special Reference to its Comparative Histology. I. Order Insectivora. Arch. of Neurology, vol. iii., 1907.

E. Wehrli, Ueber die anatomisch-histologische Grundlage der sog. Rindenblindheit und ueber die Lokalisation der corticalen Seesphere der Macula lutea und die Projection der Retina auf die Rinde des Occipitallappens. V. Graefe's Archiv., lxii., 2, 1906.

Albert Wilson, Education, Personality, and Crime. London, 1908.

STUDIES IN SPECIAL SENSE PHYSIOLOGY

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PART I.—VISUAL ADAPTATION

If one asked a number of students, taken at random, which department of physiology seemed to them the least interesting, I am confident that a majority would award the palm of dulness to that subdivision which treats of the special sense mechanisms.

It is, indeed, not difficult to understand such a result. Our knowledge of special sense physiology is at once very complete and very incomplete ; observations and experiments have accumulated to an enormous extent, yet we are far from the synthesis of these results which makes the inter-relationship of the various parts clear and enables the intelligent reader to perceive that the subject is an harmonious system, not a mere collection of disconnected fragments.

I think, therefore, the reader will more easily appreciate the scope and method of this branch of science if I choose two problems only, and examine them in detail, not so much because they are of practical importance, but as illustrations of the lines upon which modern thought and experimental work seem to advance.

In the present section, I shall sketch the course of recent inquiries into the phenomena of adaptation of the eye to various intensities of light, a subject which illustrates the practical methods of work ; in the later section I shall attempt to set out the principles of two modern theories of colour vision, and to show how far they may be regarded as really new contributions to science, and to what extent they are products of thought handed down to us from remote ages. Here, as in so much of modern science, we shall find that old and new are inextricably interwoven, that much of what is taken to be modern is so only in a geological sense.

It has long been known that the nature of the response by the

eye to a stimulus largely depends upon whether, before the experiment, the subjects have rested in a dark room or been exposed to light—that is to say, whether there be a condition of light or dark adaptation.

Many years ago, Aubert noticed that the response of the eye to feeble stimulation was increased by resting in the dark, and also laid down the rule that the threshold value of a stimulus in such cases varied inversely as the area of surface stimulated. This general statement received ample confirmation; Charpentier (1), for instance, found that the central part of the "dark" [1] retina, although exhibiting an increased response as compared with the same region in the "light" eye, was far less sensitive than the periphery. This increased responsiveness was very marked in respect of the short waved regions of the spectrum, indeed it is denied by many good observers that adaptation affects the response to red light at all (Parinaud and v. Kries), while nobody has demonstrated a large increase.

Of the many who have studied the changes of responsiveness in adaptation, all agree that they are far more prominent in the peripheral than in the central region, but much dispute has arisen as to whether any part is absolutely unaffected. On the whole, it may be said that no satisfactory proof is forthcoming that such a part exists. Experimentally, the problem is beset with difficulties, for it is hard to be certain of the exact limits of a very small stimulated field, and it is possible that the time required for adaptation is not the same in the fovea and the peripheral regions, being probably longer in the former (Tschermak [2]).

These changes in responsiveness immediately lead us to the consideration of Purkinje's "phenomenon," an effect which may be described in the following terms. If one examines an ordinary spectrum, the brightest part of it seems to occupy the neighbourhood of the yellow or orange-yellow; if now its physical intensity be diminished—for instance, by moving the source of light farther away from the prism or grating—the maximum of brightness is shifted towards the violet end. With the feeblest illumination which enables us to detect the spectral colours at all, the brightest part is at the junction of the green and blue.

Hering (3) by means of a simple experiment has made it seem

[1] For brevity, I shall speak of an eye which has been rested in darkness as a "dark" and one previously exposed to light as a "light" eye.

probable that these changes are due to adaptation. Two rooms which could be independently darkened are separated by a light-proof partition in which two slits are cut and covered with pigmented glass. The amount of light transmitted by these slits can be varied independently with the aid of reflectors. So long as the room occupied by the observer is kept at a constant illumination, diminishing the physical intensity of the light traversing the two slits, which are covered with blue and red glass respectively, does not change their relative intensities. If, however, the observation room is darkened, the blue slit immediately appears brighter than the red one, even while the physical intensity of light passing through them is unaltered. This effect is enhanced by a prolonged stay in darkness, and is more noticeable in indirect (peripheral) than direct (central or foveal) vision. Burch, in a series of experiments which I shall discuss later, has obtained similar results, so that we may conclude that Purkinje's "phenomenon" depends not on physical intensity but visual adaptation, and is a particular case of the general change already mentioned. These facts naturally incline us to examine more closely the differences between peripheral and central vision, and we shall find that all work tends to show that the former is more susceptible to adaptive changes and characterised by a heightened responsiveness to feeble stimuli.

Before going further, however, we must ask ourselves what is meant by saying that different colours are equally or unequally bright. As a matter of fact, this question is more easily asked than answered. A similar difficulty is experienced in attempting to ascertain what one means by saying that two notes of different pitch are unequally loud. If we attempt to define our meaning in terms of the physical properties of exciting stimuli, we become confused, and perhaps the only valid excuse for employing the expression is an empirical one. Ask a dozen normal persons to look at a spectrum in daylight, and they will agree that the yellow is the brightest part of it, meaning, I suppose, that the region in question produces, somehow, a predominant effect in consciousness. This uniformity of results is a justification, perhaps the only justification, of the method, and allows us to compare different colours with respect to brightness.

Bearing in mind the empirical and sensational nature of the investigation, we can attain comparative results in numerous ways.

One of the best is the "flicker" method which has been carefully studied in England by Haycraft ([4]) and Rivers ([5]). If a series of sectors are whirled round on a colour mixer, the rapidity necessary to produce a fused sensation depends upon the brightness of the sectors; hence with different sets of sectors equal in size, the velocity of rotation which just extinguishes the sensation of flicker will afford us a measure of brightness, this varying, within certain limits, inversely as the rapidity of rotation. Many other plans can be, and have been, adopted, some of which will be mentioned later. The above should give the reader some idea as to how researches can be arranged.

Hering, in 1890, noted the relative darkening of red as one passes from central to peripheral vision; he compared a pure red, a spectral mixture of red and blue green (656 $\mu\mu$ + 470 $\mu\mu$) and daylight. The converse was found to hold for spectral green (505 $\mu\mu$), but his results were not quite pure, since momentary dark adaptation occurred during the experiments ([6]). Tschermak ([2]), who studied the whole question systematically in the "light" eye, found with indirect vision a relative diminution in brightness for light of wave length between 693 and 525 $\mu\mu$, no change from 525 to 516 $\mu\mu$, an increase from 516 to 466 $\mu\mu$. Similar changes were observable in "dark" eyes.

Another line of research was to start with a large field of colourless light, produced by mixing together complementaries, and then to diminish its size. It has been found that a colourless mixture of spectral red and bluish-green becomes, with such areal diminution, redder and darker; if the change of size be an increase, it becomes greener and brighter. In fact, both for "light" and "dark" eyes, colourless matches valid for the periphery do not hold for the centrum and *vice versa*. Apart from adaptation, it is interesting to see whether merely changing the physical intensities of the two mixtures renders the match invalid. It is agreed that mere intensity variation does not affect central matches, but there is much dispute as to the periphery. V. Kries and his fellow-workers have brought forward experimental evidence on the affirmative side, but difference of opinion exists. Thus, v. Kries ([7]) found the equation R + G = Y, no longer valid on diminishing the intensities of both fields, the binary colour growing paler and brighter. We must remember that it is extremely difficult to avoid changes in the state of adaptation, and as these

are especially important at the periphery, it is probable that some of the results have been vitiated by this circumstance (Tschermak [2]).

In connection with the supposed relation between physical intensity and apparent brightness, an interesting set of observations may be noted regarding what is called the "achromatic threshold of coloured light." In studying Purkinje's "phenomenon" we found that if the intensity of a spectrum were steadily diminished, a point was reached at which the brightest region appeared to have been moved towards the violet. What, it may be asked, happens if the illumination be still further diminished? Under normal circumstances we soon reach a point at which the whole spectrum appears colourless, differing, however, in brightness in the various regions. Reduction beyond this yields an intensity which is associated with no sensation at all. Hence it seemed necessary to distinguish between the absolute liminal intensity of a spectrum,[1] that is, the least intensity corresponding to a colourless sensation, and the "specific" threshold or liminal value for which the spectral zones could be seen to differ in hue.

A good many workers, including Purkinje, Helmholtz, Aubert, Landolt, &c., observed this phenomenon, and the actual absolute threshold values for various spectral lights and different parts of the retina have been studied. Charpentier (1) found the "photochromatic interval" (*i.e.* the difference between specific and absolute threshold intensities) least for red and greatest for blue light, and that the absolute thresholds were diminished by dark adaptation, while the specific liminal values were not affected. It also appeared that these results were more noticeable with peripheral than central vision.

It was soon noticed, however, that the phenomena were in reality complex. Some workers (*e.g.* Parinaud and v. Kries) never obtained an achromatic value for red, and doubts arose as to the existence of such intervals at all. Finally, on comparing the brightness of central and peripheral lights, rendered colourless by a reduction of physical intensity, unexpected and puzzling results were obtained.

Stegmann (3) performed the following experiments. Matches were made between a series of lights from 640 to 480 $\mu\mu$, and a

[1] The liminal value or threshold value of a stimulus is that intensity which corresponds to a "just-noticeable" sensation.

screen of blue-green or orange paper, illuminated by lamp light passing through an absorbing medium, the fixed illuminant being so chosen that no colour was discernible. The tested lights were arranged in the first series of experiments at an eccentricity of twenty degrees; in the second, at one of four degrees. In the first set of observations, Stegmann found that, after five to fifteen minutes' dark adaptation, a diminution of 21 to 45 per cent. in orange intensity, and an increase of 23 to 50 per cent. in blue-green intensity were necessary in order to match the fixed standard; that is to say, below the chromatic threshold, the peripheral responsiveness was increased with respect to the long waved light and diminished with regard to the short-waved light, *i.e.* a change the exact converse of that associated with the ordinary Purkinje effect. V. Kries concluded that these results depended on the feeble intensity of the stimulus employed, and that with light stronger but still below the chromatic threshold, the results agreed with the Purkinje effect, the discrepancy being therefore a consequence of physical intensity; this view has not, however, been generally accepted. Recently, G. J. Burch has published the results of some interesting experiments on achromatic thresholds (9). In the first place, Burch performed some qualitative experiments. A Bunsen burner was completely covered by a metal chimney so as to prevent any escape of light while not interfering with ventilation. By bringing the flame into contact with the metal chimney the latter could be heated gradually to a point at which it became luminous. If the experiment were performed in a room with windows covered by ordinary blinds—that is to say, in a room from which light had not been absolutely excluded—the first appearance of light was a pearl-grey tint—the achromatic threshold—as had been previously stated. But when the room was changed to one without windows and absolutely dark, the first appearance of luminosity was not grey but dull red. On repeating this experiment, *after spending a few minutes in a lighted room*, the former grey appearance was once more obtained.

Burch then made exact measurements, using spectral red and violet, a Nicol prism and paper reflector (Fig. 1). He found that after a prolonged rest in total darkness, a period of two hours being necessary, no achromatic threshold existed for either light.

Adaptation Values (*Burch*).

A. During the period of increasing adaptation.

Time in Dark. (Mins.)	Intensity of Minimum Visible Red.	Intensity of Minimum Visible Blue-Violet.	Ratio, V : R.
9	16·63	254·76	15·32
21	11·14	57·61	5·17
60	2·4	5·39	2·24

B. After spending two hours in the dark room.

Time in Dark. (Mins.)	Intensity of Minimum Visible Red.	Intensity of Minimum Visible Blue-Violet.	Ratio, V : R.
120	1·0	1·0	1·0
122	1·20	1·63	1·34
125	2·69	5·14	1·91
127	5·04	12·44	2·47
130	50·02	225·72	4·51

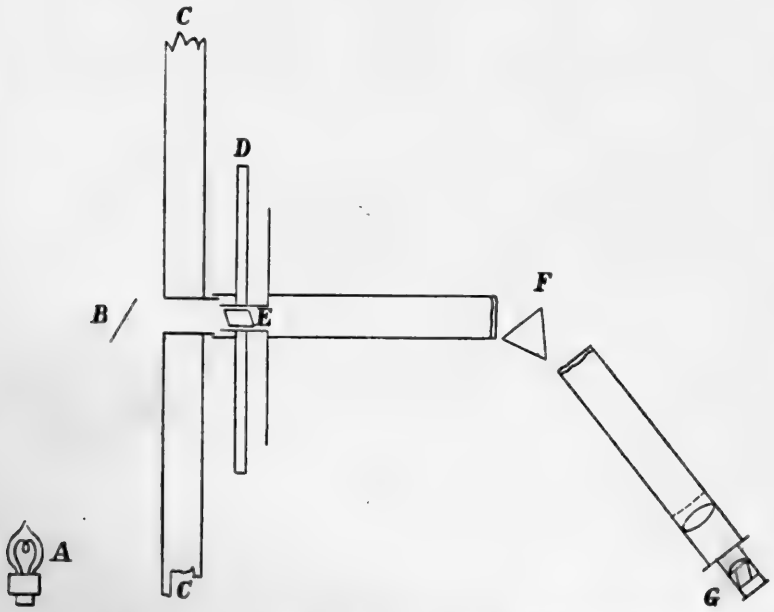


FIG. 1.—Burch's apparatus for the study of "achromatic thresholds."

A. An electric lamp, 16 candle-power.
B. Paper reflector.
CC. Wall of dark room.
D. Stand with polarising prism (E).
F. Spectroscope with double image prism (G) over eye-piece.

There is a stop with two slits (allowing red and blue-violet light to pass through) in the eye-piece. By rotation of the polarising prism the relative intensities of the red and blue-violet lights can be varied.

Burch, therefore, while confirming the statement that adaptation increases the stimulus value of blue-violet relatively to that of red, inferred that the achromatic threshold had no existence, and that the positive results obtained by other workers were due to a compounding of the immediate stimulus with the effects of previous exposure to light—*i.e.* after-images. By careful observations in a dark room he ascertained that diffused luminous effects—his "dazzle tints"—persist for as long as two and a half hours after entering the dark room, and that when these had disappeared no achromatic interval existed for his own eye.

This evidence is sufficiently strong to render the existence of an absolute as distinct from a specific threshold for coloured light exceedingly doubtful in the case of foveal vision. On the other hand, it is not clear from Burch's paper that special attention was, or could be, paid to the behaviour of the periphery; so that we are not entitled to conclude from it that an achromatic interval does not exist when the peripheral retina is stimulated; indeed the careful researches of Tschermak and others, who worked with prolonged dark adaptation ([2]), are opposed to such a belief.

Burch's results merely, I think, emphasise the view I am endeavouring to develop that central and peripheral vision differ in kind and degree. His work does not appear to be fundamentally new, except in experimental technique, for Parinaud in 1898 remarked in his most suggestive and valuable book: "At the fovea, on the contrary, a simple light of sufficient purity is perceived primarily as a colour, whatever be the intensity of the light, or whether the retina be or be not adapted" ([10], p. 51).

Without therefore going the length of asserting that an achromatic interval depends in some vague way on previous stimulation, we must be very cautious in interpreting results, such as Stegmann's, obtained by this method.

So far, then, direct experiment seems to have established the following points:—

(1) The peripheral regions of the retina are relatively more sensitive than the fovea to light of moderate or short wave length.

(2) Adaptation to darkness is characterised by an increase in responsiveness to short waved light, and this change is predominantly, if not entirely, extra-foveal.

The following tables illustrate these statements. The intensity values are arbitrary, the measurement of eccentricity is in terms of the angle subtended at the nodal point.

A. *Relative Stimulus Values of different Spectral Regions* (*Parinaud*[10]).

Fraunhofer Lines.	Adapted Retina.	Unadapted Retina.
B	$\frac{1}{400}$	$\frac{1}{400}$
C	$\frac{1}{100}$	$\frac{1}{100}$
D	$\frac{1}{10}$	$\frac{1}{60}$
E	1	$\frac{1}{100}$
F	1	$\frac{1}{300}$
G	$\frac{1}{100}$	$\frac{1}{1800}$
H	$\frac{1}{230}$	?

B. *Increased Responsiveness of Peripheral Retina* (*Dark-adapted*).

Stimulus: A bluish-white object, 35 degrees in diameter (v. Kries,[11] p. 171).[1]

Responsiveness (Arbitrary Scale).	Temporal Eccentricity in Degrees.	Nasal Eccentricity in Degrees.	Insensitive Zone.
1·0	1·07	0·85	1·92
1·78	1·22	1·06	2·28
7·12	1·70	1·38	3·08
16·02	2·3	1·92	4·22
28·48	3·0	2·58	5·58
44·50	3·75	3·33	7·08
64·08	4·04	4·04	8·08

[1] Distances from the fovea centralis of any point on the retina can be conveniently measured in terms of the angle subtended at the nodal point by a segment of the retina cut by a plane passing through the fovea, nodal point, and position of

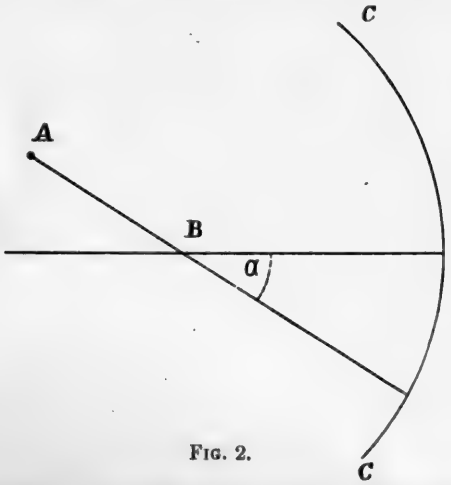


FIG. 2.

the object and bounded by a straight line through the nodal point from the object intersecting the retinal segment and by the principal axis. *E.g.* if A be an object, B the nodal point, and CC a section of the retina, the position (eccentricity) of the image of the point A is defined by the angle *a*.

