On the relation of the nervous system to disease and disorder in the viscera / by Alexander Morison.

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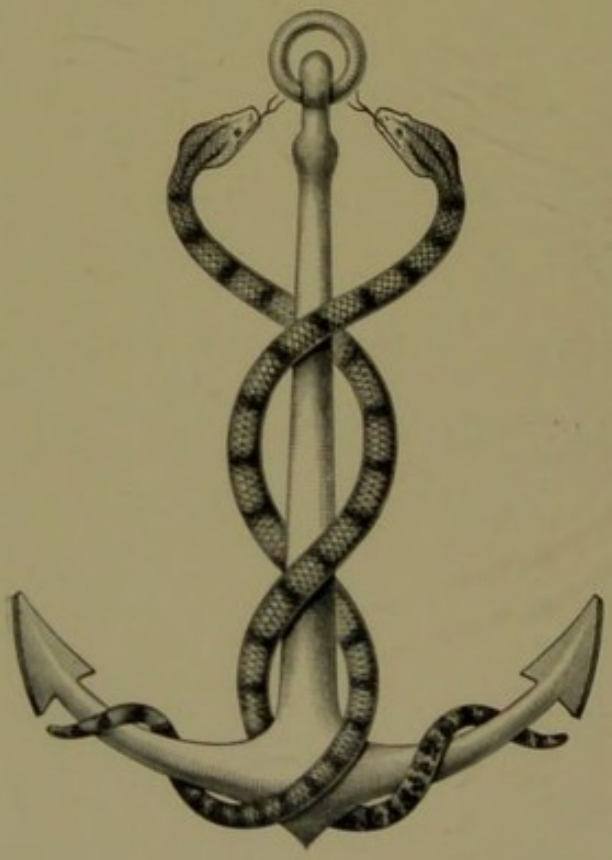
THE NERVOUS SYSTEM AND DISEASE AND DISORDER IN THE VISCERA.



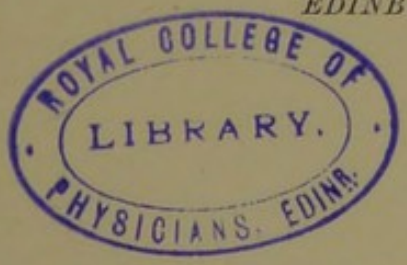
NUNQUAM ALIUD NATURA, ALIUD SAPIENTIA DICIT.

ON THE RELATION OF THE NERVOUS SYSTEM

TO

DISEASE AND DISORDER IN THE VISCERA.

BEING THE MORISON LECTURES DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS IN EDINBURGH IN 1897 AND 1898.



BY

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THESE PHYSICO-PSYCHOLOGICAL LECTURES

ARE INSCRIBED

AS A CENTENNIAL TOKEN OF AFFECTIONATE REMEMBRANCE

TO THE MEMORY OF

SIR ALEXANDER MORISON

OF BANKHEAD, MIDLOTHIAN, KNT.,

FELLOW AND PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS IN EDINBURGH;
FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS IN LONDON, ETC.,

WHO GRADUATED AT THE UNIVERSITY OF EDINBURGH IN 1799;

AND

TO THE MEMORY OF

JOHN FORBES

(OF BLACKHALL AND PITSLIGO),

MASTER OF ARTS OF UNIVERSITY AND KING'S COLLEGE, ABERDEEN;
MINISTER OF THE PARISHES OF LOGIE-COLDSTONE AND
KINCARDINE O'NEIL;

"*Doctrinae, facundiae, prudentiae, amicitiae,*
pietatis ac pacis laudibus illustris."

PREFACE.

In the present issue of the following lectures, which have already appeared *in extenso* in the *Edinburgh Medical Journal*, and as full abstracts in the *Lancet*, some verbal corrections have been made, and a little additional matter interpolated to make my meaning clearer. Some illustrations which were unsatisfactory have been omitted, and others added. In connection with these, I desire to express my great obligations to my friend Mr. Frank Crosbie of London, who spared neither time nor his well-known skill as a photographer, in producing the photo-micrographs. I have also to thank my friend Dr. Forbes Ross of London, for the assistance he rendered both Mr. Crosbie and myself. My obligations to others are expressed in the text.

14 Upper Berkeley Street,
Portman Square, London
May 1899.

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THE NERVOUS SYSTEM AND DISEASE AND DISORDER OF THE VISCERA.

LECTURE I.

THE ANATOMY OF VISCERAL INNERVATION.

Mr. President and Fellows.—When the Council expressed to me the desire of the College that I should deliver the Morison Lectures in 1897 and 1898, I need not assure you that I was as much surprised as gratified by the unexpected honour you had done me. My first impulse was, respectfully to decline your proffered kindness, and the more so because a honorarium is attached to the lectureship, the appointment to which has, in consequence of the agreement of the College with the founder, lain in my hands.

On reflection, however, I conceived that the monetary difficulty might be capable of arrangement, and felt that the privilege of addressing you, which your indulgence proposed to confer upon me, was not to be declined without serious consideration. For having rendered it possible for me to accept the office, I beg to offer you my thanks.

I am well aware that my own position and attainments were little worthy of your consideration. My gratification, nevertheless, in addressing you from this place, rests upon the double ground of my fellowship of the College, and my kinship with the founder of the lectureship.

The continuous or perpetuated consciousness or *esprit de corps* which pervades and actuates large and important bodies of men, like the Royal College of Physicians, influences likewise the smaller and humbler human aggregate of the family. It is therefore, as I have said, doubly pleasing to me to have the

opportunity of offering, in my own generation, filial homage to the memory of my grandfather, in this hall, to which he was ever warmly attached, and before this company, among whom, had he been alive, he would have rejoiced to have seen me numbered, and to be numbered among whom I regard as the chief honour of my professional life.

When I remember the distinguished names which have been associated with the lectureship—the names of Dr. William Seller, of Sir Arthur Mitchell, of Sir John Batty Tuke, of Drs. Clouston and Sibbald, of Professors Gairdner and Hamilton, and of Drs. Keiller and Alexander Bruce, I am even now appalled at my temerity in having accepted the post, and crave your indulgence should my efforts fall short of the standard of excellence established by them.

The subject-matter for my lectures presented another difficulty. A large proportion of those delivered have dealt with mental disturbances of the brain from the alienist's point of view, and to special knowledge in this sphere I could lay no claim. A smaller proportion, however, were concerned with the nervous system from the point of view of the anatomist, the pathologist, and the general physician; and it was with the latter that I felt I could most appropriately associate myself.

My attention had for some time been directed to the relation of the nervous system to disease and disorder in the viscera, partly on account of the admitted obscurity of the subject, and partly because of the frequent opportunities presented to me in hospital and private practice of examining cases in which that relation seemed, while obscure, to be nevertheless indubitable. I concluded, therefore, that this subject would be worthy of more systematic examination, and might have some interest for others as well as myself.

As the honorary secretary of the College was good enough to convey to me your wish that I should deliver the lectures for 1897 and 1898, I determined to deal with the matter in its more purely scientific aspects this year, namely, in its anatomical and physiological aspects, as distinguished from the bearing of these fundamental considerations upon the pathology and clinical phenomena manifested by disease and disorder of visceral innervation, which I propose treating in the next series.

It would be impossible, in the time at my disposal, to enter with detail into the neural anatomy and physiology of all the viscera, and were it possible it would be tedious to do so. I shall

therefore endeavour to study the matter on representative lines so as to elucidate, however dimly, those principles which guide us in the rational discovery and treatment of disease affecting the organs which we conventionally term viscera, although it might be legitimately argued that the whole organism is but a complex viscus.

Before examining the anatomical relations of nerves to viscera, however, it may be of interest, and not unprofitable, to refer shortly to the *methods* suitable for their detection and examination.

The essentials of vision are visual power on the part of the instrument of sight, and visibility of the object looked at. The earlier microscopists trusted chiefly to the translucency of the object and the power of the microscope to discover detail; and when we look at the beautiful delineations of detail in works such as those of Lionel Beale, delineations in some instances representing an enlargement of 1800 diameters, we recognise what excellent work was done before the era of modern methods. The endeavour of the modern microscopist is, by staining methods of various kinds, to render the object examined more visible—a circumstance which naturally renders the use of the higher powers of the microscope less necessary.

For the examination of detail, central and peripheral, in the nervous system, the use by Camillo Golgi in 1880–81, and by Santiago Ramon y Cajal in 1889, of the chrome-silver method, has caused a revolution in our conceptions of the ultimate nervous system, a revolution which has been powerfully promoted by the adhesion to that method, and his own researches by its means into the minute anatomy of the nervous system, by Albert von Kölliker, the revered *doyen* of European histologists, to whom some of us can offer the homage of pupils to their master.

The Golgi-Cajal method is, however, notwithstanding its indubitable value, not an easy method of examination, and this, by their own confession, even in the hands of some who are justly acknowledged to be experienced and trustworthy histologists. My own experience of the method in the examination of nerve-endings in viscera was disheartening in the extreme, and for such results as I have obtained I had to betake myself to another method which I shall mention presently. I was convinced, however, that the fault lay with me, not with the method, in my failure, and I determined to betake myself to my old teacher, Geheimrath Albert von Kölliker, for information, as I saw from

the last edition of his "Gewebelehre" that he had employed it very successfully. The result of my visit to Würzburg I have pleasure in stating here, as I believe it may save others much disappointment and loss of time, and save, likewise, this invaluable method from the aspersions of the unsuccessful. I had an opportunity of examining many specimens of the central and peripheral nervous systems with Herr G. Peter Hofmann, the curator of Professor Kölliker's museum, who made all or most of the preparations which illustrate the last edition of the "Gewebelehre," and saw for the first time the perfection to which the Golgi-Cajal method could be brought.

The method pursued by Herr Hofmann, under Professor Kölliker's supervision, is not essentially novel, but some points which have at times been lost sight of are emphasised and rigorously adhered to.

The tissue to be examined must be fresh—*lebend warm*—and when cut in moderately thin sections, placed at once in the osmic acid and bichromate of potash solution, without previous hardening in Müller's fluid. The mixture consists of a 1 per cent. solution of osmic acid and a 3 per cent. solution of bichromate of potash in distilled water, in the proportions of one of the former to four of the latter. The tissue is left in this mixture at a temperature of 30° to 33° C. for three days, and shaken from time to time, to prevent the deposit of precipitate upon it, a manœuvre which appears to contribute to the remarkable clearness of the Würzburg preparations; thereafter, it is transferred directly to a ·75 per cent. solution of nitrate of silver in distilled water for at least two days, and it may be allowed to remain in this solution for any length of time, that is, until used in the next step in the method. On being first placed in the silver solution, there is, of course, a precipitate, which necessitates its transference in half an hour to fresh solution, in which it may remain without further changing. It is when the tissue is removed from the silver solution for further treatment that the necessity for care, and especially for promptness of action, arises. Upon this the result, satisfactory or otherwise, seems mainly to depend. It should be placed for one hour in absolute alcohol. Then for half an hour in thin celloidin, followed by an immersion of a few minutes only (two or three) in thick celloidin, and mounted for section. The celloidin block should then be placed in 70 per cent. alcohol till hardened, a process which takes from one to three hours. Sections should be made, however, within an hour

of embedding, if possible, and the preparations mounted without a cover-glass. Herr Hofmann informed me that he had found a longer postponement of section-cutting involved a loss of fine detail, and that this was also the case if good preparations were mounted under glass, without having previously been fixed by hydrochinon treatment—a somewhat tedious process, in no way essential for practical purposes.

The expression "quick Golgi method" is usually applied to that which does away with a preliminary hardening of texture in Müller's fluid for a week or two, but it might be more profitably used in connection with the quickness necessary in the operations following the removal of the stained tissue from the nitrate of silver solution.

Berkley[1] appears to have got good results by a method which differs from that described, chiefly by a preliminary immersion of thin sections of tissue in a saturated solution of picric acid. This is certainly not necessary for obtaining the best conceivable results, and, in my hands, has appeared to present a barrier to the penetration of the essential solutions, by coagulating the surface of the tissue.

Other methods employed in the examination of the central have likewise, in the hands of some, been of service in the investigation of the peripheral nervous system. For the staining of peripheral ganglion cell's Nissl's method may yield good results, and I shall show under the microscope the distal sympathetic cells of the heart so stained.

Dogiel's modification of Ehrlich's methylene blue method has been fruitful of good results in his hands.

The method I have personally found most useful is that employed by Sihler of Ohio,[2] which was brought to my notice by Dr. Fred. E. Batten, who used it in the preparation of the specimens on which his recent valuable paper on muscle spindles was based.[3]

The difficulty of staining the peripheral nervous system consists in its fineness, and its being surrounded by texture more or less dense. Stains appear to require application as directly as possible, and with sufficient potency to effect their purpose. Thus, while Ehrlich's intravenous injection of methylene blue stains peripheral nerves, Seme Meyer's subcutaneous injection of

[1] *Johns Hopkins Hosp. Rep.*, Baltimore, 1894, p. 50.
[2] *Arch. f. Physiol.*, Leipzig, 1895, S. 202.
[3] *Brain*, London, 1897, pts. 77 and 78.

the same material, while it acts admirably on the central nervous system, is of little value for peripheral work. For this reason also, Dogiel's direct application of methylene blue appears to act much better on peripheral nerves than the more indirect modes of using that stain which I have mentioned.

Sihler's method is a direct method, and consists—(1) In macerating the tissues to be stained in acetic acid, glycerine, and a 1 per cent. solution of chloral hydrate in distilled water, in the proportions of one each of the two first to six of the last. (2) In staining the macerated tissue for a week or ten days in a mixture which differs from that first used only in containing Ehrlich's hæmatoxylin instead of acetic acid. (3) In placing the stained tissue in pure glycerine. (4) If considered desirable in removing overstaining by acetic acid or Pal's solution.

In using this method, I made thin sections of the organs with Cathcart's freezing microtome, left them for a fortnight or longer in the stain, and in glycerine for an indefinite period. The longer they remained in glycerine the better I found the result to be, as the staining seemed to be continued in that medium, and the tissue to become softer and more easily teased or squeezed. This I believe was also the experience of Dr. Batten. I am also under the impression that the stain and the medium (Farrants' solution), in which the preparation is mounted, continue to define detail for a time after mounting, and am strengthened in this belief by a statement recently made to me in conversation by Dr. Lionel Beale, that he had had the same experience with the glycerine-carmine method which he has so fruitfully practised.