We must next consider certain facts which seem to bear indirectly upon the problem under examination; of these the most important are connected with the condition of total colour-blindness.

Total colour-blindness is almost always a congenital defect, and is characterised, apparently, by a complete absence of colour perception—in the ordinary sense. A person in this state may see a spectrum merely as a grey strip unequally bright in the different regions which seem to us of various colours. To describe the sensations of a second human being is, of course, an impossibility; but perhaps we may say, for the sake of comparison and without pretending to any real precision, that a totally colour-blind man receives from a coloured print impressions similar to those excited in ourselves by an uncoloured one. The following summary of observations by Hering ([12]) will give the reader a tolerably clear impression of the facts.

The subject was a man of twenty years, whose colour vision had always been abnormal. He said that he could read without difficulty, provided the light were not too intense, but that his eyes were readily fatigued by bright illumination. In twilight his vision was especially good, particularly if the light were very feeble. On examination, the following results were obtained. No objective changes were detected with the ophthalmoscope, nor was any part of the retina insensitive; there was no scotoma. His power of distinguishing two spots unequally bright—physically—was much below that of a normal person, in bright light; in a dark room, it was much superior. Working with a spectrum, it was found that the area of red which produced any sensation was much diminished; there was shortening of the red end, and those parts which were effective seemed less bright than to a normal eye. The violet end, on the other hand, was not shortened, and it seemed relatively brighter than to the normal "light" eye, while the region of maximum brightness was in the neighbourhood of the Fraunhofer E and C lines. Brightness matches between coloured sectors and mixtures of black and white gave the results indicated in the table, which contains comparative values for the normal "light" eye. It is to be noted that the colour-blind's matches were valid, *i.e.* good matches, for a normal "dark" eye.

Hering's Case of Total Colour-blindness.

Coloured Circle.	Equally Bright Circle for Colour-blind.		White Valency.[1]	White Valency of a Grey Circle matching the Coloured Circle for a Normal "Light" Eye.
	White.	Black.		
	Degrees.	Degrees.	Degrees.	Degrees.
Bluish red . .	13·0	347·0	18·8	40
Yellowish red .	5·5	354·5	11·4	46
Orange . .	37·0	323·0	43·4	159
Yellow . .	136·5	223·5	140·2	283
Arsenic green .	228 0	132·0	230·5	205
Green . . .	152·0	208·0	155·5	137
Greenish blue .	109·5	250·5	113·7	89
Ultramarine blue	88·3	271·7	92·8	34
Violet . . .	47·5	312·5	52·7	32

Tests were also carried out by means of an ingenious polariscopic method. At one end of a horizontal tube, blackened inside, a cork plate was fixed; the plate was perforated in the middle and a doubly refracting prism inserted. The other end of the tube was closed by a lid in which two equal and symmetrically placed semicircular openings were made. With this contrivance the ordinary and extraordinary images obtained by polarisation appeared to form a series of spherical surfaces when the tube was directed to a source of light—*e.g.* a piece of baryta paper stretched over a glass plate. Between the eye and the prism a small telescope and a Nicol prism were introduced, together with a graduated arc. The diaphragm of the telescope removed the lateral images, leaving only two magnified white circles, the halves of which could have their brightness altered in opposite directions by rotating the Nicol. In front of one opening in the tube a coloured glass was placed, and the Nicol so arranged that for the normal "dark" or for the totally colour-blind eye, both halves appeared equally bright. The next table gives the readings for two observers. Some of the variations may be explained by the fact that the normal-sighted person was unpractised in this sort of work.

[1] For methods of measuring white "valency" consult Hering ([12]), p. 567, &c. For the present purpose the figures in the third column of the table may be regarded as a recalculation of the amounts of white in the sectors which match the coloured circles, so as to admit of comparison with the figures of the fourth column.

Precisely similar results were obtained in matching spectral colours.

Polariscopic Matches (Hering).

Yellow Glass.		Blue Glass.	
Total Colour-blind.	Normal Dark-adapted Eye.	Total Colour-blind.	Normal Dark-adapted Eye.
Degrees of Rotation.	Degrees of Rotation.	Degrees of Rotation.	Degrees of Rotation.
22·3	22·9	18·2	18·35
22·6	22·6	18·0	17·95
22·3	23·0	18·0	18·15
21·9	22·5	18·1	18·4
22·3	22·7	17·8	18·9
21·8	23·1		
22·1	21·8		

The analogy between normal vision under conditions of dark adaptation and the vision of the totally colour-blind will also be apparent from the next two tables. The first gives the intensity values of the different parts of the spectrum for a normal "dark" eye, as determined by Schaternikoff ([13]), and the second Abney's observations ([14]) on two other cases of total colour-blindness. The units of intensity in the two cases are not comparable, but it will be observed that the two maxima occur in the same part of the spectrum.

"Twilight" Values of a Spectrum (Schaternikoff).

Wave Length.	Intensity Value.	Wave Length.	Intensity Value.
In millionths of a mm.		In millionths of a mm.	
670·8	18·0	529·3	2736·0
651·8	36·5	522·3	2532·3
634·3	83·3	515·4	2219·3
618·1	216·9	508·7	1944·0
603·1	423·2	502·2	1475·8
589·3	881·7	490·0	1016·0
577·1	1424·9	478·6	633·0
566·4	2110·7	468·0	364·5
556·0	2609·7	458·7	208·8
546·0	2899·0	451·1	111·2
537·2	3000·0	443·9	69·6

Luminosity Values of two Cases of Total Colour-blindness (Abney).

(No. 40 in Abney's scale is close to the E line.)

Scale of Spectrum.	K. B.'s Luminosity Value.	P.'s Luminosity Value.
56	2·5	...
54	9·0	...
52	16·0	7·0
50	27·5	19·0
48	42·5	39·0
46	61·0	65·0
44	82·5	85·0
42	96·0	98·0
40	100·0	99·0
38	95·5	91·5
36	87·5	90·0
34	75 0	80·0
32	61·5	65·0
30	43·0	50·0
28	37·0	36·0
26	30·0	26·5
24	24·0	19·5
22	18·5	14·0
20	14·5	10·0
18	11·5	...
16	9·0	5·5
14	7·0	...
12	5·0	...

As we have already seen that direct evidence points to dark adaptation being chiefly an affair of the extra-foveal part of the retina, it is reasonable to suppose that, in the totally colour-blind, the fovea centralis is relatively insensitive. It has indeed been asserted that a central scotoma, or totally insensitive area, is found in these cases, and much dispute has arisen on this point. Summarising the results of examination, we find that, out of eighteen cases investigated (Grunert [15]), in seven an absolute or relative central or para-central scotoma was definitely made out; in the other eleven this was absent. The importance of a central scotoma has been greatly over-estimated for theoretical reasons, as we shall see later. In most cases, very imperfect fixation or actual nystagmus was observed. On reviewing the facts, it will, I think, be admitted that the agreement in type between the vision of the totally colour-blind and that of the normal "dark" eye

is exceedingly close. The importance of these facts in forming conclusions as to the mechanism of visual processes will be pointed out when we have considered a few more experimental observations regarding central and peripheral vision in the two phases of adaptation.

A set of experiments, apparently of little practical importance, has proved very interesting with respect to the phenomena of adaptation. These deal with the effects which follow the application of luminous stimuli for very short intervals of time.

Such experiments can be carried out in at least two ways. By a contrivance, similar to a photographic camera shutter, the eye can be stimulated for a very short time, or, the gaze being fixed, a source of light may be moved across the field of vision. For the latter experiment, we may employ a rotating mirror and a projection lantern, or a disc with a slit in it may be rotated in front of a source of light. If the length of the object be l and v be the velocity of movement, then l/v measures the time during which each retinal area is exposed to the action of the stimulus, and by a suitable choice of object and velocity this time becomes as short as we please.

In principle the methods are alike, but the second is easier in practice, and the results obtained of special interest.

The earliest observer seems to have been D'Arcy ([16]), who, in 1765, measured the duration of the response produced by a glowing coal which was attached to the circumference of a wheel; the wheel was rotated faster and faster until a complete circle of light was seen. If a bright object be rotated against a dark background, in the manner described, the whole sensory effect is somewhat complicated, comprising under favourable circumstances the following six phases:—

(1) A primary image; the immediate consequence of the stimulus, its first and strongest effect. As compared with the image due to a stationary illuminant it is more or less elongated into a streak of light.

(2) Immediately following upon the primary image is a short dark streak.

(3) After the dark streak we obtain a second phase of illumination which, if the stimulus be coloured, appears complementarily tinged (this is often called, after its discoverer, the Purkinje after-

image). This phase, which is the most striking part of the whole experiment, produces the effect of a second bright object coming behind the first, so that its appearance was termed "recurrent vision" (Young, Davis), the "ghost" (Bidwell), or the "satellite" (Hamaker).

(4) The end of the satellite is not sharply defined and is followed by another interval of darkness.

(5) After this, the field once more brightens, and a faint bright or homoiochromatic phase is obtained (of the same colour as the original stimulus). If this part of the phenomenon be well developed, it is found that with a velocity such that the satellite is distinct a bright haze fills the whole field, hence more than one rotation should not be made.

(6) Sixthly, and lastly, another dark interval occurs.

It will be plain, even from this enumeration, that the phenomena under consideration are by no means simple; hence nobody will be surprised to learn that divergences, even flat contradictions, exist in the literature of the subject not merely as to the interpretation of these results, but even as to their *bona-fide* existence. I shall follow, for the most part, the lucid statement of the case which we owe to Professor J. von Kries ([17]), indicating why I believe his results to be reliable.

With respect to the experiment as a whole, we have three phases of illumination—the primary image, the secondary or satellite image, and the tertiary. In apparent brightness, these are arranged in the order of their appearance. With low illuminations, primary and secondary images alone are visible; with still lower intensities, the secondary also disappears. Further, the lengths of the images can be made to vary, the dark intervals being lost. Fixing our attention for a moment on the primary, we may note the following points. Very frequently it exhibits a striped appearance, similar to the well-known Charpentier "bands" ([18]) seen on slow rotation of a white field containing a black sector. Apart from this, it seems to the "light" eye uniformly bright. As, however, dark adaptation proceeds, we find that the primary image not only increases in extension and brightness, but with chromatic stimuli ceases to be uniform. Thus, with blue light, only the anterior border is deep blue, being followed by a white stripe. Macdougall ([19]) finds this latter to commence at a distance corresponding, in his experiments, to a time interval of $\frac{1}{18}$ second.

With other colours, *except red*, the same result is obtained, but less distinctly.

Although anticipating our theoretical summary, I must point out how strongly this suggests the activity of two distinct mechanisms with different latent periods. An analogous, but not identical, result is the old illusion of the "fluttering hearts." Small heart-shaped scraps of blue paper are pasted upon a red surface and the whole examined in dim light. On moving the sheet backwards and forwards, the blue scraps appear to lag behind the red background. This phenomenon does not occur on stimulation of the fovea centralis.

The secondary, ghost, or satellite, begins $\frac{1}{5}$ to $\frac{1}{4}$ second after the commencement of the primary, and is, in general, complementary to it. This rule must, however, be modified in the following way. If the primary be pure white, the secondary is bluish; indeed, the secondary is always modified in the direction of bluishness. Even with a feeble blue primary, the secondary may still be bluish. It is only with a saturated blue primary that a secondary of a really complementary (yellow) hue is obtained. As regards brightness, the result depends on the adaptation value of the primary. Two lights of equal stimulus values for the "dark" eye give equally bright secondaries. Red, with its relatively low stimulating power as regards the "dark" eye, only gives a secondary when its physical brightness is great.

As we should expect from its characteristics, the secondary is dependent on dark adaptation, increasing to a maximum of distinctness as adaptation proceeds and then diminishing, although Macdougall has obtained it after prolonged dark adaptation. We thus see in the causative factors of the secondary image the phenomena we have already learned to associate with peripheral vision: (1) Relatively greater efficiency of short waves; (2) increased intensity with increasing dark adaptation. It only remains to add failure over the fovea centralis. "If one observes it in the form of an after-coming image and fixates carefully a luminous point in the track of the object, one sees clearly that the satellite leaps over a small central area, while it follows without a break similar points of light moved over a paracentral region. Also, with stationary objects, momentarily illuminated, of suitable form and size, an analogous appearance can be demonstrated. Small objects which lie entirely within the foveal region do not exhibit the

characteristic secondary illumination; small lines passing through the fixation point exhibit a distinct interruption in the secondary image" (v. Kries,[17] p. 225).

The great theoretical importance of this failure at the centrum has led to much, at times, acrimonious discussion. Hess ([20]) objected that v. Kries' experiments were vitiated by the use of bright objects as fixation marks and too short intervals between successive stimulations. He showed that no interruption of the secondary image of a bright line occurred at the fovea, and obtained with chromatic stimuli similar results, except that for strong red light the secondary was not complementary but homoiochromatic. Hess, accordingly, was of opinion that no central difference exists with regard to the secondary image.

These objections have been considered by v. Kries in an interesting and lucid article ([21]).

Failure of a central secondary can be demonstrated by rotating a screen with a slit in it before an ordinary projection lantern. The best results are obtained with an arrangement such that the object takes the form of a line $\frac{1}{4}°$ to $\frac{1}{2}°$ broad. If adaptation and physical brightness are so chosen that the secondary is distinctly separated from the primary, the latter's failure over the fovea is clearly demonstrated. Experiments conducted without bright fixation points and with long intervals between the successive stimulations gave the same results. V. Kries, however, found that the experiment failed if crossed lines were used or three small fields in a row. This seems to be due to psychological factors, especially the difficulty of concentrating the attention on any particular point. Thus in the line experiments of Hess, the failure to obtain a central interruption may be referred to an inability to fixate steadily any given point, so that the relations of the moving images are disturbed and a distinction becomes impossible.

The results of v. Kries have been essentially confirmed by Macdougall ([19]), and Hamaker ([22]) also failed to obtain foveal secondaries for blue and green stimuli. On the whole, the evidence in favour of v. Kries' view is strong, and we may consider the third point suggesting the peripheral nature of the secondary image—its failure at the fovea—as established.

Passing to the tertiary image, the following characteristics have been made out. The hue is best appreciated when one uses red light, and may, in this case, be very distinct. With increasing

dark adaptation, the tertiary gains in brightness and loses in chromatic value; indeed, owing to the high adaptive powers of blue and green lights, when these are used at moderate intensities, the colouration of the tertiary image is only visible at the beginning of the experiment.

There is some difference of opinion as to whether the tertiary can be obtained in direct vision; since red light is the most suitable stimulus for calling up this image, it is reasonable to suppose that it should be perceived by direct fixation. The suggestion is, therefore, that the customary form of the tertiary image is due to a chromatic element, unaffected by dark adaptation, and a brightness element which is so affected.

We are almost in a position to attempt a sorting out of the various experimental facts described; only one group remains for examination, namely, some researches into peripheral changes which accompany the retinal alterations, and are important as objective signs of the latter.

Schirmer asserted that the pupil width and its reaction were related to the adaptive condition of the eye. With complete adaptation to a given grade of light, the pupil reaches after initial widening or narrowing a physiological mean position. Garten ([23]) found that momentary illumination produces in the "light" eye a weak sudden, in the "dark" eye a slow powerful contraction. Proceeding further on these lines, Sachs ([23]) discovered that the pupillo-motor response to coloured lights followed closely their adaptation values. Abelsdorff ([23]) confirmed these results, using the apparatus sketched (Fig. 3). One of the two lights serves as a standard; the subject looking through the strong convex lens at the slit sees a bright point surrounded by a diffusion circle. If the light falling on the eye be changed the diffusion circle increases or diminishes in size. By rotation of a Nicol prism the new intensity can be increased or diminished and the intensity is found for which the diffusion circle produced by the standard light is not increased or diminished by changing to the tested colour. Naturally, the method does not yield very exact quantitative measurements; the mean error is said to be about 7 per cent. The next table (see p. 370) gives some of Abelsdorff's results.

The close agreement between the pupillo-motor values and those of apparent brightness justifies the method, and its importance lies in the fact that we can employ it in experiments on animals.

We have no direct means of investigating adaptive changes in any animals except man, but we can measure this pupillary response; if we find it changing in the manner described, it is not an unfair inference to suppose that visual responsiveness may be similarly affected by adaptation.

It has been found that intensities of red and blue which appeared equally bright to and exerted the same pupillo-motor effect upon a human "light" eye, did not produce identical changes

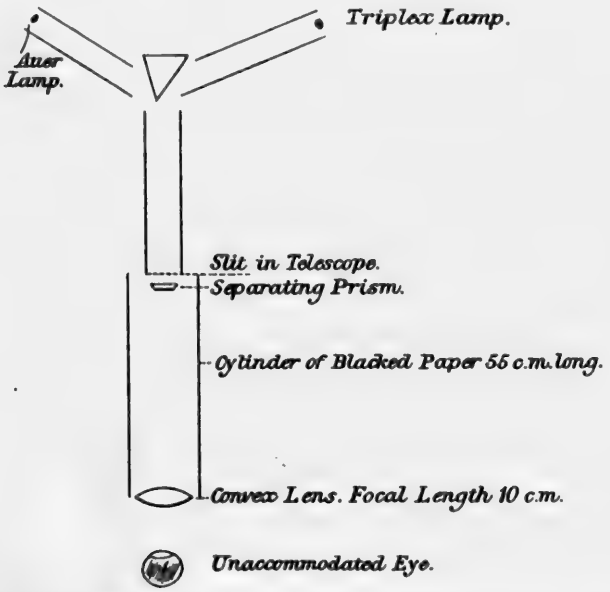


FIG. 3.—Abelsdorff's apparatus for studying the pupillo-motor response.

in the pupils of the dove and the owl. For the former the red, for the latter the blue was the stronger stimulus. Indeed the pupillo-motor response to blue in the owl's eye was greater than in the case of a total-colour-blind (Abelsdorff).