For the detection of nerve-endings in muscle, and for showing the relation of distal ganglionic cells to nerve trunks, I found this method very satisfactory; but for the investigation of intercellular nerve-endings in secreting glands, it was less successful in my hands. The profuse nuclear staining which results from the use of hæmatoxylin is a disadvantage in this respect, and, in the case of fœtal structures especially, tends to obscure detail. I did not decolorise many of my specimens, as doing so seemed to me to render the detection of the finer nerves more difficult.

It is just fifty years since Bidder of Dorpat, in 1847, published his pamphlet "Zur Lehre von dem Verhaltniss der ganglien Körper zu den Nerven fasern," with an appendix by Volkmann of Halle, in which he gives a résumé of the knowledge at that time of the relation of ganglia to nerves. He mentions the heated controversy between two young observers of the period, Valentin

and Remak, in which the former denied and the latter affirmed the origin of nerve fibres from ganglion cells.

It is provocative of reverential admiration that, in this early brochure, Bidder mentions the favourable reception—unaccountable to him—accorded to the discovery published in 1844 by a young scientist of Zurich, that ganglia could originate fibres which shortly assumed the double contour of medullated nerves. That scientist was Albert Kölliker, who still, as an octogenarian, graces the ranks of medicine, and this retrospect alone conveys to the mind the long and valuable services of him who in 1896 published a new edition of his histology of the nervous system, and contemplates, with the enthusiasm of perennial vigour, still further work. That he may live to accomplish this must be the desire of all who honour distinguished service in the cause of science, and especially of those who, like myself, have had the privilege of his personal instruction.

Notwithstanding the admirable work of many investigators in the interval, the anatomy and physiology of the sympathetic system, and its relation to the cerebro-spinal centres, remained in many respects obscure, until a comparatively recent period, and debatable questions in connection with it cannot even yet be regarded as settled.

During the last decade our knowledge of visceral innervation has been greatly increased. The invisible (as in other spheres) was previously regarded as the non-existent in many organs, which are now known to be richly endowed with nerves.

The researches of Golgi, Ramon y Cajal, Kölliker, Gustaf Retzius, Van Gehuchten, Sala, Von Lenhossek, Ehrlich, and the Dogiels abroad, and of Berkley and Sihler in America, have done much to elucidate a dark field of inquiry.

To our own countrymen we also owe much, and before referring to later investigators it would be unpardonable not to acknowledge our indebtedness to Lionel Beale, whose position to-day is not identical with that of many histologists, as regards the manner of nerve termination, but whose accurate observations have a permanent value. Gaskell, Langley, and F. M. Balfour of Cambridge, have each, by different methods, rendered clearer to us a subject once the despair of anatomists, physiologists, and physicians alike ; and the more recent work of Professor Paterson on the embryology of the sympathetic system has placed in a clearer light the original relation of the sympathetic to the

cerebro-spinal system, a relation, as influencing function, to which I shall have occasion to refer again.

We may determine the character and course of a river by following it from its source to its outflow into the ocean; or we may trace it from its distribution to its fountain-head. In examining the innervation of the viscera, I propose adopting the latter method.

The stream of visceral innervation may, in its ultimate distribution, be likened to a delta with three mouths, these points being (1) the secreting cell, (2) the cell of involuntary muscular fibre, and (3) an intermediate or compound and more obscure condition, the innervation of metabolism and excretion.

The innervation of the secreting cell.—A. S. Dogiel of Tomsk, in his paper on nerve-endings in the tear gland of mammals,[1] before proceeding to give particulars of his own investigations, refers to the previous work of others with other glands as establishing a general identity of method in nerve distribution, in secreting glands as a whole. Although some have figured what appear to be nerve-terminals on cells, the general result of investigations hitherto has been, that the actual termination in a cell has not been established. Even the apparent fine endings on or between cells Dogiel regards as due to incomplete staining of continuous nerve fibrils. His own results, he considers, show that non-medullated fibres surround vessels and ducts; that fibres arising from these primary branches surround in loops the ducts of the gland, and form a plexus on the membrana propria; that small twigs from the latter pierce the membrane and form a network over the cells; and that, finally, extremely fine fibrils, arising from the cellular plexus, find their way between the cells, forming a pericellular or circumcellular plexus, in the meshes of which the cells are, as it were, embedded. Dogiel thus supports the well-known contention of Lionel Beale, that apparent nerve-endings are a fallacious conclusion from imperfect observation,—a view which is opposed to the opinion of the majority of histologists of the present day. Dr. Beale's opinion remains the same as in the days of his active histological work. He recently remarked to me, aphorismically, "A nerve-ending has no end." Kölliker, on the other hand,[2] states that the penultimate plexus, which is frequently observed, ends free, and that he is in a position to vouch for this fact in the case of intestinal villi, the spleen, the

[1] *Arch. f. mikr. Anat.*, Bonn, Bd. xlii. S. 632.

[2] "Gewebelehre," S. 870.

kidneys, the muscles of the intestinal wall, and the mucosa of gut. Gustaf Retzius also joins issue with Dogiel. He admits with Kölliker and others the occurrence of terminal plexuses, but not of terminal nets or loops.[1] The controversy between Valentin and Remak concerning the origin of nerve-fibres is thus pushed by the discoveries of the intervening period to the extreme limits of the nervous system; and although it cannot even now be considered to be settled in favour of the terminalists, the balance of evidence is on their side.

A point of great interest, and one which it appears to me can only be determined by the method of induced degeneration, is the discrimination of intraglandular sensory or afferent fibres from the efferent secretory fibres proper. Sensibility is probably essential to all perfect vital action, but the execution of all peripheral functions, as will be asserted again, is in the sphere of the motor division of the nervous system; and to distinguish between these secretory motor fibres and intraglandular sensory fibres by the microscope is not at present possible. These intraglandular sensory fibres are not to be confused with others which cause increased discharges of secretion. This may arise from the most distant stimuli—mental and other. The intraglandular sensory fibres are, nevertheless, the afferent channels for the intrinsic irritability of the cell, and necessary to the quiet and continuous elaboration of secretion characteristic of healthy gland tissue.

A fallacy against which one must be on one's guard in the examination of the intercellular distribution of nerve fibrils, is the possibility of mistaking the staining of the nuclei of intercellular capillary vessels for nerve elements. In my own examination of this point by Sihler's method, so far, I regret to state that, while I have stained some good penultimate plexuses, I have not met with the success I had hoped for, and have been deceived more than once by the possible fallacy I have mentioned. I have, therefore, had to rely upon the results obtained by other and more skilful histologists, and throw on the screen reproductions of Dogiel's and Retzius' illustrations as representing the views at present entertained by the two opposing schools as to the final distribution of glandular nerves.

[1] *Biol. Untersuch.*, Stockholm, N. F., Bd. v. S. 50. An explanation of these conflicting views may perhaps be sought in the fact that horizontal sections, which afford a "bird's eye" view of the nerve distribution, in many instances may give the appearance of retiform continuity to nerve terminals, which seem to end free in sections cut at right angles to the innervated surface.

These contending views do not appear to invalidate the conclusion we are at present justified in drawing, that it is by contact of the nerve elements with the secreting cell, not by their incorporation with it, that the activity of the latter is maintained and controlled.

The innervation of the cell of involuntary muscle.—In the case of the voluntary muscle the motor end-plates or end-organs are well-defined bodies, and if the termination of the muscle spindle, so well described by Dr. Batten, be viewed with Sherrington as the end-organ of muscular sensibility, these also are no less well defined, and are to all appearance ultimate, and not penultimate, structures.

In the case of involuntary muscle, on the other hand, there is still room for controversy as to the nature of the ultimate innervation of the muscle cell. The difficulty of examining this question until recently has been so great, that it is not long since histologists of reputation regarded even so considerable a muscle as the cardiac ventricle as very sparsely supplied with nerves. Even now the "ganglion-free apex" plays a considerable rôle in physiological conceptions of the nature of rhythmical movement.

The Golgi methods have shown us, however, that not only is the cardiac ventricle well supplied with nerves, but that it is so richly supplied that there is reason to believe that ilka muscle cell, to vary the poet's language, has its ain twig o' nerve. This is the conclusion come to by Heyman of Ghent,[1] who showed many beautiful specimens of the innervation of the frog's heart, prepared by the quick Golgi method, at the meeting of the British Medical Association in London in 1895, and which probably many present had an opportunity of examining. Numerous observations, prior to and since his, lend support to this view.

The end-organs described as characteristic of cardiac muscle are knob-like bodies, first observed by Krause, and frequently seen since. What I have taken to be such, however, appear to me to be continuous rather than freely-ending structures, and to be enlargements on the fine fibres of a circumfibrillar plexus, similar to the circumcellular plexuses described by Dogiel in secreting glands. Terminal knobs, it is true, may be observed which do not appear to be continuous with any nervous element beyond them, but they so much resemble small enlargements upon nerve elements, which are undoubtedly continuous with

[1] *Berl. Phys. Soc.*, Feb. 17, 1893.

similar knob-like enlargements in a continuous chain, that the possibility suggests itself to me, as it did to Dogiel in the case of glandular nerves, that defective staining may account for the apparently abrupt termination of the fibril in some cases. The majority of present-day histologists, however, appear to be as convinced of the free ending of muscular nerves in all involuntary structures as they are of such a termination in the case of voluntary muscle. It is certainly difficult to conceive how otherwise the separate functions of nerve elements, of which there is good physiological evidence, can be secured.

In the light of modern histology, the ganglionic plexuses which innervate the muscular fibres of the intestine and bladder must be regarded as penultimate, not ultimate, structures. The plexuses, for example, of Auerbach and Meissner, treated by the Golgi method, reveal a far-reaching system of fine processes. This is well shown by a specimen of Kölliker's, which I saw at Würzburg, and which is figured in his book.[1] The drawing is a minutely faithful delineation of the original preparation from the plexus of Meissner of a kitten two days old.

The innervation of the intestinal muscles is probably double, as Gaskell and others have pointed out,[2] non-medullated fibres of the vagus supplying the circular muscles throughout the greater part of the alimentary canal, and viscero-motor fibres from spinal nerves, the longitudinal fibres.

The discrimination by the microscope of motor fibres from more sources than one, and of motor from sensory fibres in involuntary muscles, is no more possible at present than it is to distinguish secretory-motor from sensory fibres in glands. As regards the detection of sensory fibres, in the case of those supplying such special sense organs as the Pacinian bodies of the mesentery, and similar bodies which have been found in other organs (for example, the pancreas), we are justified in assuming that we are dealing with a sensory nerve termination. But no such guide to the detection of a sensory, as distinguished from a motor, nerve-ending is at present known in involuntary muscular fibre. If, however, we agree with Kölliker that a medullated nerve-fibre, found in the distant periphery, is to be regarded as cerebro spinal and sensory,[3] we may have in this a guide to the penultimate distribution of sensory nerves in the viscera.

[1] "Gewebelehre," Fig. 843, S. 868.

[2] *Journ. Physiol.*, Cambridge and London, vol. vii. p. 18.

[3] *Op. cit.*, S. 858.

Specimens from the pelvis of the kidney of a mouse (Figs. 1 and 2) show the fine fibres arising from such a source—a plexus, the fine subsidiary divisions of which are countless, but which, in view of the present opinion of the majority of histologists, may be assumed ultimately to end free, as indeed at some points it appears to do in the sections which are figured.

In the case of the heart, also, similar plexuses may be observed coursing transversely across the muscle bundles. While these probably terminate parallel to the fibres, giving off twigs to the

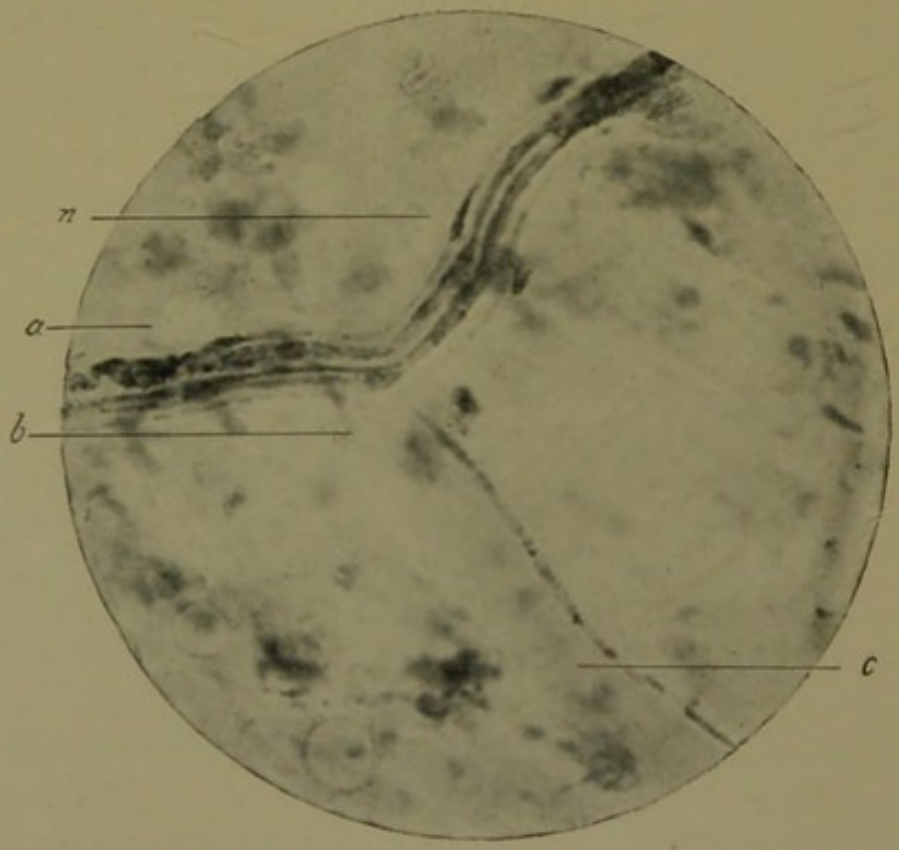

FIG. 1.—Dark bordered sensory nerve (*a*) from the pelvis of the kidney of a mouse; (*b*) nodal point whence a branch (*c*) springs, highly magnified; (*n*) nucleus of sheath.

cells, they are conceivably from another source than some of those found running parallel to muscle fibres, and terminating or appearing to terminate in the end-bulbs already mentioned. The importance of this double cardiac nerve supply we shall have to deal with later. Such plexuses are shown in Fig. 3.