We have now completed a brief review of the experimental facts and are at liberty to consider their importance in our general conception of visual processes.

First of all, is there any functional difference between the spot of distinctest vision, the fovea centralis retinæ, and the paracentral or peripheral regions of the retina?

Pupillo-Motor Values.

Wave Length. μμ.	Comparison Lights.		
	600 μμ.	Light Adaptation. 480 μμ.	Dark Adaptation. 480 μμ.
	Mm.	Mm.	Mm.
640	·5271	·3920	·2666
620	·8523	·8376	·5670
600	·9720	·9822	·7260
580	·9536	·9090	·8065
560	·8303	·8739	·8865
540	·5518	·6141	·9200
520	·3333	·2936	·5755
500	·1181	·09141	·1612

Brightness Values.

(Readings obtained when the same subject adjusted the intensities of the lights until they seemed to be equally bright.)

Wave Length. μμ.	Comparison Lights.		
	600 μμ.	Light Adaptation. 480 μμ.	Dark Adaptation. 480 μμ.
	Mm.	Mm.	Mm.
640	·5253	·3518	·2529
620	·8204	·7230	·5515
600	·9431	·9090	·8536
580	·9431	·9090	·8535
560	·8811	·8613	·9540
540	·6259	·6354	·9540
520	·3700	·3189	·5750
500	·1168	·0944	·1612

In view of the long series of experiments bearing upon the Purkinje effect, the increase in brightness of the short waved spectral lights at the expense of the long waved vibrations, the reader is probably satisfied that this effect if not solely peripheral is at least mainly so. I do not wish to disregard those who have obtained central adaptation, but even they admit the increase to be far less marked than the peripheral alterations; we may, without undue scepticism, entertain some doubts as to whether the positive results might not have been due to some slight eccentricity of fixation. However that may be, we are beyond question

justified in assigning to the periphery a predominating share in the work of dark adaptation.

We have also seen that these adaptive changes consist in a greatly increased responsiveness to light of short wave length, such appearing more intense than under " light " conditions.

We have thus to account theoretically for a localised change in responsiveness with respect to certain forms of stimulation.

The difference in histological structure between the fovea centralis and the surrounding area caused Schultze forty years ago ([24]) to suggest a functional separation which he supported on evidence drawn from comparative anatomy. In his time, however, our experimental knowledge of adaptive changes was little advanced and his conception went unheeded. The first detailed investigation was due to H. Parinaud ([25]), who has developed a theory of adaptation in a series of memoirs dating from 1881. Similar views have been carefully elaborated by Professor J. v. Kries of Freiburg and his colleagues and pupils in a large number of well-planned researches.

Essentially the theories of Parinaud and v. Kries may be summarised quite simply. Two distinct visual mechanisms exist: one, subserving both chromatic and achromatic responsiveness, and represented in the retina by the cones; the other dealing with achromatic sensations alone, represented by the rods and visual purple. The former mechanism is alone active in bright daylight and is unaffected by resting in the dark; the latter is brought into play by shielding the eye from stimulation, being the sole or chief agency of twilight vision; it is characterised by special responsiveness to ethereal vibrations of short wave length. In view of the double nature of the mechanisms postulated, the theory has been christened the Duplicity Theory (Duplizitätstheorie). Let us see how far the hypothesis covers the experimental observations I have enumerated.

If the theory be true, we should expect (1) spectral maximum brightness to change in weak light in favour of the violet end; (2) this change not to occur for images formed at the fovea centralis; (3) no achromatic threshold (*vid. sup.*) to be obtained for any light at the fovea or for red light anywhere.

We have seen that each of these deductions is supported by good experimental evidence.

Again, have we any forms of vision in which, apparently, the

basal mechanism is similar to that associated by the theory with twilight vision and uncomplicated by the existence of a second type of reaction? The subjects of total-colour-blindness appear to enable us to answer the question affirmatively. We found that the brightness judgments of these people agree well with those of normal men in a state of dark adaptation; that there is evidence in such cases of diminished or absent foveal sensitivity, bad fixation, inferior acuteness of vision, nystagmus, central scotoma (sometimes) and abnormally good vision in twilight.

Conversely, are there any cases in which the hypothetical daylight mechanism alone reacts?

Parinaud ([10]) has investigated several cases of "night-blindness" or hemeralopia. He found that in such, vision was of the foveal type; the colour sense was normal, but the spectrum shortened at the violet end; responsiveness to short waved light was abnormally low. The investigations of Messmer ([26]) and others make it probable, however, that the condition of night-blindness is not simple, different forms and degrees being classified under the same heading. In some cases, dark adaptation is very slowly induced, but after a sufficiently long interval is normal in degree. In others some adaptation comes on in a normal time but is of inferior extent. It is important to bear these cautions in mind because night-blindness is markedly heritable and has been used, in the writer's opinion illogically, as an argument in favour of the validity of the Mendelian theory of inheritance. For our present purpose, we must admit that night-blindness does not afford us so much information respecting visual processes as the apparently opposite condition of total-colour-blindness. Provisionally, we may, perhaps, say that the latter condition is consistent with the activity of the hypothetical twilight mechanism functioning by itself, while *some* examples of the former peculiarity suggest that the daylight mechanism alone exists. But it is to be remembered that scarcely any theory, however absurd, which has been advanced in explanation of a difficulty in sense physiology has failed to obtain the support of some pathological phenomena which have been tortured into a semblance of agreement with its postulates.

The complex results in sensation which follow the application of short or moving stimuli to the retina have perhaps confused some readers; let us see whether our hypothesis is capable of arranging them in an orderly manner.

I have already pointed out that the peculiar striping of the primary image, the blue tailing off into white, suggests the interplay of two processes; I also emphasised the dependence of the secondary image on adaptation and its (probable) absence at the fovea. We can perhaps sum up the effects in terms of our hypothesis thus:— The cone mechanism responds by two effects, the main part of the primary and the colour component in the tertiary. The rod apparatus responds in a threefold manner; it gives us the white tail of the primary, the whole of the secondary, and contributes, although slightly, to increasing the brightness of the tertiary. This way of putting the facts does, I think, clarify our ideas, but it certainly fails to remove all difficulties. Thus, if we are to regard our twilight mechanism as solely responsible for the secondary image, it is clear that we derive sensations of colour as well as sensations of luminosity without hue from that mechanism, since the secondary image is often coloured. Hence the mechanism cannot be identical with that of a totally colour-blind eye; so that we must either give up the view that total-colour-blindness is a condition in which the rods and purple react *as in a normal eye*, or regard the secondary as due to something beyond rod stimulation. V. Kries is disposed to adopt the latter alternative, but in that case it is difficult to understand why the secondary is entirely peripheral, and therefore how it is that the cones can only respond with the rods in this case.

This I believe to be the most serious difficulty in the way of an acceptance of the duplicity hypothesis. It is easy to evade the objection by transferring the production of secondary images to the brain (? consciousness), a course adopted by Parinaud, but this is undesirable, and I think it better to leave the difficulty where it is. We can only say, in the stereotyped phrase of the embarrassed physiologist, further work is necessary to clear up the point.

We have so far examined the duplicity theory by the light of the chief experimental facts, but a little more evidence has to be considered.

It has long been known that the relative numbers of rods and cones differ in various animals. Thus the rods are very large and almost exclusively present in the retinæ of nocturnal animals, such as owls, bats, and hedgehogs. In many other creatures, on the other hand, including most birds, cones predominate. It was indeed on the strength of this that Schultze advanced a theory

essentially similar to the one we are considering. Kühne subsequently showed ([27]) that visual purple was present only in retinæ containing rods. He was not, however, able to extract this pigment from all rod-containing eyes, a notable exception being the bat; recently, Trendelenburg ([28]) has obtained abundance of visual purple from more than one species of bat. Experimentally, as we have seen, Abelsdorff has shown that the owl is specially sensitive to short waves and the dove relatively insensitive (tested by the pupillo-motor response).

We all know that most nocturnal animals see badly in broad daylight, while such birds as the pigeon exhibit normally a marked degree of night-blindness. In Parinaud's words :—

"It is a matter of common observation that hens and pigeons see very imperfectly in artificial light and defend themselves with difficulty against the hand that tries to seize them; that as soon as the sun goes down these animals seek their night shelter. The old adage, 'To go to bed with the hens,' meaning to go to bed early, evidently having its origin in this fact" ([10], p. 66).

Biological investigation appears to show, therefore, a co-existence of rods and visual purple with vision of the twilight variety and of cones with optimal vision in daylight. It is easy to lay too much stress on this sort of evidence. Reasoning from analogy is dangerous and especially equivocal when dealing with sense physiology. Take the history of opinion regarding a bat's vision. The objectors to the theory of duplicity pointed out that no visual purple had been extracted from the bat's retina. Its partisans retorted that the bat relied on sensory mechanisms other than sight, possibly scent currents, as seems to be the case with moths. My friend Mr. Arthur Bacot points out to me that the remarkably rapid darting movements of a bat in pursuit of prey, movements which are comparable in point of velocity with the swift's flight, seem hardly compatible with the type of twilight vision we have agreed to associate with the rods, characterised as that is by poor acuity of vision. We are now aware that many species of bat possess visual purple. Hence, if the previous train of reasoning be at all correct, the value of an outfit of rods and visual purple to the twilight animals is rendered doubtful. In precisely the same way, the early roosting of diurnal birds may be due to causes other than a condition of night-blindness.

It is necessary to dwell upon these points because in no de-

partment of physiology is there a greater tendency to advance equivocal evidence in favour of an hypothesis than in that concerned with the special senses.

I can now sum up the case presented. I hope I have rendered it probable that—

(1) There is a marked difference between central and peripheral vision, in regard to the phenomenon of darkness adaptation, the former being little if at all affected in the process.

(2) These differences may be provisionally interpreted on the supposition that visual sensations are bound up with two distinct mechanisms : (*a*) That of the cones, with which chromatic sensitivity and achromatic sensations under daylight conditions are associated ; (*b*) that of the rods upon which depend achromatic sensations under conditions of dark adaptation.

The objections to this view are neither few nor unimportant. It has not been proved that no central adaptation whatever occurs. The equations (colour matches) of totally colour-blind persons and those of the normal "dark" eye agree well but not absolutely. There is also a difficulty in interpreting the secondary image of recurrent vision.

That the first of these objections (as well as the kindred one that a central scotoma does not exist in all cases of total-colour-blindness) may be parried by supposing a trace of visual purple and a few scattered rods to be present in the fovea, is clear. Recent measurement by Fritsch ([17], p. 188) on a negro's fovea gave an absolutely rod-free zone of only ·2 mm., corresponding to an angular distance of less than a degree ; we could not allow much weight to failures in the demonstration of such small adaptable areas, even supposing them to be absolutely rod-free.

The difficulty regarding "total-colour-blinds" and normal "dark" equations is not formidable. The fact is that sufficient measurements have not been made to enable us to affirm that the differences are significant. The more serious question as to the real significance of the secondary image in recurrent vision has been already considered ; it may prove the crucial point in the theory. Accepting the above view of the rôle of the visual purple and rods as an important element in the physiological processes of vision with low intensities of light, one is tempted to speculate as to the nature of their activity. Parinaud was of opinion that the process depended upon fluorescence of the retina mainly due to the presence

of visual purple. This view is certainly incorrect. A bleached retina is more strongly fluorescent than one in which the visual purple is unreduced (Kühne [27]), although the bleached substance itself may possess fluorescent properties, since Nagel and Himstedt ([28]) observed that a bleached solution of visual purple was more strongly fluorescent than the solvent alone.

If then we accept, as a working hypothesis, the view that the rods and visual purple form a link in the chain of processes by means of which certain forms of stimuli are, under particular conditions, associated with sensations, we must not, in the present state of the question, attempt to assign to them any precise physical or physiological share in the process.

In conclusion, the reader need not suppose that the cones of the periphery are functionless, that in broad daylight peripheral vision is at all of the type we have been studying. As a matter of fact, at the extreme periphery which is normally quite colour-blind, brightness values are altogether different from those of the " dark " eye, as is shown in the following table (v. Kries,[17] p. 199) :—

Na line = 100									
Wave length . .	680	651	629	608	589	573	558	530	513
Peripheral value daylight . .	9·6	37·5	77·5	101	100	79·6	52·2	28·5	14·6
Peripheral value twilight . .	?	3·4	14·0	35·5	100	256	351	321	198

The study of this problem of visual adaptation illustrates well the patient and laborious experimental work necessary to demonstrate even a limited range of phenomena, the complexity of results which appear at first simple and the necessity of caution in framing satisfactory hypotheses. It has been chosen to describe because it is so instructive from these points of view.

BIBLIOGRAPHY

(This list is not, of course, complete. The papers marked with an asterisk contain extensive bibliographies.)

[1] *Charpentier*, Arch. d'Opthalmologie, vol. iv., pp. 291–323.

[2] *A. Tschermak*, Pflüger's Arch., vol. 70, pp. 297–328. A critical summary of work up to 1902 will be found in * Die Helldunkeladaptation des Auges und die Funktion der Stäbchen und Zapfen, by A. Tschermak, Ergebnisse der Physiologie, 1st Jahrgang, 2nd part, pp. 695, &c.

[3] *Hering*, Pflüg. Arch., vol. 60, pp. 519–542.

[4] *Haycraft*, Journal of Physiology, vol. 21, p. 126.

[5] *Rivers*, Journ. of Physiol., vol. 22, p. 137.

[6] *Hering*, Pflüg. Arch., vol. 47, p. 417.

[7] *V. Kries* and *Nagel*, Zeitschrift f. Psychol. u. Physiol. der Sinnesorgane, vol. 23, p. 161.

[8] *Tschermak*, Ergeb. d. Physiol., 1st Jahrg., 2nd part, p. 731.

[9] *Burch*, Proc. Roy. Soc., B, vol. 76, p. 199. See also Nagel and Schaefer, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 34, p. 271; Loeser, ibid., vol. 36, p. 1.

[10] *Parinaud*, La Vision, Paris, 1898 (Doin), p. 51.

[11] * *J. v. Kries*, Die Gesichtsempfindungen, Handb. d. Physiol. d. Mensch., herausgegeben v. W. Nagel, vol. 3, pp. 109–282.

[12] *Hering*, Pflüg. Arch., vol. 49, p. 563.

[13] *Schaternikoff*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 29, p. 255. See also *Fujita*, *ibid.*, vol. 43 (pt. ii.), p. 243.

[14] *Abney*, Proc. Roy. Soc., vol. 66, p. 179.

[15] * *Crunert*, Arch. f. Opthalmol., vol. 56, p. 132. Other papers on total-colour-blindness are:—*Hering*, Pflüg. Arch., vol. 49, p. 563. *Hess*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 29, p. 99. *Hess* and *Hering*, Pflüg. Arch., vol. 71, p. 105. *V. Hippel*, Klinische Monatsblätter f. Augenheilkunde, vol. 36, p. 324. *Nagel*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 29, p. 118. *Uhtoff*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 20, p. 326; and vol. 27, p. 344.

[16] Quoted in * Helmholtz's Handbuch d. Physiol. Optik., 2nd edit., p. 501.

[17] *V. Kries*, Nagel's Handb. d. Physiol., &c., vol. 3, pp. 220–226.

[18] *Charpentier*, Archives de Physiol., 1892, p. 541; also C. R. de l'Acad. des Sciences, vol. 113, p. 149.

[19] *Macdougall*, British Journal of Psychology, vol. 1, p. 78.

[20] *Hess*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 27, p. 1.

[21] *V. Kries*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 29, p. 81.

[22] *Hamaker*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 21, p. 1. Other papers on recurrent vision are:—*Bidwell*, Proc. Roy. Soc., vol. 56, p. 132. *Charpentier*, C. R. de l'Acad. d. Scien., vol. 113, p. 149. *Hess*, Pflüg. Arch., vol. 49, p. 190. *Hess*, Arch. f. Opthalmol., vol. 44, p. 445; vol. 51, p. 225. *V. Kries*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 12, p. 81; vol. 19, p. 175; vol. 25, p. 239.

[23] *Garten*, Pflüg. Arch., vol. 68, p. 68. *Sachs*, Pflüg. Arch., vol. 52, p. 79. *Abelsdorff*, Zeits. f. Psy. u. Phys. d. Sinnes., vol. 22, pp. 81, 451; vol. 34, p. 111 (with *Feitchenfeld*).

[24] *Schultze*, Arch. f. Mikrosk. Anatm., vol. 2, pp. 175–273.

[25] *Parinaud*, Arch. Génér. de Med., 7th Series, vol. 7 (1881), pp. 403–414. C. R. de l'Acad. d. Sciences, vol. 93, p. 286.

[26] *Messmer*, Zeits. f. Psy. u. Phys. d. Sinnes. (2te Abth. f. Sinnesphysiologie (1907), vol. 42, p. 83.

[27] *Kühne*, Hermann's Handbuch der Phys., vol. 3, p. 235 (twenty-two other papers published, 1877–9).

[28] *Trendelenburg*, Arch. f. Physiol., 1904, Suppl. Bnd., p. 228.

[29] *Nagel* and *Himstedt*, Festschr. d. Univ. Freiburg i. Br., 1902 (quoted in Nagel's Handb., vol. 3, p. 96).

STUDIES IN SPECIAL SENSE PHYSIOLOGY

PART II

Section I.—Historical Introduction

Any one who examines the current text-books of physiology will find that in discussing colour vision great prominence is given to two theories, those of Helmholtz and Hering respectively. As the reader will also find it admitted that neither theory resumes in an altogether satisfactory manner the data of observation and experiment, he may be tempted to ask why so much stress is put upon them. An obvious explanation is the authority attaching to any utterances of men who have notably advanced our knowledge in various fields. This cannot, however, be the sole reason; physiologists not less distinguished than Helmholtz and Hering have before now promulgated theories which, being inconsistent with the subsequent results of investigation, have perished. The vitality of these particular theories of colour vision must therefore be referred to some principle other than that of mere authority.

The object of this essay is to show that these admittedly incomplete theories are important because each brings into prominence one aspect of the problem; the harmonising of these two aspects must occupy those who come after us and examine the question by the light of fuller knowledge than we possess.

With this end in view, it will be necessary, before considering the theories themselves and their relation to known facts, to examine briefly some opinions as to the nature of visual processes which were held long ago but have by no means lost all interest for us. Of these speculations, the most important are due to the Greek philosophers and men of science.[1]

In attempting to estimate the scientific value of the Greek theories of vision, it is necessary to bear in mind certain limitations

[1] A valuable account of Greek Sense Physiology and Psychology will be found in "Greek Theories of Elementary Cognition from Alcmæon to Aristotle," by Professor J. I. Beare (Clarendon Press, 1906, p. 354).

which were imposed upon them by imperfect means of investigation. Even with modern apparatus, it is not easy to obtain a precise idea of the elaborate structures contained in the eye—as every student knows—hence workers unprovided with the simplest microscope knew almost nothing of what is now common knowledge. Roughly, we may say that all the early theories agree in regarding the "pupil" of the eye and the "image" within it as of primary importance. Again, the flash of light seen on pressing or rapidly moving the eye was held to prove the existence of an inherent or native "fire," also of great significance. Thirdly, the presence of a watery substance within the eyeball had to be accounted for. The problem, as it presented itself to the earliest writers, was to assign their proper shares in the visual act to the "fire," the "image," and the "water."

One of the earliest of the Greek writers on this subject was Alcmæon of Cretona (fl. B.C. 500). Our knowledge of his views seems fragmentary; he thought that seeing is accomplished by rays passing from the ocular "fire" to the object, and that these returning to the eye, altered in some way, are reflected in the diaphanous "water." The "fire" is therefore the active element in vision. The hypothesis hardly appears consistent with itself, because the conception of a visual ray from the "fire" cannot readily be harmonised with a mirror-like action of the "water."

Empedocles' (circa B.C. 450) theory was more subtle and elaborate, although it is not easy to reconcile different statements attributed to him.

According to the first doctrine enunciated by Empedocles, *like perceives like*. All bodies whatever are characterised by—(1) All are made up of four elements, earth, air, fire, and water. (2) All are permeated by minute passages or pores, and all give off emanations which enter the pores. Thus, in perception, emanations from the object pass into the pores of the percipient organ.[1] But, that this passage may be effected, it is necessary that the emanations and the pores should correspond; if the former are too large or too small for the latter, no perception can occur.

Hence with the eye alone can we perceive emanations of colour

[1] Cf. Lucretius, *De Rer. Nat.*, bk. ii., 833—

"Noscere ut hinc possis prius omnem efflare colorem
Particulas, quam discedant ad semina rerum."

See also bk. iv., 72–86.

because these are "symmetrical" with the pores of the eye alone. This correspondence is the basis of sense specificity. Further there is a symmetrical arrangement within the eye itself with respect to the different forms of stimulation. By means of the intra-ocular fire we perceive the emanations of fire—*i.e.* white—with the "water" we see water—*i.e.* black—and so on.

"With earth we see earth, with water we see water, with air we see the bright air; just as with love we (perceive) love, and with hate, baleful hate" (1). Empedocles is said to have regarded four colours, white, black, red, and green, as primaries (Stobæus), but only examines white and black in detail. He also taught that rays issued from the visual "fire," but how this process was associated with his general doctrine of pores and emanations is not certain.

Democritus (? 460–357) agreed with Empedocles in postulating the entrance of particles from an object into pores contained in the perceiving structure and in the dictum that "like is perceived by like." But he denied that there are four qualitatively distinct elements, and believed that all things are made up of homogeneous atoms moving in a vacuum and infinitely numerous. Vision is due to the mirroring of an object in the eye, the latter's character being somehow determined by its moist and porous nature. This part of Democritus' theory was sharply criticised by Aristotle, who remarked: "It is absurd also that it should not have occurred to him to doubt why the eye alone sees, but nothing else in which energies are apparent. That the sight is aqueous is true; yet it does not happen that it sees because it is aqueous but because it is diaphanous, which is also common to air" (2).

Democritus seems to have been the first writer to attempt a detailed theory of colours, the simple ones being white, black, red, and green; his account, which is somewhat elaborate, has not played a sufficiently important part in the history of opinion to need further description, but it is well to remember that he (anticipating Berkeley [1]) held that colour had no objective reality. "... the ultimate elements—the *plenum* and the *vacuum*—are destitute of all sensible qualities, while the things composed of them possess colour (as they do every sensible quality) owing merely to the *order*, *figure*, and *position* of the atoms, *i.e.* (*a*) to their

[1] Cf. "The First Dialogue between Hylas and Philonous," especially pp. 314–318 (Sampson's edition, vol. i.). Lucretius, *loc. cit.*

order relatively to one another; (*b*) to their several shapes; and (*c*) to the position of each in its place. The subjective aspects—the qualities—of sensible objects are all due to these three things. Colour has no objective existence, since the colours of bodies are due to the position of the atoms in them " (3).

The views of Anaxagoras (B.C. 499–428) and Diogenes of Apollonia (5th cent. B.C.) may be passed over rapidly. Anaxagoras held, in opposition to his contemporaries, although the opposition is more formal than real, that perception is the result not of like operating upon like, but of the reaction between contrary and contrary. The " image " is not reflected upon a part of like colour to the object but upon a different colour. Diogenes, who believed that an all-pervading " air " was the ultimate agency in nature, has left no distinct theory of colour vision.

One would naturally expect that Plato (429–347), to whom we now turn, would have powerfully contributed to the advancement of our knowledge of the physiological psychology of vision, but this is not the case. His account of the physical side of the problem is contained in a passage in the " Timæus," of which the following quotation gives an idea :—

" And of the organs they first contrived the eyes to give light, fixing them by a cause on this wise. They contrived that as much of fire as would not have the power of burning, but would only give a gentle light, the light of every-day life, should be formed into a body; and the pure fire which is within us and akin to this they made to flow through the eyes in a single entire and smooth substance, at the same time compressing the centre of the eye so as to retain all the grosser element and only to allow this to be sifted through pure. When therefore the light of day surrounds the stream of vision, then like falls upon like, and there is a union, and one body is formed by natural affinity according to the direction of the eyes, wherever the light that falls from within meets that which comes from an external body. And everything being affected by likeness, whatever touches or is touched by the stream of vision, their motions are diffused over the whole body and reach the soul, producing that perception which we call sight " (4).

In the genesis of colour, particles are discharged from external things and impinge upon the eye, some being larger, some smaller, and some equal in magnitude to the parts of the eye. All colours

are compounded of four; white, black, bright, and red. Bright when mixed with red and white becomes golden-yellow; red blended with black and white yields violet.

From statements in the "Timæus" and "Republic" it would seem that Plato, unlike Democritus, believed in the objective existence of colour in things; but, as Helmholtz remarks (5), his views seem to have varied. In the "Theætetus," colour is considered from an entirely different standpoint, as will be clear from the next quotation:—

"We shall see that every colour, white, black, and every other colour, arises out of the eye meeting the appropriate motion, and that what we term the substance of each colour is neither the active nor the passive element, but something which passes between them and is peculiar to each percipient. . . ."

"When the eye and the appropriate object meet together and give birth to whiteness and the sensation of whiteness which could not have been given by either of them going to any other object; while the sight is flowing from the eye, and whiteness from the colour-producing element, the eye becomes fulfilled with sight and sees, and becomes not sight but a seeing eye; the object which combines in forming the colour is fulfilled with whiteness and becomes not whiteness but white" (6).

Aristotle's (B.C. 384–322) theory of vision is of very great importance in the further development of the subject, and indeed still survives in a modified form. We must therefore examine it more closely.

According to Aristotle, the *object* of sight is colour. Colour is at the surface of all visible objects, but, in order to be seen, requires the presence of light, which is the medium of vision.[1]

Light again pre-supposes a diaphanous substrate which in its turn is the medium of light. Examples of this "diaphanous" are air, water, and many solids. The realisation or actualisation of this potential quality of being diaphanous is light, its absence darkness. When the former condition of actual light is established in the diaphanous medium, any coloured body sets up a

[1] Cf. Lucretius, *De Rer. Nat.*, bk. ii., 795—

"Praeteria quoniam nequent sine luce colores
Esse, neque in lucem existunt primordia rerum,
Scire licet quam sint nullo velata colore."

The whole passage, from 730 to 833, is of much interest in this connection.

movement in it, between object and eye; this is the essential process in colour perception.

The diaphanous substrate, upon which depends the existence of light and, *a fortiori*, colour, is not peculiar to the bodies called transparent or diaphanous, but is a species of universally diffused natural power; it is not indeed capable of existence independently of "body" but subsists in varying degrees in all bodies. The colour of a body either forms its surface or is upon that surface, the latter opinion being the more exact since the indeterminate "diaphanous" of air and water exhibits colour, which, however, owing to the indeterminate boundary, is variable. This explains the changing hues of sea or sky.

Bodies with a definite boundary have a fixed colour, so that one might again define colour as the surface limit of the "diaphanous" in determinately bounded body. This definition is consistent with the first given, viz. that which stimulates the actualised "diaphanous" (light) between the object and the eye, but the latter is a definition in terms of vision and the medium of vision, the former in terms of the object as it exists apart from vision.

Colour is a genus comprising seven species; it is a quality and cannot therefore exist without a substrate. The seven species are white, black, golden-yellow, crimson, violet, leek-green, and deep blue. The colour genus (like all other genera of sensible qualities) consists of species lying between extremes; outside these extremes there can be no colours, between them are specific boundaries. By subdividing the scale limited by the extremes, we cannot obtain an infinite number of distinct colours because a sensible quality is discrete not continuous. By dividing the substrate we do not arrive at any new colour, the halves of a white object are white. It is true that by sufficiently fine division no colour whatever may be perceptible, but on reuniting these portions we again obtain white. The two limits are black and white; when one is *actually* existent the other is only *potential*. The transition from white to black is effected through the successive degrees which are the species of colour. The substratum, of which these are the qualities, is one, and is in strictness that which is changed; the colours alternate.

Colour is not purely subjective. It is true that it depends upon the eye, but it also depends upon the object. Actual colour depends upon the possibilities of these two being realised together,

but the coloured object existed in nature as a potential colour before the act of vision and apart from it. "It is light that at once transforms the potential colour to actuality and the potentially seeing to an actually seeing eye" (7).

In the colour scale (as among the elements) there is a sort of opposition of positive and negative. White is the positive, black the negative.

This is Aristotle's general account of colour and of the "diaphanous" its vehicle—omitting his views of reflection which are not important from the physiological or psychological standpoint. He also treats of certain colours in detail.

The presence of some fire-like element is the cause of light in the diaphanous, and in its absence we have darkness. In all determinately bounded bodies we may assume something analogous with the presence and absence of this fiery element. Its absence means blackness, its presence whiteness. Therefore, in determinately bounded bodies, blackness is privation of whiteness. Thus, blackness and whiteness are contraries within one sensory province, that of colour, and from them all the other colours are to be explained. "The transition from white to black is possible through continuous degrees of privation; that from white to black is likewise possible by an ascending scale in the opposite direction. The various colours are species which fall between the two contraries and are generated of certain combinations of these" (8). For instance, in passing from white to black we first come to crimson. As the intervening stages in the passage mark relative extremes, change can start from any point.[1]

With regard to the actual mode of origin of the intermediate colours, what is actually effected in the above-mentioned process? Aristotle discusses and condemns the doctrine of atomic juxtaposition and that of superposition, taking the view that a complete blending occurred. No individual part of the compound colour retains its primitive characters unmodified.[2]

As specific illustrations of this theory, we may take red, which is produced by light streaming through black, and purple, distinguished from crimson in possessing more of the dark ingredient.

[1] Goethe, of course, maintained the correctness of this theory in the *Farbenlehre*. (Cf. Goethe's Theory of Colours, translated by Eastlake, London, 1840.)

[2] Aristotle does not give this account in all his works. *Vide* Beare, op. cit., pp. 74–76.

Thus the sun shining through a fog is red; the feebler lamp ray sometimes appears purple.

In this connection, Aristotle refers to positive and negative after-images. After looking at the sun and closing the eyes we see the object at first of the same colour as before; this changes to crimson, then to purple, then black, and finally vanishes. This illustrates the genesis of colours from the blending of black and white. Simultaneous contrast is explained along these lines—the brightest rainbow appears in the darkest cloud, white wool has its colour intensified when placed next black wool, &c.

Aristotle rejected altogether the theory of emanations and pores (Empedocles, &c.), while his conception of a vibratile movement imparted to the actualised "diaphanous" may, perhaps, be regarded as a partial anticipation of the modern doctrine of a luminiferous ether. We cannot, however, push this comparison very far, since he maintained, in opposition to Empedocles, that light does not travel. It is not, I think, necessary to summarise the Aristotelian teaching in so far as it deals with structure, since, for the reasons already mentioned, it is of purely antiquarian interest. The curious reader will find ample material, if he desires to pursue the matter further, in the works cited by Professor Beare.

We can now consider for a moment the relations subsisting between Greek doctrines and the modern development of visual physiology and psychology.

The reader will have noticed already that the opinions I have summarised are concerned both with the theory of visual sensations proper, and the nature and functions of the eye itself. Or, roughly, they are, in the modern terminology, partly psycho-physiological and partly anatomical or histological.

Subsequent progress in these two departments has not been equal. Thus, while we are less ignorant than the Greeks regarding the structure of the eye and have framed formulæ more accurately descriptive of physical concepts, the development of physiological psychology has not been so great and is largely the work of recent times. The result has been that our present way of looking at and thinking about the structure of the eye and the physical changes associated with colour vision owes comparatively little to the Greeks, and may be said to date from the epoch-making discoveries of Newton. Theories of colour sensations, on the other hand,

may be traced through Hering to Goethe, and the latter almost explicitly founded his work on that of Aristotle.

It is true that the study of visual psychology received a considerable impetus at the beginning of the eighteenth century from the work of Berkeley. But Berkeley's writings are perhaps rather a contribution to epistemology than to physiological psychology as we now understand it.[1]

I shall therefore pass to the development of our knowledge as to the actual process of stimulation, so far as experiment has tended to display it, and the theoretical developments this has received in modern times. We can then again take up the thread of the narrative treating of visual sensations and attempt an estimate of its modern outcome. Before leaving this preliminary sketch, however, it is well to point out one difficulty in framing an hypothesis of vision, which hampered the acutest thinker of the Greek period, but from which we have partially escaped.

It will have been seen that practically all these philosophers either explicitly or implicitly adopted the postulate that like acts upon like. Anaxagoras might appear to be an exception, but a little thought convinces one that the exception is only formal. In adopting the literal converse of the proposition he too is committed to the belief that there is some necessary connection *in kind* between the processes occurring within the eye—or the mind—and those supposed to exist outside of it. This idea pervades all the Greek speculations—thus, since the external medium is transparent, there must be some internal transparency; since "fire" is visible, there must be some internal "fire" by which it is perceived, and so forth. In fact this "similarity hypothesis" might be regarded as the most primitive of all forms of speculation. There is reason to believe that sympathetic or homœopathic magic, an obvious extension of the same idea, is culturally older than any religions, while most of the latter embody the conception in some more or less changed form.

The real importance of what is called Müller's Law of Specific Sense Energy, is that it contains an explicit denial of any necessary

[1] For Berkeley's views on colour, see "The First Dialogue between Hylas and Philonous" (vol. i., p. 314 *et seq.*). "Alciphoron," Fourth Dialogue (vol. ii. p 288, &c.). Cf. also "An Essay towards a New Theory of Vision" (vol. i., p. 79 *et seq.*). The references are to Sampson's edition (Bell, 1898).

qualitative connection or resemblance between the physical processes of stimulation and the psycho-physiological changes associated therewith in the sense organ and "consciousness." For this reason, and although no definite proof of its applicability to all cases of sensory stimulation has been furnished, the law marked an important step forward in the study of physiological psychology.

Section II.—Normal Visual Stimuli

The physical basis of experimental work on colour stimulation is to be found in the conception of a simple or homogeneous light, and dates from Newton's researches in prismatic analysis. By homogeneous light we understand ethereal vibrations all having the same wave length or vibration frequency (within assigned limits). Prisms and gratings allow us to filter such lights from a mixture and employ them for our experiments. A pure light is uniquely defined by its wave length, and any such light may possess any intensity. Unfortunately, the physical unit of intensity is not readily fixed.[1]

In any spectrum, the intensities of individual lights depend on the source of illumination and the method of analysis—*i.e.* on the extent of surface over which light of a given wave length is dispersed. In an interference spectrum, dispersion is uniform; in a prismatic spectrum, on the other hand, it increases from red to violet, so that the short-waved light is relatively less intense than the long-waved. Spectra obtained by the two methods are not therefore directly comparable.

By colour or light mixing we understand an arrangement by means of which two or more homogeneous lights fall upon the same retinal area. Numerous experimental methods have been devised for this purpose, and the results obtained [2] enable us to formulate certain general statements respecting chromatic stimuli.

[1] The application by Krarup (H. Krarup, *Physisch-opthalmologische Grenzprobleme*, Leipzig, 1906) of Angström's energy measurements is a step in the right direction.

[2] As this essay is chiefly concerned with the theories of colour vision, I assume the reader to be acquainted with the main experimental data and methods. Such knowledge can be obtained by consulting any good text-book, for instance Dr. Rivers' article in the second volume of Schäfer's Text-book, or Prof. v. Kries' article in the third volume of Nagel's *Handbuch*.

These statements owe their present form to Grassmann, and can be summarised in the following way :—

1. If in a mixture one component be continuously varied, the appearance of the mixture will likewise vary ; unequal lights mixed with equal lights produce unequal mixtures.

2. On the other hand, lights which appear equal give, when mixed, equal mixtures. A corollary is that proportional increase of the intensity of each component does not destroy a match.