Future research by staining methods, or by these in combination with the Wallerian method of degeneration, may enable us more accurately to distinguish between the ultimate distribution of visceral motor and sensory nerves, to the benefit of correct anatomy, and as affording a valuable check upon ingenious physiological surmise.

The nervous mechanism of excretion and metabolism. — The essential conditions for excretion are a medium containing the

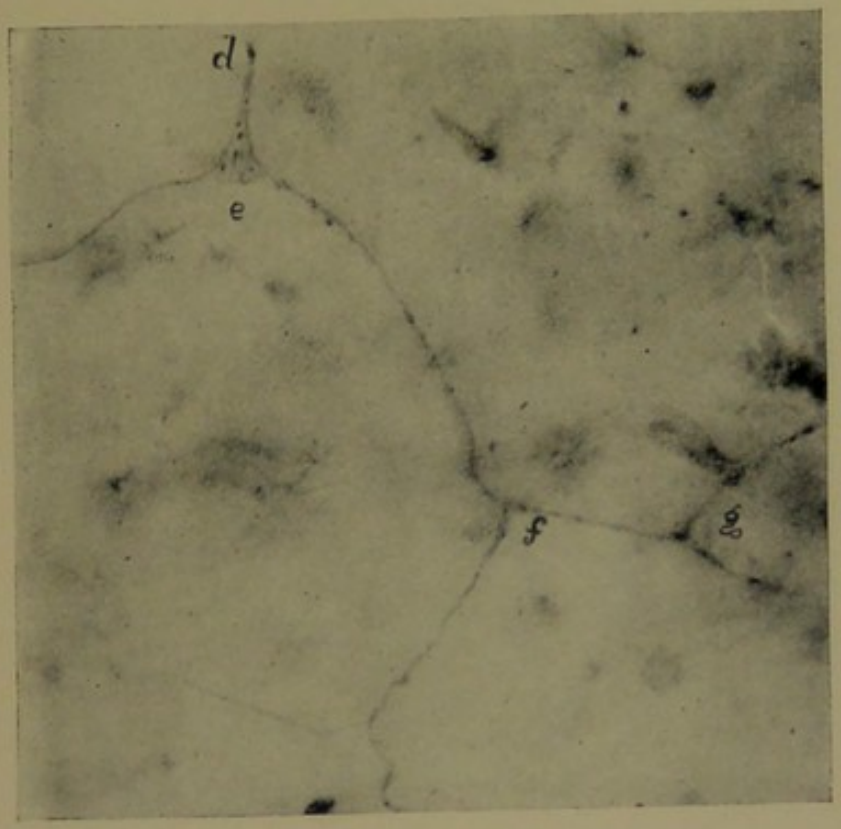

FIG. 2.—Penultimate plexus from the pelvis of the kidney of a mouse. (*d*) Continuation of (*c*) in Fig. 1 ; (*e*, *f*, *g*) nuclear points of dichotomous division.

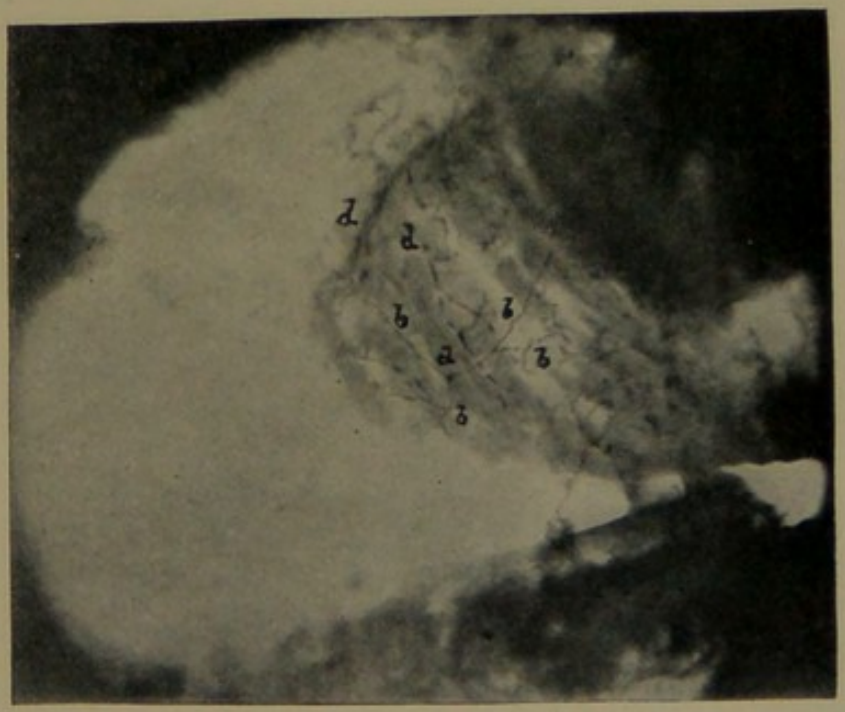

FIG. 3.—Penultimate plexus from the heart of a mouse. (*a*) Nuclear point of division like (*e*) in Fig. 2 ; (*b*,*b*,*b*,*b*) branching fibrils ; (*c*) Krause's knobs ; (*d*) main nerve.

excretion and vessels to convey it to a point at which it is to be excreted, where appropriate arrangements for its conveyance out of the body exist.

If we take the kidney as exhibiting these conditions in a typical manner, we shall be able to study the nervous anatomy of this process, so far as we at present know it. While this organ, however, exhibits the essentials of excretion mentioned, it is also one beset with considerable difficulties for the histologist of the peripheral nervous system. Its close texture and general density render the use of staining methods, as applied to the finer nerve elements, a difficult matter. So great a master in histological