Passing to the actual observations, we at once note that the effect of mixing spectral extremes is the production of a colour, purple, not present in the spectrum at all. It thus follows that any graphical representation of our results must take the form of a closed curve, since, passing from red to violet, we can either travel over the range of spectral colours or by way of purple.

If we mix lights not belonging to the extreme ends of the range our results are quite different. The simplest cases are those of mixing colours of wave length not less than 540 $\mu\mu$. For instance, a red (670 $\mu\mu$) mixed with a yellow (580 $\mu\mu$) gives a pure colour of intermediate wave length ; the greater the proportion of the long wave-lengthened component in the mixture, the nearer will the position of the mixed colour be to the red end, and conversely.[1] The mixing relations for this part of the spectrum are therefore straightforward ; but the results obtained—*i.e.* that two simple lights when mixed give a colour matching that of a simple light the wave length of which is intermediate between those of its components—are only valid for a small part of the range. If we mix a blue-green (510 $\mu\mu$) with a blue (460 $\mu\mu$), the mixture, although resembling, perhaps closely, a pure intermediate, *e.g.* 490 $\mu\mu$, does not match it perfectly. The mixed colour is paler, or as we say, "less saturated," than any of the spectral colours. This is still more evident when we choose our components in such a fashion that the wave length of one is greater and that of the other less than 517 $\mu\mu$. If one constituent is taken a little nearer the red than 560 $\mu\mu$ and the other diminished, in wave length, in each experiment, then, with suitable proportions, the mixtures pass from greenish yellow becoming paler and paler until we reach

[1] It is very important to remember that when we say that two colours are "equal" or "match," we only mean that viewed under apparently the same conditions they look alike, *i.e.* are followed by the same results in consciousness. Neglect of this truism has been a fertile source of misunderstanding.

a combination which corresponds to a sensation of whiteness. As we tend to assign a unique position to white in our scale of *sensations*, it is customary to complete the mixing laws by the following addition :—

3. Any light mixture whatever can be matched by a mixture of a definite homogeneous light (or a definite purple) and white light. That our results may be as general as possible, it is well to note that there is no necessity to accord a special place to white, although it is convenient in practice.[1]

We see then that the mixing experiments give us variations in colour tone and variations in whiteness, that is, two variables, so that our results ought to be expressible graphically by some plane figure. We have also seen that we can pass from red to violet through the spectral colours and back again to red through purple, so that our graph should be a closed figure. Finally in virtue of the fact that the position of any mixed colour depends directly upon the relative proportions of its components, we infer that the method of determining the position of the centre of inertia of masses might be adapted to the task of ascertaining the position of a mixed colour, given the nature and proportions of its constituents.

If three colours, A, B, C, none of which can be mixed from the other two, be represented by three points in a plane, then, on assigning to them values in terms of any unit, the situations and quantitative values of their mixtures can be ascertained. Thus a colour mixed from a units of A and b units of B will lie on the line A B at the point at which the centre of gravity of two masses aA and bB (representing the proportions of each colour in the mixture) would be situated.

In order to establish the correctness of this method it is necessary to prove that, given the experimental laws of colour-mixing, as above defined, this construction is valid in all possible cases—*i.e.* that the situation of a mixed colour, in a diagram, coincides with that of the centre of gravity of two equivalent masses when—(1) The two constituents can be mixed from the three chosen colours ; (2) when one can and one cannot so be mixed ; (3) when neither can so be mixed.

The proof is too long for insertion in this essay, but it is quite straightforward (⁹). We can show that the co-ordinates of the point

[1] Cf. on this point, J. v. Kries, Nagel's *Handb.*, vol. iii., p. 116.

at which the mixture must be situated according to the mixing laws, are the co-ordinates of the centre of gravity of masses situated at the points at which the components are represented.

It is clear that a diagram constructed on these principles will vary in accordance with our choice of units and fixed points. Thus Newton chose white as a fixed point and arranged the simple colours at equal distances from it, so that his diagram was a circle. We should obtain this result except that the part of the curve passing from violet to red must be a straight line, since purple can only be mixed from these colours and therefore lies on the chord joining them.

Recurring to the experimental facts previously mentioned, we

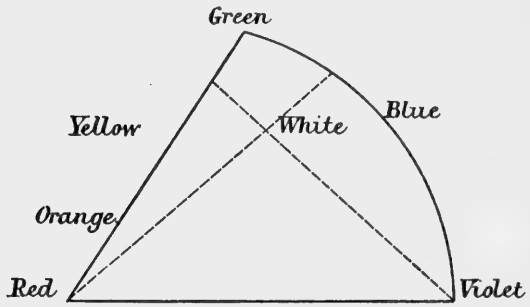


FIG. 4.—Colour Table.

see that the most convenient form of diagram will be that figured (Fig. 4). From red to yellow the curve is a straight line since we found that mixtures of colours between these limits matched pure spectral lights; we then get a sharp bend in the part of the diagram beyond green, representing the low saturation of mixtures from this region; finally we have the straight line through purple.

Suppose now we select three colours in the spectral series, *e.g.* red, green, blue, then in accordance with our previous deductions, all mixtures of these are represented in the triangle RGB. This includes a good deal of our complete diagram, but not all of it. If we choose, instead of blue, violet, then the triangle RGV comprises nearly the whole spectral diagram; in other words, nearly all colours can be matched by mixing three chosen lights in suitable proportions (*vid. infra*, p. 404). There is

not, indeed, a complete super-position, because of the bend in the spectral diagram between green and blue, which means that mixtures of green and violet are less saturated than spectral cyanide blue; we can, however, generalise a little.

If spectral greenish-blue be mixed with red in certain proportions, it matches a mixture of green and violet—

$$a.G\ Bl. + b.R. = c.Gr. + d.V.$$

Hence

$$a.G\ Bl. = c.Gr. + d.V. - b.R.$$

or we have the unmixable colour in terms of our three chosen colours.

It is to be remarked that colour equations, as they are termed, of the form

$$a.R. + b.Gr.\ C\ c.V. = d.R.$$

seem to be a justifiable way of expressing the facts. Addition is uniform, the same result being always obtained when the same quantities are summed; it is commutative, the order of operations does not affect the result; it is associative and homogeneous. Analogies may be discerned in the process of colour mixing. Green + (mixed with) Red + Violet = Red + Green + Violet = (Red + Violet) + Green.

If we define subtraction *in terms of arithmetical quantity*, as uniform, non-commutative, and non-associative, similar analogies can be observed. This, however, is of little importance; the justification of using the symbol of addition in an arithmetical sense is sufficient for our purposes.

We can now consider some experimental points. Since practically all chromatic stimuli may be expressed in terms of three, researches can be planned in the following way. A definite spectrum, *e.g.* the prismatic spectrum of an Auer gas lamp, and three lights of arbitrary but constant intensity, *e.g.* a red, a green, and a violet, are selected; each part of the spectrum is then matched by a mixture of all the three or of two, or by only one of them. In this way, Koenig and Dieterici investigated normal colour vision ([10]). Details of the results need not detain us; all I wish to emphasise here is the general conclusion that the experimental facts of colour *stimulation* can be graphically represented by a plane figure and the possible forms of stimuli reduced to

terms of three independent variables; that is to say, from the point of view of stimulations, normal colour vision is trichromatic.

It is important to notice that a choice of variables is, from the theoretical standpoint, arbitrary; indeed, if a table be constructed in terms of three primaries, A′, B′, C′, a second can be deduced in terms of another three, A″, B″, C″, because, in view of what has been said, we can evidently define any one of the new variables, *e.g.* A″, in terms of the old ones by a linear relation of the form

$$A'' = a.A' + b.B' + c.C'.$$

The process, in fact, merely involves a change of the co-ordinate axes. Of course, if we choose the three primaries so close together that we cannot experimentally reproduce all the spectral stimulus values, our table will involve negative directions, but this is of no theoretical importance.

Summarising the points dealt with in the last few pages, we find that—

(1) Fixing our attention on stimuli alone, mixing results are functions of two variables and graphically expressible by means of a plane figure.

(2) Colour differences can be expressed in terms of three chosen stimuli, the choice being *theoretically* unrestricted, but in practice certain real stimuli are selected for convenience.

I must reiterate here the fact that all these statements purport to be merely descriptive and to resume experimental observations as briefly as possible. Colour diagrams and the assertion that colour vision is trichromatic are only short ways of expressing experimental results; they contain no hidden theoretical assumptions, and their truth, or falsehood, is purely a matter of observation and necessary inference from such observations. It is essential to separate the theory I propose to discuss from the data which have given birth to it.

Section III.—Partial Colour-blindness

We have seen that, from the purely experimental point of view, the characteristics of normal colour vision admit of relatively simple arrangement, that in fact all the results of stimulation can be expressed in terms of three different stimuli and no more; we

must next consider some types of vision which, although abnormal, throw light upon the normal mechanism. These are the commoner forms of congenital partial colour-blindness.

The existence of abnormal colour perception in certain people has been recognised for more than two centuries (11); but John Dalton, the great chemist, was the first who attracted much attention to the subject (12).

Goethe in his *Farbenlehre*, which appeared in 1812, gives the following description: (13)—

"We will here first advert to a very remarkable state in which the vision of many persons is found to be. As it presents a deviation from the ordinary mode of seeing colours, it might fairly be classed under morbid impressions; but as it is consistent with itself, as it often occurs, may extend to many members of a family and probably does not admit of cure, we may consider it as bordering only on the nosological cases and therefore place it first.

"I was acquainted with two individuals not more than twenty years of age, who were thus affected. . . . They agreed with the rest of the world in denominating white, black, and grey in the usual manner. . . . They appeared to see yellow, red-yellow, and yellow-red like others. . . . But now a striking difference presented itself. If the carmine were passed thinly over the white saucer, they would compare the light colour thus produced to the colour of the sky and call it blue. If a rose were shown them beside it, they would in like manner call it blue; and in all the trials that were made, it appeared that they could not distinguish light blue from rose colour.

"They confounded rose colour, blue, and violet on all occasions; these colours only appeared to them to be distinguished from each other by delicate shades of lighter, darker, intenser, or fainter appearance.

"Again they could not distinguish green from dark orange, nor, more especially, from a red-brown.

"If any one accidentally conversing with these individuals, happened to question them about surrounding objects, their answers occasioned the greatest perplexity, and the interrogator began to fancy his own wits were out of order. With some method we may, however, approach to a nearer knowledge of the law of this deviation from the general law.

"These persons, as may be gathered from what has been stated,

saw fewer colours than other people : hence arose the confusion of different colours. . . ."

Since the time of Goethe a great deal of attention has been devoted to the subject and its literature has attained to formidable proportions. I only propose to consider that aspect of the subject which seems to be of theoretical interest.

The most obvious distinction between the vision of partial colour-blinds and our own is their inability to perceive differences which are plain to us. As Goethe says, they see fewer colours than we do. This difficulty is of special interest because it is something definite ; it is easy to find out whether a person can distinguish between the effect produced on him by two stimuli which certainly affect us differently, while what the actual nature of the effect is, remains unknown. How, *e.g.*, a certain green light affects a colour-blind eye, by what sensation it is followed, we can only guess ; but we know that the effect cannot be distinguished by the subject from that produced by a certain physical intensity of red light.

We have thus to deal with a condition in which the conscious responses to varied physical stimuli are fewer than in normal persons ; the question is whether experimental results can be summarised in the simple manner that was possible in the case of normal vision. It will be found that the results appear capable of even simpler description.

We concluded that, for most experimental purposes, normal colour stimulation is expressible in terms of three colours ; the vision of partial colour-blinds is expressible in terms of two only. If we choose as our fixed lights a red and a blue, these, mixed in suitable proportions, match any part of the spectrum, as the latter appears to the partially colour-blind, and a mixture of the two also matches unanalysed daylight. In the sense in which normal colour vision is trichromatic, this form is dichromatic.

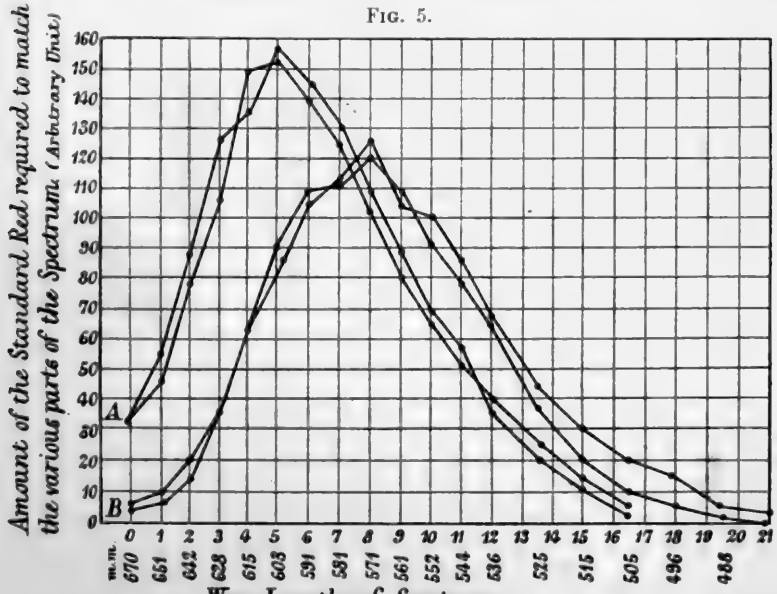
But, just as in normal persons the actual proportions of the constituents in mixtures equal to various spectral lights do not agree completely,[1] we also find different types of dichromatic vision, distinguished by their respective mixing ratios. The two classes

[1] The question of so-called abnormal trichromatic systems cannot be discussed here. Consult Koenig, *Zeits. f. phys. und psych. d. Sinnes.*, vol. 4, p. 317. Donders, *Arch. f. Anat. u. Phys.* (Physiol. Abth.), 1884, p. 518. V. Kries, *Zeits. f. Psy. u. Physiol. d. Sinnesorg.*, vol. 19, p. 63.

Proportions of Standard Red and Blue in a Mixture of apparently the same Tint as various Spectral Colours in four cases of Partial Colour Blindness (v. Kries).

Spectral Wave Lengths in millionths of a millim.	Deuteranope (1).		Deuteranope (2).		Protanope (1).		Protanope (2).	
	Red.	Blue.	Red.	Blue.	Red.	Blue.	Red.	Blue.
670·8	33·0	...	34·4	...	5·3	...	4·9	...
656·0	48·0	...	56·4	...	9·1	...	8·4	...
642·0	79·0	...	95·0	...	19·0	...	18·0	...
628·0	107·0	...	126·0	...	38·0	...	38·5	...
615·0	147·0	...	138·0	...	63·0	...	63·0	...
603·0	151·0	...	155·0	...	90·0	...	84·0	...
591·0	137·0	...	144·0	...	109·0	...	105·0	...
581·0	124·0	...	129·0	...	111·0	...	113·0	...
571·0	103·0	...	108·0	...	120·0	...	126·0	...
561·0	82·0	...	89·0	...	108·0	...	106·0	...
552·0	64·0	...	65·0	...	92·0	...	101·0	...
544·0	52·0	...	56·0	...	78·0	...	85·0	...
536·0	41·0	6·3	37·4	6·0	65·0	...	67·5	...
525·0	26·0	12·0	21·0	10·3	38·3	11·0	46·8	...
515·0	15·0	28·0	13·7	21·6	20·6	34·0	32·8	13·0
505·0	7·7	36·0	7·5	32·2	9·8	35·0	17·2	29·0
496·0	3·7	48·0	4·1	46·3	4·8	47·0	8·4	33·0
488·0	1·6	62·0	1·9	58·0	2·2	57·0	5·3	49·0
480·0	0·9	64·0	0·9	67·0	0·9	66·0	2·9	71·0
469·0	0·3	70·0	0·3	65·6	0·3	67·0	1·0	69·0
460·8	...	67·0	...	68·6	...	54·0	...	66·0

FIG. 5.



Red Values for Partial Colour Blinds (v. Kries).
The two curves A are Deuteranopes, the two B Protanopes.

Amounts of Red (Lithium Line) required to match a Standard Yellow (Sodium Line) by 11 Protanopes and 9 Deuteranopes (v. Kries).

Protanopes.	Deuteranopes.
214·0	36·5 [1]
213·0	36·3 [1]
211·0	36·3 [1]
205·0	36·5 [1]
196·0	38·4
198·0	37·3
210·0	37·0
200·0	37·0
210·0	37·8
203·0	37·0
225·0	36·9
...	38·0

Ratio is 5 : 1 (Approx.).

which have been most studied are known as Protanopes and Deuteranopes. Their special characters will be described briefly.

Experimentally, we proceed as in the examination of normal colour vision. A certain red and a certain blue are chosen; the whole spectrum matched and expressed in terms of the standard lights. The tables and diagram (p. 395) embody the results obtained by J. v. Kries ([14]).

An examination of the curves shows that the cases fall into two groups in respect of red values. The four sets of blue values, on the other hand, are not very dissimilar; in fact, remembering that the physical differences of macular absorption would be most influential in that region of the spectrum where the blue values agree worst, we may regard the similarity as fairly close.

Referring to the tables, we see that for matching spectral lights of wave length greater than 530 $\mu\mu$ no blue at all is necessary, so that the forms of the red curves beyond this point are especially instructive. In one group the curve rises fairly sharply to a maximum in the neighbourhood of 571 $\mu\mu$, and then falls sharply, suggesting a relatively low stimulus value for long-waved light; in the other group the rise is more gradual, attaining a maximum at 603 $\mu\mu$, while the curve does not fall to so low a point at the red end.

[1] One subject.

Hence, within the region under examination, we may say with fair accuracy, that the four subjects are grouped into a pair relatively more sensitive to short-waved light and a pair relatively more sensitive to long-waved light. The former are called protanopes, the latter deuteranopes.

But we have thus far only examined four cases, and must see if the results can be substantiated with the help of a larger number of subjects. If the conclusions just stated be valid, in matching yellow some partial colour-blinds will require enormously more red than others (protanopes); and this experiment, which can be readily performed, will test our conclusions. V. Kries made the test on twenty cases, using red (lithium line) and a fixed yellow (sodium line). As will be seen from the table (p. 396) the subjects do in fact fall into groups, one set (protanopes) requiring approximately five times as much red as the other class (deuteranopes) to match the standard yellow. The classification is therefore a tolerably definite one.

This relative insensibility to long-waved light explains the observation that in protanopes—who correspond to the class badly named "Red Blinds"—the red end of the spectrum appears shortened. The shortening is, however, of little interest from our present standpoint.

It is to be remarked that individual differences occur within each class. In the two protanopic cases, from 552 $\mu\mu$ onwards to violet, one subject constantly demanded more red in his mixture than the other. The subject requiring less red may be presumed to have a deeply pigmented macula, so that the homogeneous light was weakened by selective absorption, because the diminution in red values agrees with the known increments of absorption as we pass towards the violet. The difference is of some importance in connection with an interesting peculiarity of dichromatic vision. Since daylight can be matched, for the dichromatic eye, by a mixture of red and blue, and since all spectral colours can be matched by mixing these standards, we should expect some spectral colour to match more or less closely unanalysed daylight. The situation of such a colour is called the "Neutral Point" of the spectrum. As for protanopes the stimulus value of lights falls off rapidly towards the red, their neutral point should be nearer the violet than that of deuteranopes, and this is generally the case. But, if there is a good deal of macular pigmentation, the mixed

light undergoes selective absorption, and the homogeneous match is nearer the red end. Thus the typical difference may be obliterated and a simple determination of the neutral point would not enable us to distinguish the two forms.

A study of the neutral point, however, immediately brings to our notice that characteristic which has attracted the attention of practical men. Spectral light between 490 and 500 $\mu\mu$ induces normally the sensation green; for the dichromatic it has the same effect as unanalysed daylight *or* a mixture of red and blue. Now this mixture contains much red and little blue, so that a normal person asked to name the simple colour and the mixed colour which look alike to the dichromatic would probably call them green and red; so that we can say that both protanopes and deuteranopes confound red with green. Even here we observe a class difference. In matching a given bluish-green, the protanope, being relative insensitive to long waves, requires much red in the red-blue mixture; the deuteranope takes about the same amount of blue but much less red. Accordingly, a protanope will match a light bluish red (physically speaking) with a green that appears to us much darker, *e.g.* a scarlet with olive green; a deuteranope matches a far bluer red with a green which we should take to be about equally bright. Hence, although both groups confuse certain reds with certain greens, the matches of one class are not usually valid for the other.

These then being the chief characteristics of the two common forms of colour-blindness, we must endeavour to ascertain what relations their visual systems bear to those of normal persons. The mere fact that the systems are dichromatic would tell us comparatively little; we should indeed conclude that, owing to the reduction of different stimulus forms, sensations of colour are less numerous for dichromatics than for ourselves, but they might be quite different, and what we seek is a relation between stimuli.

As early as 1837, Seebeck expressed the opinion that two lights or mixtures of lights which appeared equal to the normal eye, never appeared unequal when examined by a partial colour-blind. If this be true, it is of importance, because it would show that these people lack something possessed by a normal person, but have nothing, no stimulus reaction, which is not shared by the normal eye; in other words, colour-blindness is purely an error of

defect not excess. The validity of normal equations for the two groups of partial colour-blindness has been recently tested by v. Kries. His conclusions are clearly expressed in the following passage :—

"One employs the frequently cited equations between a homogeneous yellow and a mixture of red and yellowish-green (670·8 and 550 $\mu\mu$). As all lights in this region are of equal stimulus value for the colour-blind, whatever be the ratio of red : yellowish-green, one can always give the homogeneous yellow an intensity such that the match is good either for a protanope or a deuteranope, but in general the matches of the one are not valid for the other. As we should expect, a strongly red mixture is for the protanope equivalent to a yellow of relatively feeble intensity ; a deuteranope finds in a match arranged by the protanope, the mixture too bright and the pure yellow too dark. The relation is reversed for strongly green mixtures. With extraordinary accuracy, however, we find that for the ratio of red : yellowish-green that has for the trichromatic an equal colour tone with the homogeneous yellow, both groups agree ; trichromatic equations are valid for both protanopes and deuteranopes. Conversely, if we try to find an equation valid for both groups, we arrive precisely at the one valid for a normal person." [1]

Additional evidence is afforded by the following considerations. Suppose we prepare a table giving the mixing ratios for a normal person in matching spectral colours between 670·8 $\mu\mu$ and 550 $\mu\mu$. The results are as follows :—

Spectral Region.	Proportions of Standard Colours.	
Wave Length.	670·8 $\mu\mu$.	552 $\mu\mu$.
670·8	88·5	...
628·0	251·0	10
615·0	276·0	27
603·0	270·0	49
591·0	202·0	67
581·0	123·0	76
571·0	73·0	91
561·0	21·0	80
552·0	...	71

[1] Nagel's *Handb.*, vol. iii. p. 160.

We also find that a certain deuteranope requires 33 units of the standard 670·8 to match the spectral 670·8, and 64 units of the same standard to match the spectral 552.

If deuteranopic vision be merely a reduction form, we ought to be able to calculate from these data the stimulus values of the intervening lights. Take as an example 591, which is matched by 202 units of 670·8 plus 67 units of 552. We must change from the arbitrary units of the normal system by dividing by 88·5 and 71 respectively, and then express in the deuteranope's intensity system by multiplying by 33 and 64. The stimulus value should be therefore: $202 \times 33 \div 88{\cdot}5 + 67 \times 64 \div 71 = 135$ (approx.) units.

This, then, is the stimulus value of 591 $\mu\mu$ expressed in terms of the intensity values of 670·8 and 552 $\mu\mu$ on the hypothesis that a match good for a trichromatic eye is valid for a dichromatic. The observed value was 137. In this way the following table was obtained: ([15])—

Stimulus Values for Deuteranope and Protanope.

Wave Length.	Deuteranope.		Protanope.	
	Calculated.	Observed.	Calculated.	Observed.
670	33	33	4·9	4·9
628	106	107	28·8	38·5
615	126	145	54·2	63·0
603	145	151	86·0	84·0
591	135	137	108·0	105·0
581	114	124	117·0	113·0
571	110	103	137·0	126·0
561	76	82	111·0	106·0
552	64	64	101·0	101·0

A further, but less satisfactory test is afforded by the construction of a colour diagram or "triangle" combining observations made upon the two classes of colour-blinds. As this would involve the discussion of some rather technical details, and involves certain assumptions of questionable validity, it will not be further considered in this essay.[1]

[1] See the memoir by v. Kries cited in the last footnote, also Nagel's *Handb.*, vol. iii., p. 162, and especially for the theory of a dichromatic "Fehlpunkt," Helmholtz, op. cit., pp. 363, &c. I am deeply indebted to Professor v. Kries for information respecting his work on dichromatic systems.

Summing up this rather difficult piece of work, I think the reader will agree that :—

(1) The two commoner forms of partial colour-blindness are distinguished one from another by a different responsiveness to stimulation by long and medium wave-lengthened light. Protanopes are relatively insensitive to long waves, deuteranopes to moderately long waves.

(2) Each is an example of dichromatic vision, using the term in a purely experimental sense.

(3) Each may be regarded as, to some extent, a reduction form of normal vision, although, as we shall see later, this conclusion cannot be pushed very far.

The forms of partial colour-blindness just described are of everyday occurrence, and their recognition of obvious practical importance ; [1] another type less common, and therefore less completely studied, is that known as blue or blue-yellow blindness. This condition, unlike the last two, is not as a rule congenital, usually one-sided, and associated with definite pathological changes in the retina ; it affects, generally, only a portion of the visual field. Koenig's observations make it probable that this type also is dichromatic ; [2] two suitably chosen lights will match the entire

[1] For the practical tests employed in the detection of colour-blindness, the reader must consult the special treatises. It may be remarked that considerable difference of opinion exists among ophthalmologists as to the reliability of the test in common use.

[2] For the reader's convenience, I give a list of the chief papers dealing with blue-yellow blindness.

(1) *J. Stilling*, Beiträge z. Lehre v. den Farbenempfindungen Klinische Monatsbl. f. Augenheilk. Jahrg. 13 (1875), 2nd Supp. p. 41, Jahrg. 14, 3rd Supp. p. 1. Stuttgart, 1875–6.

(2) *Cohn*, Studien über angeborene Farbenblindheit, Breslau, 1879, pp. 139–148 (five cases with good bibliography).

(3) *Donders*, Annales d'Oculistique, 12th series, vol. 4, 1880, p. 212.

(4) *Holmgrén*, Centralbl. f. Augenheil., 5th Jahrgang, 1881, p. 476.

(5) *Hermann*, Ein Beitrag z. Casuistik d. Farbenblindheit. Inaugural Dissertation, Dorpat, 1882. (Not seen.)

(6) *V. Vintschgau*, Pflüger's Arch., vol. 48, p. 431. (A full account, without theoretical bias, of a case in which no pathological changes were observed and a precis of the observations contained in 1–5.)

(7) *V. Vintschgau*, Pfl. Arch., vol. 57, p. 191. (Continuation of (6).)

(8) *Hering*, Pfl. Arch., vol. 57, p. 308. (A study of v. Vintschgau's case, which Hering regards as yellow-blue blindness combined with a weak red-green sense.)

(9) *Wundt's* Philosophische Studien, vol. 8, p. 173, 1892. (Not seen.)

(10) *Koenig*, Ueber Blaublindheit, Sitzungsbericht. d. Preuss. Akad. d. Wissenschaft. in Berlin, 29th Juli, 1897, xxxiv. p. 718 (Pathological).

spectrum. The neutral point is in the yellow, between 566 and 570 $\mu\mu$.

At the risk of being tedious, I must emphasise the fact that the truth or falsehood of the foregoing account depends entirely upon the trustworthiness of the various observations. None of the statements rely on any hypothesis as to the mode of action of the visual elements.

Section IV.—After-Images

Considerations of space make it impossible to discuss, even in outline, the numerous interesting observations which have been made upon visual after-images. I will merely, for the purpose of reminding the reader of facts with which he is doubtless familiar, tabulate the main results of modern work.

(1) The distinction between "positive" and "negative" after-images is not absolute but relative, depending on the nature of the reacting stimulus.

(2) An image-producing or "retuning" stimulus changes the stimulus value of a "reacting" (subsequently applied) light, but only in such a way that the sensation response following exposure to the "reacting" light is increased or diminished quantitatively. Colour equations do not lose their validity.

(3) The latter statement is true in the case of foveal vision, but not for peripheral stimulation.

(4) We do not know the time relations of the retuning process, nor whether it proceeds uniformly or in pulses.[1]

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(11) *Piper*, Zeitsch. f. Psy. u. Phys. d. Sinnesorg., vol. 38, p. 155, 1905 (Pathological).

(12) *Levy*, Arch. f. Opthalmologie, vol. 62, 1906, p. 464.

(13) *Collins* und *Nagel*, Zeitsc. f. Psy. u. Phys. d. Sinnesorg., vol. 41, 2nd part, p. 74, 1906 (Pathological).

(14) *Schenck*, Pfl. Arch., vol. 118, p. 161, 1907. (This memoir is mainly theoretical; it describes a case, however.)

[1] For full information, in addition to the treatises of Helmholtz and v. Kries, already frequently cited, see v. Tschermak, *Über das Verhältnis von Gegenfarbe, Kompensationsfarbe und Kontrastfarbe*, Pfl. Arch., 1907, vol. 117, p. 473. G. J. Burch, Proc. Roy. Soc. (1900), vol. 66, p. 204. Some amusing observations by Goethe will be found in his *Farbenlehre* (Eastlake's translation, p. 22).

Section V.—The Three-Colour Hypothesis of Young as Modified by Helmholtz

As we saw, in an earlier section, Newton's researches demonstrating the (conceptually) complex nature of white light and the physical substratum of chromatic stimuli—as co-ordinated by the undulatory hypothesis—enable us to frame a coherent, if not necessarily final account of the physical elements involved in retinal stimulation. On the other hand, the specificity of physiological response, which finds a not quite accurate expression in Müller's law, releases us from some of the difficulties attendant upon the primitive theories of vision, the propounders of which were hampered by their acceptance of the dogma of physico-physiological identity.

On so broad a basis, it is of course possible to erect many, more or less, substantial edifices. In a famous passage, R. L. Stevenson relates that he once overheard two persons arguing. "What I advance," said one, "is true." "Yes," replied the other, "but not the whole truth." "Sir," was the retort, "there is no such thing as the whole truth." It is well to bear that saying in mind when one considers the theories of colour vision.

In attempting to arrive at an adequate interpretation of any experimental facts, more than one route is generally open. As a rule, it does not much matter which path we choose so long as we keep count of any assumptions made and avoid the introduction of unnecessary steps. Let us start, then, from the experimental laws of colour mixing, and see where we arrive by following the most obvious route. We saw that, for most experimental purposes, we could say that a sensation "produced by" a colour stimulus could be matched by a sensation due to a stimulus obtained by mixing not more than three lights. We saw that these three lights did not coincide accurately with any spectral colours, but that, if we admitted negative values into our colour equations, our vision could be regarded as definitely trichromatic, even in terms of known stimuli. In order, however, to avoid this, let us so choose our stimuli that only positive values of each are employed. This means that they must be so chosen that the colour table is

circumscribed by the lines joining their representative points in a plane, *e.g.* :—

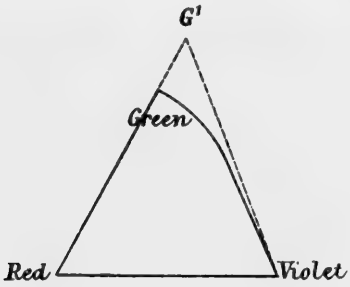

FIG. 6.

This is our first assumption, and is little more than a generalisation of experimental facts.

Thus far, we have merely asserted that any stimulus, R′, say, can be expressed by the equation $R' = x.R + y.G + z.V$, where x, y, z are positive real quantities. But, our only measure of stimulation equality being corresponding sensation equality, we imply (and this is our second and most important assumption) that there is a definite relationship between the physiological excitatory processes which lead up, somehow, to sensations, and the stimulus magnitudes.

This assumption is justified if we can show that it leads to the formulation of a satisfactory working hypothesis, and if we assume the simplest relationship consistent with the experimental facts. What, then, is the simplest relation we can suppose to subsist between the stimulatory and excitatory processes? Clearly that, just as stimuli may be reduced to terms of three independent variables, excitatory processes are represented by three independent variables. Thus, taking our previous example, any stimulus, $R' = x.R + y.G + z.V$, then $A = f_1(x, y, z)$, $B = f_2(x, y, z)$, $C = f_3(x, y, z)$, and conversely, $x = F_1(A, B, C)$, $y = F_2(A, B, C)$, $z = F_3(A, B, C)$.

These latter expressions may be taken as "elements" or unit excitatory processes, or any *linear* functions of them may be so taken.[1]

[1] The proof of this statement, although simple, requires some knowledge of analytical notation, and cannot therefore be reproduced here. See Helmholtz, *Handb. d. Phys. Opt.*, 2nd edition, pp. 342–3.

The conception is merely that three independent physiological processes exist, each of which is defined by an equation connecting it with the three independent stimulus values which, as we have seen, determine the effect of any given stimulus.

This statement represents the fundamental part of the hypothesis, first sketched by Thomas Young, and elaborated by Helmholtz. It is important to distinguish the essentials of the theory from its subsidiary parts.

The effect produced by any chromatic stimulus is supposed to depend upon the resultant changes set up in three independent "substances," nothing whatever being postulated with respect to these substances except that the magnitude of change in each is a function of, *i.e.* depends on, the proportions of three independently variable stimuli in terms of which the given stimulus can be expressed. Conversely, any given stimulus value is a function of the independent activities of three visual "substances." The nature of the substances, also the exact relation between them and the stimuli, are left open. For convenience of illustration, Young and Helmholtz assumed that the activity of each substance was associated with a single colour sensation, and chose red, green, and violet as "elementary sensations" from the present standpoint. "Substance" A, when stimulated, was supposed to give rise to the sensation of red; B, under similar conditions, to that of green; and C to that of violet; in this way the well-known "valency curves" of the text-books were obtained. The advantage of this method is that the theory seems more definite, but the disadvantage is entailed that if the illustration proves irreconcilable with facts of experiment, the reader omits to notice that what is found wanting is merely an *illustration, not* the basal theory.

It is especially important to remember that the colour equations discussed in Section II. do not pretend to describe any direct relationship between the hypothetical "substances" and stimulus magnitudes.

In precisely the same way, for the sake of illustration, Helmholtz suggested the existence somewhere in the retino-cerebral apparatus of three sets of fibres, each corresponding to one of the hypothetical substances.

This suggestion was less happy because its utility was not so great as, and the chance of misunderstanding greater than, in the previous case. The red, green, and violet fibres have reigned long

and ingloriously over the student's imagination: it is time to remember that they are pure abstractions, no more essential to the theory just sketched than the employment in algebra of the letter x to denote an unknown quantity is an essential procedure in that science. To avoid this source of misunderstanding, I shall use Prof. v. Kries' term, Components, and speak of the theory as the "Three Components Hypothesis."

Another mistake is illustrated by the following quotation from a paper by Miss Calkins: ([16])—

"From the point of view of a psychological analysis of our conscious sensations of colour, the postulates of this theory are not in accordance with the facts of observation; for, even granting that violet is a simple fundamental colour sensation (which many observers regard as complex), it can hardly be denied that yellow is just as well characterised and definite a sensation as red or green. Yellow looks yellow, and does not seem at all like a mixture of red and green, or indeed any other colour mixture."

Objections of this type are simply irrelevant. The theory is only an attempt to express physiological processes, of admittedly hypothetical character, in terms of experimental facts; [1] it has nothing to do with a psychological analysis of sensations. Whether such analysis be possible may be doubted; in any case it is and can be no part of our present inquiry, which is only concerned with visual sensations in so far as the latter are signs of the existence of a physiological reaction.