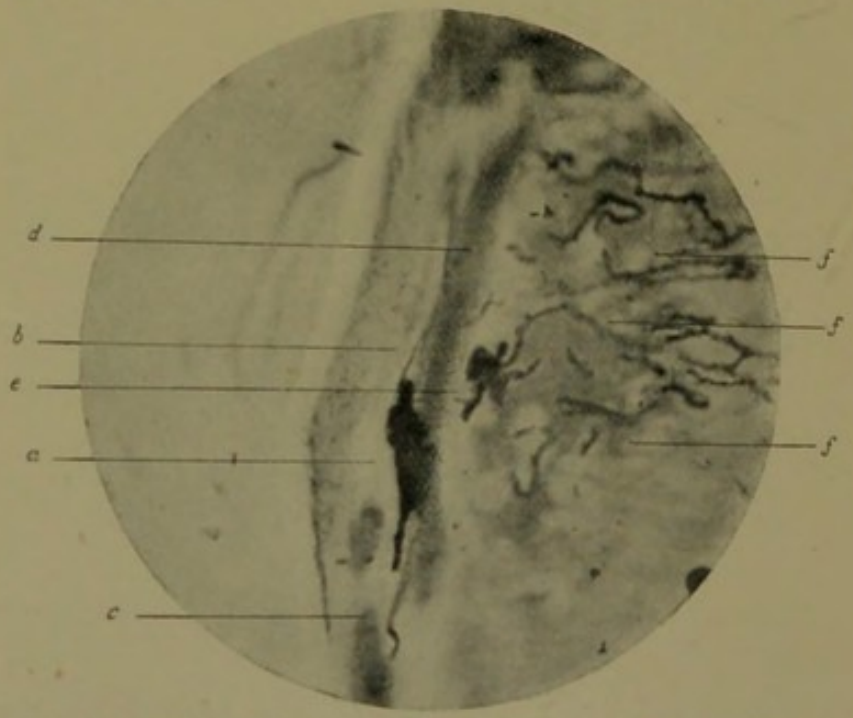

FIG. 4.—Innervation of a vessel in the kidney. (*a*) Ganglionic cluster; (*b*, *c*) nerve fibres; (*d*) artery; (*e*) retiform ramification of nerve fibrils in vessel; (*f*, *f*, *f*) capillary vessels.

methods as Gustaf Retzius recognised and acknowledged this difficulty, and stated that even by Golgi's method the nerves of the kidney did not stain well.[1] He succeeded, however, in staining the vascular nerves as far as the glomerulus, but not further, as many specimens show.

My own attempts to use the chrome-silver method for this purpose were made before my visit to Würzburg, and resulted in little beyond the staining of blood vessels and a few questionable nerves.

A specimen, however, which Herr Hofmann gave me, shows the vascular innervation of the kidney very well. Hofmann also found the organ difficult to stain by the Golgi method, and did

[1] *Biol. Untersuch.*, Stockholm, N. F., Bd. v. S. 35.

not succeed in doing so beyond the point reached by Retzius. A ganglionic cluster, with fine retiform ramification of fibrils, is shown in the preparation (Fig. 4). That the blackened cluster is ganglionic, is argued from a somewhat similar appearance, presented by indubitably ganglionic material, shown in a preparation of my own on the wall of a blood vessel supplying one of the cervical sympathetic ganglia in a child.

The nerves in the case of the kidney, as in other organs, follow the course of the blood vessels. This relation of visceral nerves to blood vessels is well shown by the preparations which are figured.

FIG. 5.—Relation of large nerves (*a*, *a*) to vessel (*b*) from the pancreas of a mouse.

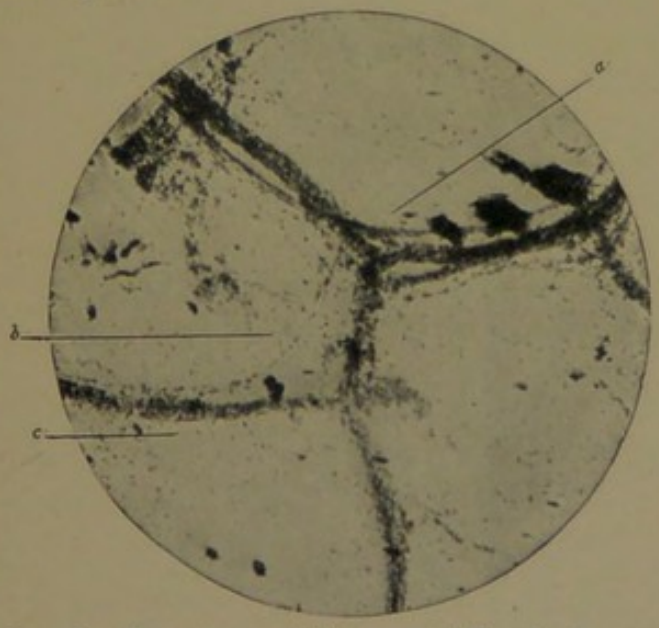

FIG. 6.—Mesentery of kitten. (*a*) Trunk of nerve; (*b*) branch going to supply the vessel (*c*).

The control of the blood-flow in a viscus is no less the note of empire in an organ than is the control of the waterways of our planet the ensign of sovereignty among nations (Figs. 5 and 6).

While we have thus failed hitherto, so far as I know, in demonstrating the complete innervation of the glomerular capsule and its connections, there can be little doubt that the nerves are there for staining, and with improvements in method will, sooner or later, be stained.

It is perhaps allowable to make a guarded inference from the innervation of the somewhat homologous Malpighian body in the

spleen. I am fortunate enough to be able to show a good Golgi specimen of the ultimate innervation of the spleen, for which I am indebted to Herr Hofmann. It will be observed that nerve fibrils reach and surround the Malpighian body, even anastomosing over it in the manner in which precellular cerebro-spinal fibrils touch and embrace the ganglionic cells of the sympathetic system. On careful examination, it will be seen that the vascular fallacy may be excluded in this case, as a Malpighian twig may be observed to arise from an unquestionable nerve fibril (Fig. 7). That these bodies, differing in function with the organ in which they occur, may

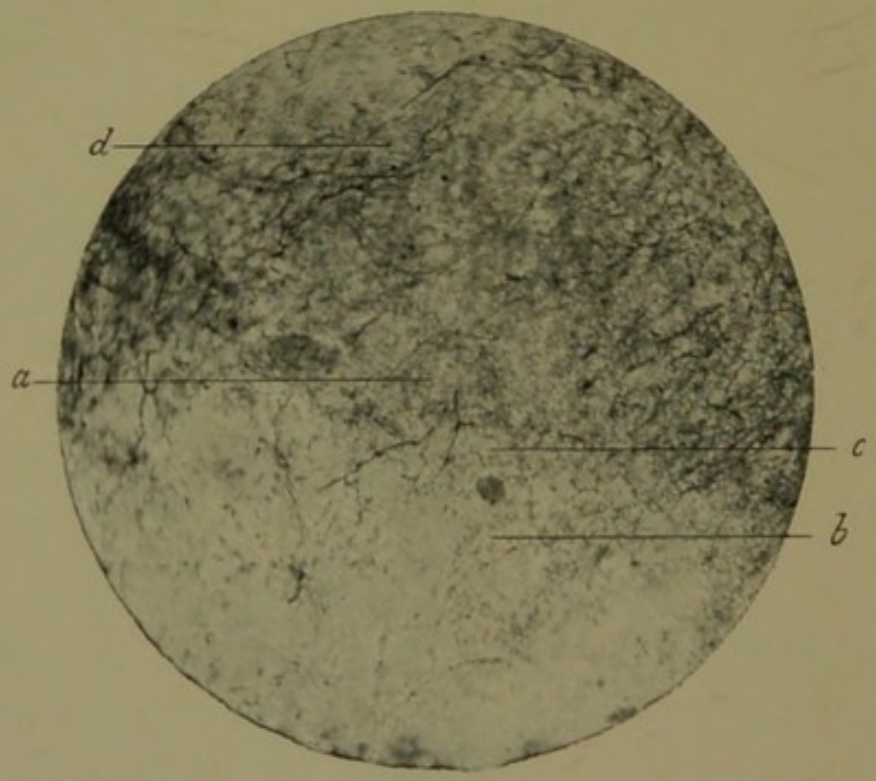

FIG. 7.—Golgi preparation of nerves in the spleen of a calf. (*a*) Nerve fibre; (*b*) Malpighian corpuscle; (*c*) connecting fibril; (*d*) nerve fibres and fibrils, some of which have gangliform enlargements.

be regarded as probably endowed with nerves in a similar manner, is, I think, a legitimate inference from the ascertained nerve supply of both. The greater facilities which the soft spleen affords for histological treatment, as compared with the hard kidney, may account for the greater success of the Golgi and other methods in the one case, and its comparative failure in the other.