Having reduced the hypothesis to its simplest terms, let us apply it to the facts reviewed in the former sections of this article. Abnormal trichromatic systems are satisfactorily described if we suppose one of the visual components to be defined in a peculiar way. Thus, if a component A is normally defined as $f_a(x, y, z)$, in these cases it is some other function, $f_{a_1}(x, y, z)$, say, of the stimulus values.

Turning to dichromatic systems, we have seen that, from the experimental standpoint, they are reduction forms of a normal system. Theoretically considered, the simplest reduction we could imagine would be the absence or ineffectiveness of one of the three normal components. Thus, if we take R, G, V (for the sake of clearness) as the normal components, in the absence of R all sensations (sensation being used with the meaning above defined)

[1] *i.e.* in terms of stimulus values.

are functions of G and V, a condition *approximating* to that of protanopia. If G is absent, we get a form resembling deuteranopia.

Under such conditions, not only would the relation between dichromatics and trichromatics be easily intelligible, but further we could determine, from observations on dichromatics, the components of a normal system.[1] A stimulus inoperative upon a dichromatic eye must act exclusively upon the missing component. We have learned how to find the situation of such a stimulus in the colour diagram (the "Fehlpunkt"), and the two such points obtained for the two systems of dichromatic vision determine the stimulus relations of two visual components of a trichromatic eye.

All this depends, however, on the assumption that one component is absent and everything else unchanged in a dichromatic eye. Modern work renders it doubtful whether we may make this assumption. In 1885, when the second edition of his great treatise was being prepared, Helmholtz wrote as follows to Lord Rayleigh: ([17]) "I have never doubted that our colour system depended on three variables and no more. In regard to colour-blindness, the recent observations of Donders and of my assistant Dr. A. Koenig, show that this defect cannot be referred simply to the lack of one of the fundamental colours, but that two of the primaries (red and green) appear to acquire a more even distribution in the spectrum, so that now one and now the other makes a more vigorous impression; in other words, the resulting curve approximates now more to the red and now to the normal green sensation. In addition to this we have every shade of lessened power of discrimination. Consequently different individuals require very different mixtures of lithium and thallium light in order to make up sodium light."

But if we cannot regard dichromatic vision as differing from the normal merely in the absence of a component, we can, in terms of the fundamental hypothesis, assert that it depends upon a visual system made up of *two* variables defined by such expressions as $x = \phi_1$ (A, B, C), and $y = \phi_2$ (A [illegible], C).

This way of looking at the matter is consistent and logical, but it is not free from objection. Thus we could not deduce from such an expression any definite statements respecting the components of normal systems; the interpretation of dichromatic systems is, necessarily, expressed in such highly general terms as to be hardly

[1] Or rather the stimuli which act exclusively upon such components.

capable of direct verification. To put the matter in a nut-shell, the older conception of partial colour-blindness as due to the absence of a normal component is simple and, if true, practical, but is not, in fact, quite adequate; the more general form is adequate, but not very helpful.

Next, what has the Component Hypothesis to say with regard to the phenomena of after-images?

A noteworthy feature of after-image experiments is, of course, that stimulation with a given light increases responsiveness to its complementary. It would appear, therefore, easy to imagine that activity of the three components, or any one or two of them, in a certain way diminishes their responsiveness in one direction, increasing it in an opposite direction. This amounts to supposing that we have a condition comparable with the state of the reflex arcs, so brilliantly described by Sherrington: the nervous path is occupied by one form of motor discharge, and this very occupancy paves the way for a discharge different, and even opposite in kind.

To so highly general a statement as this, no objection will be found, but if we investigate details, difficulties arise. For instance, the apparent saturation of spectral colours is greatly enhanced by previously stimulating the eye with their complementaries. Helmholtz accordingly supposed that all the spectral colours stimulate each visual component. But, if this be true, the simpler interpretation of colour-blindness once more fails. Observations of dichromatics suggest that lights having wave-lengths greater than 550 $\mu\mu$ do not affect the third component (the "blue" or "violet" component) at all, because no standard blue had to be mixed with the standard red in order to effect a good match. To a normal eye, however, the saturation of spectral yellow (589 $\mu\mu$) is unquestionably enhanced by previous exposure to blue. Either spectral colours do not affect all three components, in which case the theory does not cover after-image effects, or the simpler explanation of partial colour-blindness must be abandoned. In view of what has already been said, the reader will perhaps agree that the second alternative is the more plausible, and conclude that after-images are adequately described at the cost of strengthening our suspicion that dichromatic and trichromatic systems cannot be co-ordinated in any simple manner.

So far we have found that the Hypothesis of Three Components describes with sufficient clearness the facts of normal colour vision,

including the phenomena of after-images; that it also describes the facts of partial colour-blindness adequately enough, but in very general terms, the earlier direct explanation being insufficient. We have now to see whether any experimental evidence can be found pointing to the existence of independent visual components satisfying the above conditions, or conceivably capable of satisfying them.

Evidence of this kind is furnished by the experimental production of a peculiar form of colour-blindness by G. J. Burch. ([18]) This observer exposed his eye to direct sunlight in the focus of a two-inch lens behind coloured glasses. A gelatine film stained with magenta and combined with a medium ruby glass was found to transmit a fairly pure red, three thicknesses of green glass were used for green, and a tank of cupric ammonia-sulphate for violet. Similar arrangements were made for the other hues, and in some experiments a large spectroscope was employed. Two minutes' exposure was sufficient to produce the maximal effect in the case of red.

After exposure to red light, the following effects were noted. Scarlet geraniums appeared black, calceolarias and sunflowers green, purple flowers, such as clematis, violet. Pink roses were sky blue. Fatiguing with violet light caused objects reflecting violet light to appear black, purples and reds seemed crimson. Green stimulation made the foliage appear reddish or bluish-grey. But, after these exposures, "the colour by which the eye has been dazzled, and to which it is now blind, tints all those objects which naturally reflect none of this." The truth of this is illustrated by a simple experiment. ([19]) Suppose the eye to be somewhat fatigued by green, as during a long country walk, if under these circumstances the eye be directed to a small red spot on a black surface, *e.g.* a geranium petal on the black cover of a book, and one walks quickly with it into a dark shed or barn, the colour of the petal changes from red through orange and yellow, becoming eventually perhaps whitish. On coming into the light again the red reappears.

These experiments suggest that stimulation with red, green, and violet alters responsiveness with respect to these stimuli alone, and the same is found in the case of blue. Orange stimulation, on the other hand, affects not only the appearance of the orange but that of the red and green as well. Both positive and negative

effects pass off rapidly in the case of artificial red blindness (in ten minutes), more slowly after violet fatigue (in two hours).

It is, I think, obvious that the state of affairs presented by these experiments is highly complex. We are dealing with a change of responsiveness, analogous to the retuning effects, as they are called, produced in the study of after-images, but of greater magnitude, and in less simple form. Take the experiment quoted as to the apparent hue of a geranium petal after green stimulation: this is an ordinary after-image effect, and differs in no way from the results obtained by other workers; in the case of exposure to stronger green light, the effect is similar. How does this, we may ask, differ from the experiment with intense orange light? Simply in the fact that "retuning" with orange, red and green both act like orange itself in inducing a negative image. The conclusion that in this case the mechanism involved in the production of orange is compounded of a mechanism yielding a sensation of redness and a mechanism responding with a sensation of greenness is reasonable, and finds some confirmation in a recent experiment carried out by Burch. ([20])

We know that responsiveness to green is increased, relatively to that for red stimulation, by resting the eye in darkness; hence, if orange or yellow depends upon a fusion of two physiological processes, one concerned with green, the other with red, then, under conditions of feeble illumination and dark adaptation, the yellow should appear greenish, because the mechanism responding by a sensation of greenness, is more active under these conditions than that associated in the same way with redness.[1]

Burch found this actually to be the case; "the sodium lines appeared pale green when of the minimum visible intensity."

These results do therefore support a contention that components in the sense of our theory may possibly have a physiological counterpart. I do not think, however, that the view that four components—a red, a green, a violet, and a blue—exist is proved by Burch's experiments. To prove that any light acts upon only one component it would be necessary to show that after dazzling with, *e.g.*, blue, any mixed light was altered by the subtraction of blue, and that any light not containing blue had that colour added to it. The facts that the condition is transitory, is perhaps

[1] The reader must forgive the apparent confusion between object and subject of vision which is rendered inevitable by the necessity of being concise.

attended with some risk, and almost certainly involves psychological complications, render exact observations difficult. Under the circumstances, it is perhaps best to say that, although the experiments are perfectly consistent with a component hypothesis of the type discussed, it would be rash, on the strength of them, to make any general statement as to the nature of the components from the physiological standpoint. Theoretically it does not matter whether we adopt three or four components; the algebraical form of our theory would not be changed, but we should lose the practical advantages of considering normal colour vision to be, experimentally, trichromatic, which would be a serious objection.

Before finally summarising the case presented, two matters need attention. First, as to monochromatic vision or total colour-blindness. It has been asserted that such a condition cannot be described in terms of the Young-Helmholtz theory. As a matter of fact, the assertion is inaccurate; symbolically we could cover the facts by supposing that the functions defining the variables are identical thus: $A = f(x, y, z) = B = f(x, y, z) = C = f(x, y, z)$, or, graphically, we can put it that the three valency curves coincide. In any case, the reader will probably see reason to think that monochromatic vision depends upon a mechanism entirely distinct from the precursors of normal foveal vision, and its treatment should be kept separate from that of the phenomena with which we are here concerned.

In the second place, no reference has been made to Simultaneous Contrast. The reason is that it seems doubtful whether the phenomena of simultaneous contrast are not of quite a special kind. It is true that the original hypothesis of Helmholtz, which assumed that contrastive effects are dependent upon factors, purely psychological in nature, can hardly be maintained without some modification; the subject is, however, so complex that its discussion would not be intelligible in the space at our disposal. It must, however, be said that if subsequent work should compel us to assign a *purely* physiological basis to the facts of simultaneous contrast, it will probably be necessary to modify the theory of components in such a way that it will become somewhat more complicated than it is at present.

Leaving this matter for future consideration, we can say that the Component Hypothesis associated with the names of Young and Helmholtz supposes—(1) That colour sensations depend upon

the activity of three independent physiological substances of unknown nature and situation. (2) That the relationship between these components and the complex of stimuli is expressible quantitatively by saying that the responsiveness of each component is measured by a real linear function of three standard stimuli. (3) The results of stimulating these components are unit sensations in a *purely physiological sense*, not units of consciousness. (4) No spectral light acts upon only one hypothetical component.

The theory describes with sufficient accuracy the main facts, and there is some direct experimental evidence—that of Burch—which is consistent with its truth. Further, the main objection to the hypothesis in its modern form is its highly general nature and want of direct applicability to the immediate objects of physiological and physical research. How far this is a real objection may be a matter of discussion, but it at least inclines one to examine those theories which are, in the colloquial phrase, less up in the clouds. Such an examination will now occupy us.

Section VI.—Hering's Theory of Visual Sensations

In the preceding section, I attempted to trace out the theoretical consequences which it seemed possible to reconcile with the experimental facts of colour mixing. As I have pointed out, with wearisome frequency, perhaps, the whole process depended upon the observation that, in general, the effect of a given stimulus or of a combination of stimuli was constant, so that we might attribute to the stimulus a causal value. In other words, we have regarded the sensations as the *signs* or *differentiæ* of stimulation processes, and our theory, therefore, was in that sense not a theory of visual sensations at all but a theory of visual stimuli.

If the estimate I formed of the value of this process be at all just, it would follow that its weakness lay rather in what was left unsaid than in any incorrectness or improbability in its positive teaching. An objector, let us say the hypothetical man in the street, might perhaps express his criticism in the following terms: "You compel me," he might say, "to examine a great many facts, and force me to puzzle out some difficult quantitative reasoning, and at the end you leave me with a few highly general theorems which, you confess, only describe some of the phenomena. Whenever I

clutched at a straw of definite specific statement, that straw was instantly snatched away again. Is it worth while going through so much for so little ? "

I do not think such an objection at all unreasonable. It is good to be as simple as possible, provided we do not sacrifice truth in the process, and we find that deductions from stimulus values do *not* lead us to any very simple results. Let us see, therefore, what fortune attends us when we pursue our quest by a different path altogether ; perhaps in this way we shall attain to something more intelligible and practical.

The other line of investigation practically resumes the problem at the point at which the Greeks left it, and dates from the publication in 1810 of Goethe's *Farbenlehre*.

The comparatively slight influence that has been exercised by this work upon the development of modern physiological thought respecting the nature of visual processes, is due to causes well worth notice. The physical analysis of white light into monochromatic constituents by Newton had naturally attracted the chief, almost the exclusive, attention of those who occupied themselves with the study of colour vision. Goethe, however, saw quite clearly that the difficulties of the problem were not to be overcome by vague references to physical experiments. He saw that the problem was one of sensations, and he therefore approached it from a sensational standpoint. Had he contented himself with this, with an analysis of sensations of colour, his work must have had an enormous influence ; but he went further. The prevailing tendency to over-estimate the significance of the physical side of the problem in visual theories led Goethe into the opposite error. He sustained the thesis that the Newtonian analysis was physically incorrect, and that the alleged physical analysis of white light was not in general possible. Consequently, much of his work is devoted to an attack upon the Newtonian hypothesis from the physical side. Since this attack failed, more valuable portions of Goethe's book became involved in the discredit this produced.

I can best give an idea of the valuable parts by quoting a few significant passages.

" With regard to the German terminology, it has the advantage of possessing four monosyllabic names no longer to be traced to their origin, viz. yellow (*Gelb*), blue, red, green. They represent

the most general idea of colour to the imagination, without reference to any very specific modification. If we were to add two other qualifying terms to each of these four, as thus—red-yellow and yellow-red, red-blue and blue-red, yellow-green and green-yellow, blue-green and green-blue, we should express the gradations of the chromatic circle with sufficient distinctness; and if we were to add the designations of light and dark, and again define, in some measure, the degree of purity or its opposite by the monosyllables black, white, grey, brown, we should have a tolerably sufficient range of expressions to describe the ordinary appearances presented to us, without troubling ourselves whether they were produced dynamically or atomically." (21)

"Considered in a general point of view, colour is determined towards one of two sides. It thus presents a contrast which we call a polarity, and which we may fitly designate by the expressions *plus* and *minus*.

Plus.	Minus.
"Yellow.	Blue.
Action.	Negation.
Light.	Shadow.
Brightness.	Darkness.
Force.	Weakness.
Warmth.	Coldness.
Proximity.	Distance.
Repulsion.	Attraction.
Affinity with Acids.	Affinity with Alkalis." (22)

We see here formulated the conception of certain colour sensations as occupying unique places in our sensational field, and presenting also, as it were, a species of sensational contrast one with the other.

Not only is this conception present in the minds of those who seek to influence us through the colour sense (painters), but it is given effect to in their practice.

In a dialogue on colours by Ludovico Dolce, published in 1565, the following passage occurs: (23) "He who wishes to combine colours that are agreeable to the eye, will put grey next dusky orange, yellow-green next rose colour, blue next orange, dark purple, black, next dark green, white next black, and white next flesh colour."

Titian, according to his biographer Ridolfi, was fond of opposing

red and blue to his flesh tints, and Rubens contrasted a bright red with his "still cooler flesh colour" (Eastlake).[1]

The point to mark is the general agreement that certain of our sensations of colour are really singled out from the whole group as presenting sharply-defined, special characters. All sensational theories are primarily concerned with the definition of these characters, and secondarily with an attempt to describe the data in terms of a physiological hypothesis.

Of such attempts the views developed by Professor Ewald Hering and his pupils during the last five-and-thirty years are the most valuable results. Whatever may be our ultimate conclusion as to the validity of these theories, no one can doubt that they have greatly advanced our knowledge of visual physiology, and their study cannot be neglected by any one desirous of acquiring even a superficial idea of modern conceptions.

According to Hering's method of analysis our whole visual world can be resolved into six elementary sensation qualities—white, black, the toneless, and blue, yellow, green, red, the toned or bright (*bunte*) colours.

If we consider the tone-free qualities, we can form a series of shades or graduations passing from intensest white to deepest black. If we attend to the toned colours, they can be arranged in a circle with four divisions.

"If we choose in such a colour circle any colour as starting-point, for instance a red similar to that with which a spectrum usually begins at the long-waved end, we see the red colours arranged in one direction gradually becoming more yellowish, while the redness of the colours correspondingly diminishes, until finally, passing through orange and golden-yellow, we arrive at a yellow which contains no trace of the red which is still so apparent in the orange. To this yellow succeed other yellow colours which play more and more into the green (sulphur-yellow, canary-yellow); further on (as in sap-green) the yellowishness recedes more and

[1] In the work of Rembrandt, who is, I believe, regarded by those qualified to judge as the greatest exponent of contrastive effects, the most striking results seem to be rather light-dark contrasts, as in the Hague "Anatomie," than specific colour oppositions. For instance, in the (so-called) "Nachtwache," the yellow sunlight and yellow costume of one of the central figures, which produce such a magnificent brightening effect, are balanced by general shadow without any apparent use of the "Gegenfarbe." This seems to apply also to the "Staalmeesters." A careful study of the chief master-works of painting from the standpoint of the visual physiologist would be most interesting.

more behind the steadily increasing greenishness, until we finally reach a green which seems to be entirely free from yellow. To this succeed green colours which already play into blue (water-green); further on the bluishness of the colours becomes increasingly stronger, the greenishness weaker, until we finally reach a blue exhibiting no more greenishness at all. To this blue succeed blue colours of increasing reddishness and correspondingly diminishing bluishness (blue-violet, red-violet, purple-red), until the last trace of bluishness vanishes in a definite red." (24)

If we define a pure green as a sensation free from admixture with blue and yellow, and the other three sensation qualities in the same manner, we see that our pure colours (from this point of view) can be arranged in two pairs, yellow and blue forming one and red and green the other. The members of each pair can be placed opposite one another in a diagram, because we can only pass from yellow to blue or from red to green by traversing the province of a member of the other pair, as just explained. There is no pure yellowish-blue or reddish-green sensation quality.

But there is yet another contrast, from the standpoint of sensation quality, between yellow and red on the one hand, blue and green on the other.

Somehow, in a manner difficult to express in words yet of universal experience, the two former colours are associated with a certain heightening and increased vividness of sensation-tone, while the two latter exercise a depressing or subduing influence. This finds its expression in the classification by artists of colours into warm and cold. Goethe has emphasised these points :—

"We find from experience, again, that yellow excites a warm and agreeable impression. Hence in painting it belongs to the illumined and emphatic side.

"This impression of warmth may be experienced in a very lively manner if we look at a landscape through a yellow glass, particularly on a grey winter's day. The eye is gladdened, the heart expanded and cheered, a glow seems at once to breathe towards us." (25)

Of blue he says: "This colour has a peculiar and almost indescribable effect on the eye. As a hue it is powerful, but it is on the negative side, and in its highest purity is, as it were, a stimulating negation. Its appearance then is a kind of contradiction between excitement and repose.

". . . Rooms which are hung with pure blue appear in some degree larger, but at the same time empty and cold.

"The appearance of objects seen through a blue glass is gloomy and melancholy." (26)

How far these results depend on mental factors, *e.g.* an association of ideas, cannot be discussed in this place; it is sufficient to recognise their existence.

In the opinion of those whose theories we are examining, the facts are most satisfactorily described by saying that in any sensation-complex blue and green produce a darkening, and yellow or red a brightening effect; the toneless colours, black and white, also contribute respectively in a negative or positive sense to the sum total of effects. We have, therefore, the brightness of a colour defined in strictly sensational terms.

We have now arrived at the conception of six primary sensation qualities arranged in three pairs—white-black, red-green, yellow-blue. The first member in each case increases, the second diminishes the subjective intensity or brightness of a sensation-complex of which it forms part.[1]

"The brightness or darkness of a toned (*bunte*) colour is, according to this view, the result of the inherent brightness or darkness (*Eigenhell und Eigendunkel*) of its constituent pure colours, which as the pure constituents of that colour agreeably to their respective distinctness determine the quality of the colour. In any colour really existent for us is a definite inherent degree of brightness and darkness, and in accordance with whether the brightness or the darkness be the more distinct, we call (the colour) bright or dark.

"A toned colour may generally be regarded as made up of four primary components, two toned and two tone-free (black and white). Only in colours of the tone of a pure colour is one toned constituent present by itself. In any red-yellow colour, *e.g.* orange, we have accordingly to distinguish three bright, pure components (red, yellow, white), and one dark (black); but in any green-blue, three dark (green, blue, black) and one bright. The red-green and green-yellow colours would contain, however, two bright and two dark pure components.

[1] Sensation-Complex is a term used merely to indicate the supposed multiplicity of infra-conscious representatives, not in a perceptual sense.

"From what has been said the following rules can be deduced :—

"If two colours of equal tone and equal purity differ in brightness this is due to a difference in their black-white components.

"Two colours differing in tone may, notwithstanding equal degrees of purity and equality as regards their black-white components, differ in brightness.

"With equality of conditions as to the black-white components, a yellow, a red, or a yellow-red colour is so much the brighter, a blue, a green, or a blue-green so much the darker, the more distinct the colour tone in comparison with the black-white constituent." ([27])

This extract describes what is often called the theory of the "specific brightness" of colours. All that has gone before purports to be a faithful analysis of our visual sensations without reference to any hypothesis whatever. That this is a perfectly legitimate procedure I have already attempted to show : the next step is to translate these facts, or supposed facts, into terms of a physiological hypothesis.

Such a translation can readily be effected.

It is supposed that somewhere in the retino-cerebral apparatus, in the infra-conscious sphere, four distinct substances exist. Each of these substances can undergo a building up or anabolic and a breaking down or katabolic change. External stimuli will, depending on their natures, induce either an anabolic or katabolic change in the substances, and these are associated with a definite colour sensation. The building up of the black-white substance corresponds to a sensation of blackness, its breaking down to a sensation of whiteness ; anabolism of the red-green substance is associated with green colouration, its katabolism with red colouration ; similarly in the third substance yellow is katabolic in origin, blue anabolic.

Before discussing these views in detail, I should like to clear up certain popular misunderstandings. Some opponents have asserted or suggested that the facts upon which the theory is based differ in some perverse way from those data which are ordinarily called facts of experiment. This is not the case. The facts the hypothesis attempts to describe are as legitimately objects of inquiry as any others within the purview of physiological science.

It is further to be noted that the four physiological "sub-

stances" have just as much and just as little real existence as the three components of our other theory. It is idle to say that the postulated anabolic and katabolic processes are essentially unlike any chemical mechanisms with which we are acquainted. It is equally vain to object that stimulation processes in animal nature are, to all appearance, bound up with katabolic changes; this would be a valid objection if we tried to identify the hypothetical substances with any known retino-cerebral constituent. No such identification is attempted; the suggestion that Hering and his school identify the black-white substance with visual purple is altogether false. The fact is that this theory can only be judged on the grounds of scientific expediency, and in no other way. Does this method of presenting the facts give us a clearer insight into the phenomena of vision than the method based upon stimulus relations? This is the only question which requires to be answered.

We notice at once that the hypothesis, in the form in which it has just been epitomised, offers two considerable advantages. Firstly, it deals with the immediate data of vision, the visual sensations of colour, directly, and not in terms of stimulation magnitudes. In this sense it might be called a primary hypothesis. In the second place it is essentially simple and easy of comprehension, which is a very strong point in its favour.

But if we find, on testing this simple hypothesis with such facts of experiment as have previously been detailed, that it rapidly ceases to be simple; if we find that its apparently direct grip upon the objects of investigation is perceptibly weakened; in one word, if it ceases to be definite, then its characteristic advantages will have disappeared.

Let us first of all attempt to express the facts of successive contrast, after-images in terms of the hypothesis. After resting the eye on a white object, we should expect, under certain conditions, a positive, under others a negative after-effect. The experimental results agree perfectly with the theory. In the case of colour stimuli, we can understand why complementary reacting lights gain in saturation. For example, if the eye be stimulated with green, anabolism will occur in the red-green substance, an anabolism which will lead to the formation of a large quantity of "material." If now red light stimulates the retina, it produces not only katabolism of the normal quantity of substance, but the

new formed material also falls to pieces and the correlative sensation is greatly enhanced. All the simple phenomena of after-images are adequately described, but a detailed examination yields less promising results.

V. Kries found that the responsiveness of the eye to monochromatic light was markedly altered by previous exposure to white. He found that the stimulus value of the red he employed was diminished in the ratio of about one to four by previous retuning with white.[1] How can this come about if the black-white substance is independent of the red-green substance ?

Hering's own views on this matter deserve careful study.([28]) He objects that, in v. Kries' experiments, the colour used as a reactor (180° blue, 180° white on a disc) was not sufficiently saturated, and brings forward the following experiment :—

Two discs are arranged, A and B. A consists of a black centre surrounded by a white ring, B of a centre composed of 120° blue and 240° black, encircled by a ring containing 356° blue and 4° white. A point upon the internal margin of the white ring in A is fixated for a given time, and the experimenter then turns his eye to an exactly corresponding point in B. Hering always found that the outer ring in B, under these conditions, looked more saturated than the centre.

As the term saturated is not used by Hering in the physical sense, the exact bearing of his objection to v. Kries' experiment is not apparent. Presumably what is meant is that the "blueness" of such a disc was not distinctly separable from its "whiteness," with the result that the admitted change in the latter on retuning with white was mistaken for a change in the former. If this objection is admissible, it is, however, equally fair to retort that in Hering's counter-experiment the difference between the amounts of blue in reacting and comparison fields was so great that an enormous diminution in responsiveness over the retuned area would be necessary for the production of a good match between the centre and periphery of B. Put briefly, the contention is that after white retuning, a reacting blue and white can be made to match a pure blue in brightness by adding more white ; adding more blue will always make the reactor too saturated. Hering's experiment does not seem to prove more than that a

[1] For an account of v. Kries' work and some more recent observations of hi pupils, see Nagel's Handb., Bd. iii., p. 210, &c.

diminution of about 66⅔ per cent. in apparent intensity cannot be attained by retuning with the white he employed. That the apparent brightness *was* correspondingly reduced is indeed favourable to his hypothesis, but it is to be noted that we have under these conditions the difficulties of specific brightness comparison in their most acute form.

The discussion of conflicting experimental methods is, however, always a thankless and mostly a dull task; the reader's special attention is accordingly directed to the following remarkable passage with which Hering concludes his memoir:—

"To the change of state experienced by an element of the somatic visual field when acted upon by, *e.g.* blue light, with which the blue sensation is associated, the whole somatic visual field reacts by a change in the opposite direction which corresponds to the oppositely coloured or yellow sensation, and any light that now falls on the retina acts, in consequence of this chromatic retuning of the visual field, as if its yellow valency were increased and its blue valency correspondingly diminished. This retuning is maximal in the immediate vicinity of the element acted upon by the blue light, and diminishes with its distance from the same. . . . A white light falling on the neighbourhood of the region which has been stimulated with blue seems therefore more or less yellowish, but a white light which falls together with blue on the spot that has been stimulated with blue, seeing that it behaves as a more or less yellow-valent light, neutralises the blue valency of the blue light so much the more, the greater be the quantity of it mixed with the latter. This explains the striking fact that the chromatic quality of a saturated colour is so extremely quickly extinguished by increasing the amount of white mixed with it. . . ."

"When v. Kries, therefore, supposed that, according to the theory of opposite colours (*Gegenfarben*), the same result would be obtained from a fatigued and an unfatigued area if the same quantity of blue light were allowed to fall on both, but in addition on the fatigued area a suitably chosen quantity of white light, he was in error. In such a case, the blue valency of the blue light at the unfatigued area is unaltered since no other light is mixed with it; over the fatigued area the blue valency of the blue light is partly neutralised by the admixture of white. Accordingly the blue at this latter area must appear less saturated than at the former. In fact a transitory equality in brightness and saturation

between the two areas is only obtained when white is indeed mixed with blue for the fatigued area, but on the other hand, the blue light for the unfatigued area is suitably diminished. In general, for reasons already given, an equality in colour tone for blue can only be obtained under exceptional circumstances, when the character of the daylight is specially favourable and the tone of the blue just right." (29)

It has been said by Professor William James that John Stuart Mill was in the habit of boldly asserting in general terms the truth of a philosophical theory derived from his father, and then admitting in detail the validity of all objections to it. A trace of this method can be discerned in the passage just quoted. The whole memoir is designed to show that white retuning does not affect colour valency. Experiments apparently in favour of the rival hypothesis are met by other experiments in support of this contention. We are led to suppose that white retuning and colour retuning are independent, and naturally infer that since white retuning does not affect colour valency, colour retuning ought not to affect white valency. This, however, is specifically asserted not to be the case.

It is not, of course, to be supposed that the two propositions are logically inconsistent, but the independence of the postulated physiological processes is no longer paralleled by the facts of sensational analysis. What is (from the standpoint of sensations) a pure white has a definite colour valency. Pure white (in terms of the physiological process in the black-white substance) is just as hypothetical as anything postulated by the theory of stimuli.

It will, I think, be clear that in order to cover the facts of retuning, the sensational theory loses some of its original simplicity. It is interesting to notice that the theory becomes more difficult to follow by developing in a direction opposite to that followed by the stimulus theory; the latter became unsatisfactory, to some, by tending to be too general, the former by multiplying its details.

I have enlarged upon the question of retuning, a matter not perhaps of very special importance in itself, because, as I hope to have shown, the facts are not quite so easily described by the Hering theory as some of its supporters would lead one to imagine. These very facts have been claimed by eager adherents of both schools as decisively favouring their respective beliefs.

Perhaps the ingenuous reader will conclude that neither claim is admissible.

Space and the reader's patience do not admit of analysing in detail the further applications of the theory to visual phenomena. I will merely say a few words on the Hering theory of dichromatic systems.

It was originally thought that the theory covered these facts extremely well, and even in so good a text-book as that of Professor Howell it is suggested that an advantage of the sensational theory is its better description of the facts of partial colour-blindness. In reality, it seems very difficult to bring the facts into line with the theory.

It was once suggested that both types, protanopes and deuteranopes, depended on the non-existence of the red-green substance, the typical distinction being due to varying degrees of macular and lens pigmentation, combined with unequal responsiveness of the blue-yellow substance.

We have already seen that the characters of the two groups, protanopes and deuteranopes, cannot be due to differences in pigmentation, and the inconsistency of the colour equation, $R + G = 652$, is difficult to reconcile with this view.

Tschermak, a prominent member of Hering's school, seems definitely to abandon this attempt to describe dichromatic vision,[30] and, so far as I know, an adequate expression of the facts in terms of Hering's hypothesis is not yet forthcoming. This is not a fatal objection to the theory, because the sensational analysis of dichromatic vision is extremely difficult, owing to the fact, among others, that colour nomenclature is adapted to trichromatic vision, trichromatics forming the large majority of all civilised races. It must, however, be realised that this hypothesis does not seem likely to advance our knowledge of colour blindness further than that of three components.

Our general conclusion, therefore, may perhaps be expressed in the following terms.

The theory associated with the name of Hering is an attempt to arrive at a general conception of the visual processes by an analysis and comparison of sensations. In this way prominence is given to many interesting facts not specially or adequately considered by the theory founded on stimulus relations. If, however, we attempt to build up upon such data an hypothesis

adequate to the task of describing all the experimental facts, we encounter difficulties not less formidable than those we found to be associated with the Young-Helmholtz theory.

In attempting to meet their respective difficulties, the two theories become unsatisfactory in different ways. The stimulus hypothesis becomes too general, the sensational hypothesis too detailed. Examples have been described in the former's treatment of dichromatic vision and the latter's account of after-images.

Perhaps the most tempting inference is that these theories are in a sense complementary—that they both contain some measure of truth, surveying the vast complex of phenomena from very different points of view. Neither theory is wholly true nor yet wholly false ; nor does adhesion to the one imply total rejection of its ostensible rival.

I am only too conscious that, like Canning's clerical friend, in being brief I have by no means escaped being tedious. My only excuse, and that but a poor one, is that if we are ever able to propound a complete theory of the visual processes, this comprehensive formula will embrace both those I have described, and until that time comes a critical examination and comparison of both lines of thought will always be indispensable to those who wish to gain a real knowledge of visual physiology. In conclusion, the reader is most earnestly recommended to consult the original memoirs of Hering and the treatise of Helmholtz dealing with this subject. He will not, indeed, find them light reading—no really scientific books are ; but he will be repaid by a grasp of the matter in hand such as can never be derived from text-books, however lucid, or summaries, however long.

BIBLIOGRAPHY

[1] *Beare*, op. cit., p. 18.
[2] *Aristotle*, De Sensu et Sensilibus, Taylor's Trans., vol. iii., p. 133.
[3] *Beare*, op. cit., pp. 36–37.
[4] *Plato*, Timæus, Jowett's Translation, vol. ii., pp. 538–9.
[5] *Helmholtz*, Handb. d. Phys. Optik., 2nd edit., p. 248.
[6] *Plato*, Theætetus, Jowett's Trans., vol. iii., pp. 375, 378.
[7] *Beare*, op. cit., p. 64.
[8] *Beare*, op. cit., p. 69.
[9] *Helmholtz*, Handb. d. Phys. Opt., pp. 328–330.

[10] *Koenig* and *Dieterici*, Zeits. f. Psy. u. Physiol. d. Sinnesorg., vol. iv., p. 241.

[11] *Turberville*, Phil. Trans., 1684. *Huddart*, Phil. Trans., 1777. *Whisson*, Phil. Trans., 1778. [*Vide* Koenig's Bibliography appended to Helmholtz, Phy. Opt., 2nd ed., for full bibliography.]

[12] *J. Dalton*, Literary and Philosophical Society of Manchester, 1794.

[13] *Goethe*, Theory of Colours, translated by Eastlake, London, 1840 (Murray), pp. 45–47.

[14] *J. v. Kries*, Ueber Farbensysteme Zeits. f. Psy. u. Phys. d. Sinnes., vol. 13, pp. 241–324; and Nagel's Handb., vol. 3, pp. 153–5. The technic is partly described in Zeits. f. Psy. u. Physiol. d. Sinnesorg., vol. 12, pp. 4, &c.

[15] *J. v. Kries*, Zeits. f. Psy. u. Phys. d. Sinnesorg., vol. 13, p. 241.

[16] *Miss Calkins*, Arch. f. Physiologie, Supp. Bd., 1902, pp. 244 *et seq.*

[17] *Koenigsberger*, Life of Helmholtz, Engl. Trans. by Miss Welby, Oxford, 1907, p. 364.

[18] *G. J. Burch*, Phil. Trans., B., vol. 191, pp. 1–34. Proc. Roy. Soc., vol. 66, pp. 216–219.

[19] *Burch*, Proc. Roy. Soc., vol. 66, p. 219.

[20] *Burch*, Proc. Roy. Soc., B., 1905, p. 214.

[21] *Goethe*, op. cit. (Eastlake's trans.), pp. 243–4.

[22] *Goethe*, op. cit., p. 276.

[23] *Ibid.*, Note C.

[24] *Ewald Hering*, Grundzüge der Lehre vom Lichtsinn, Leipzig, 1905, &c. (separate publication not yet complete), p. 41.

[25] *Goethe*, op. cit., p. 307.

[26] Ibid., p. 310.

[27] *Hering*, op. cit., p. 61.

[28] *Hering*, Ueber die von der Farbenempflindlichkeit unabhängige Aenderung der Weissempflindlichkeit. Pfl. Arch., vol. 94 (1903), pp. 533, &c.

[29] *Hering*, op. cit., p. 552.

[30] *Tschermak*, Ergebn. d. Physiol., 1st Jahrg., 1902, IIte Abth., s. 795, &c.

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