The question of special nerves of metabolism, like that of special trophic nerves, which may be appropriately mentioned in this place, must be left undecided at present. That diminution of the *vis a tergo* necessary to push through metabolism to its normal physiological limit is the cause, rather than abnormal

explosion of physico-chemical material, of the defective metamorphosis met with in some diseases, is argued, I would suggest, by the commonly observed clinical phenomenon of deposits of uric acid, in conditions of exhaustion, in some persons who, in robuster health, exhibit the normal metamorphosis of urates. There is much more evidence in support of this view, which we shall consider more fully in its proper place. There is also a good deal of clinical and some experimental evidence to show that the nervous system has a distinct local trophic influence, although the separate existence of nerves for this purpose has not so far been established. We have so far examined the extreme periphery of the visceral nerve distribution, and found that, while there are still noteworthy upholders of the non-terminal conception of the peripheral nervous system, the balance of evidence and trend of histological opinion is in favour of the termination of the sensory and motor nerve supply of the viscera in free ends.

LECTURE II.

THE ANATOMY OF VISCERAL INNERVATION.

When we strike the main stream of innervation at the apex of the visceral delta of secretory, mobile, and excretory nerve distribution, our task in tracing the current is considerably simplified. Here also, however, the threefold state referred to in the con-

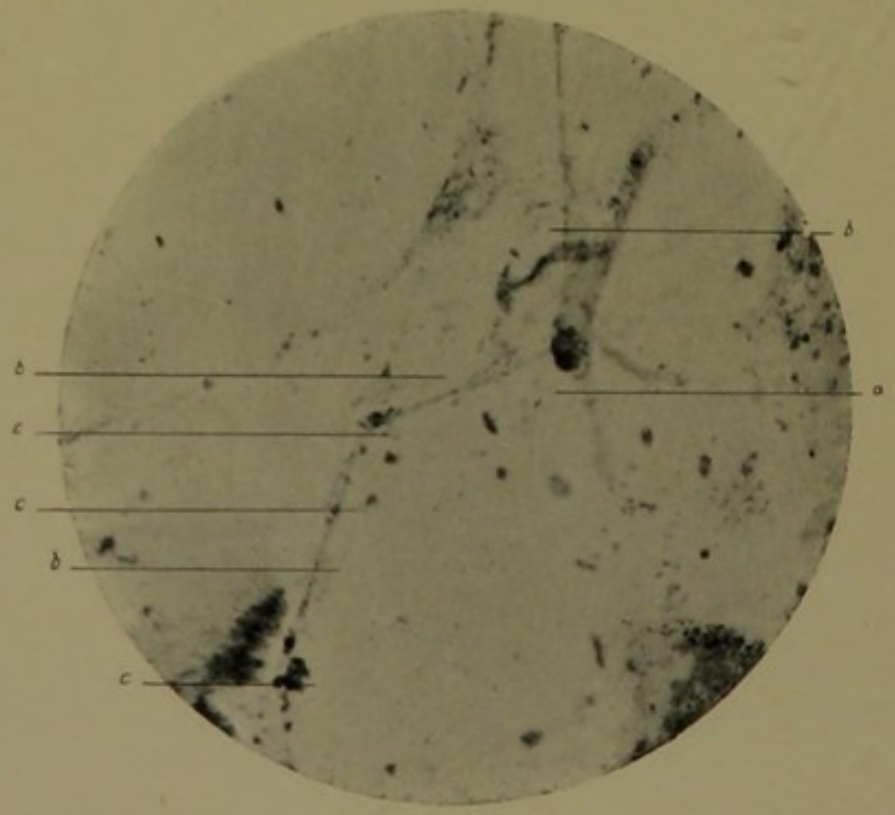

Fig. 8.—From the hepato-duodenal region of a mouse. (*a*) Large cluster of ganglion cells; (*b b b*) branches; (*c,c,c*) ganglion cells.

ditions of the ultimate distribution is taken by the triple conditions and their associated questions, of medullated and non-medullated fibres, and of the ganglion cells, regarded as anatomical entities and conglomerate structures.

The vast majority of the fibres constituting the nerve bundles

in the branches near their ultimate distribution, are non-medullated fibres—the fibres of Remak, a term which Kölliker applies to certain fibres only, of those originally described by Remak as belonging to the sympathetic system.[1] These fibres have been shown by the higher powers of the microscope to consist of many smaller fibrils. They may be distinguished from connective tissue, according to Kölliker, by their becoming opaque, not transparent on boiling, and on the application of weak solutions of acetic acid.

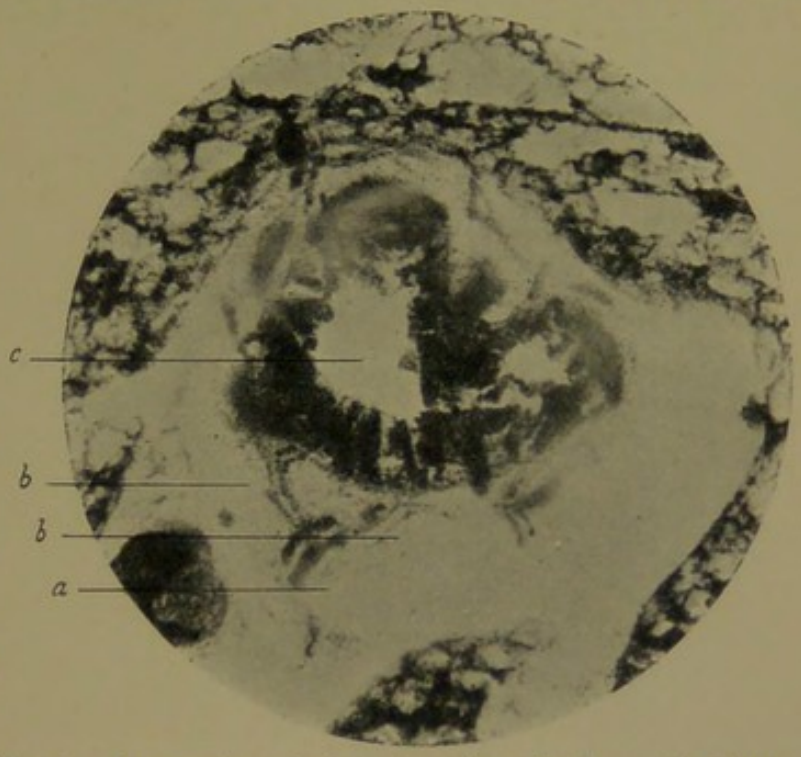

FIG. 9.—Innervation of a bronchus from the lung of a kitten. (*a*) Nerve trunk with a cluster of ganglion cells; (*b b*) branches of (*a*); (*c*) lumen of bronchus.

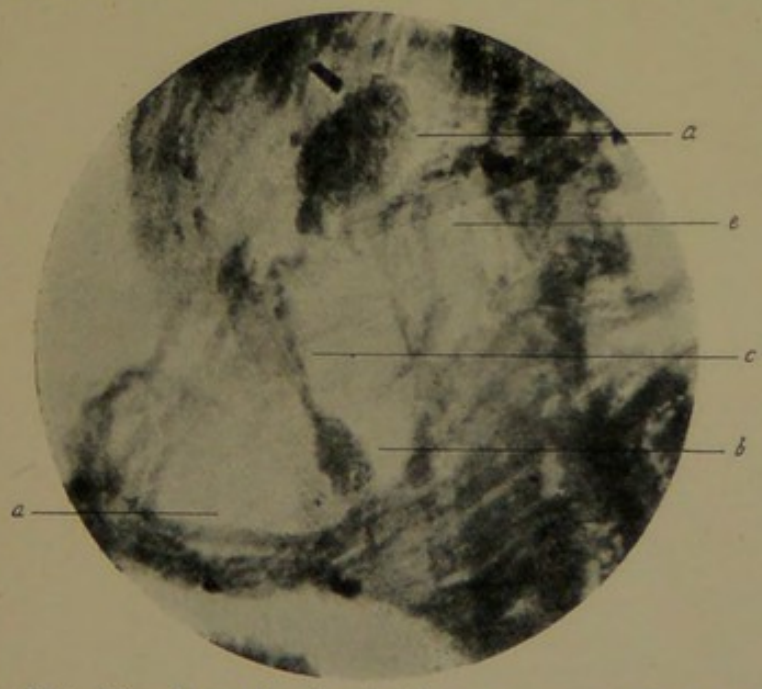

FIG. 10.—From the heart of a mouse. (*a*) Trunk of vagus; (*b*) fusiform cluster or ganglion cells on (*a*); (*c*) fibres issuing from (*b*) as the continued trunk of the vagus; (*d*) fat cells; (*e*) hair of mouse.

In addition to these non-medullated fibres, a much smaller number of *medullated* fibres may be observed in the peripheral visceral nerves, especially in transverse sections of those treated with osmic acid. As

[1] *Op. cit.*, Bd. ii. Hälfte 1, S. 30.

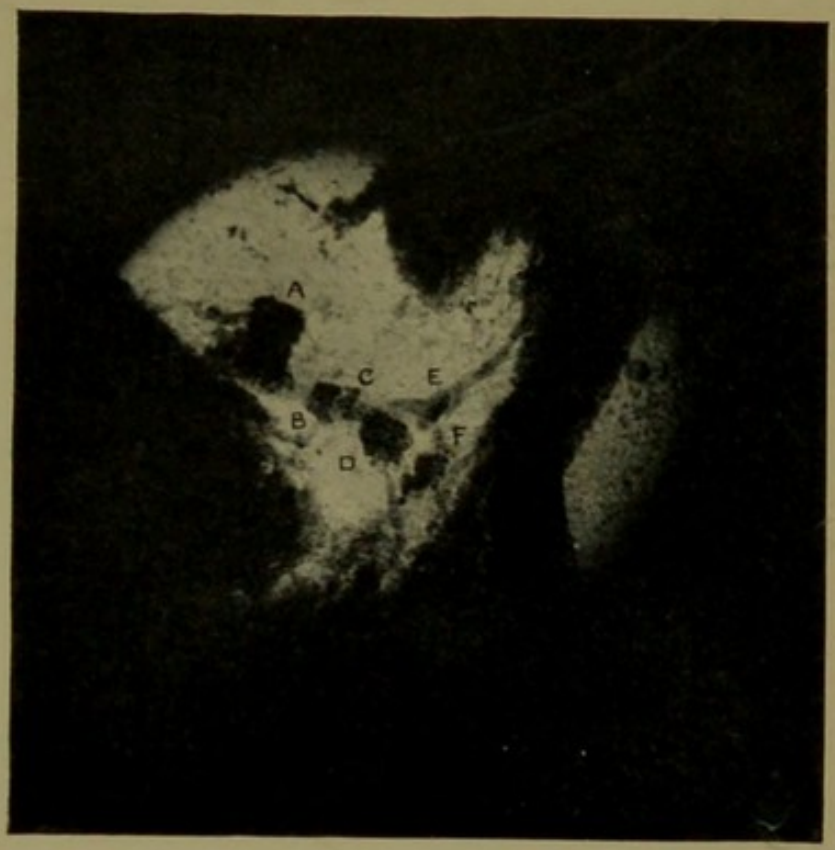

FIG. 11.—Large ganglia on the vagus (*A B C D E F*), Swift's obj. $\frac{1}{3}$.

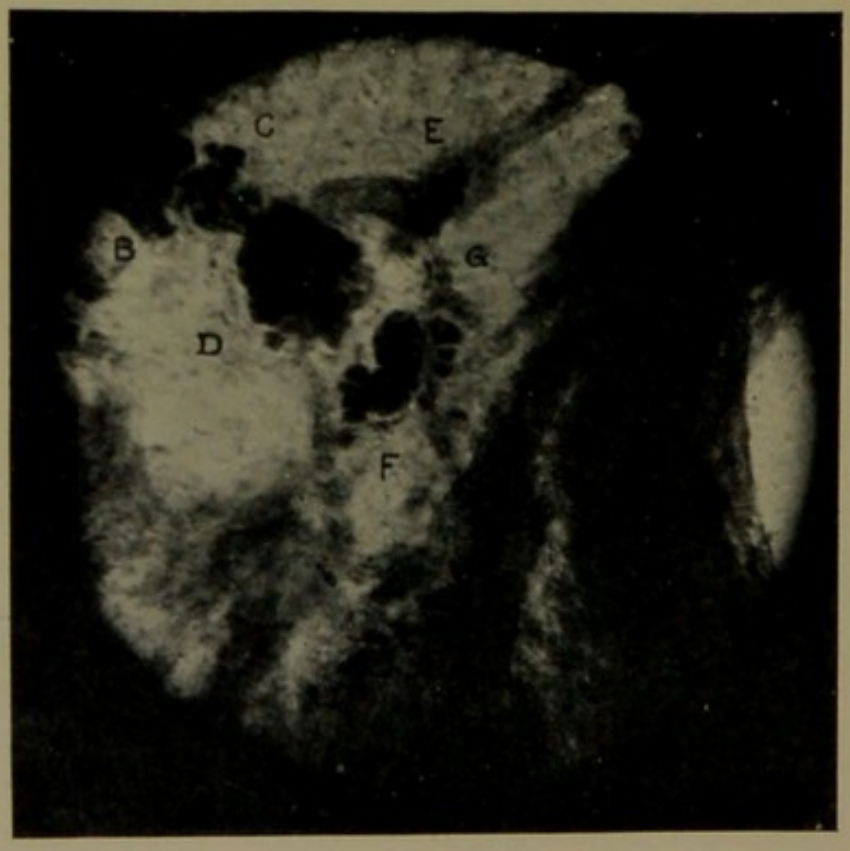

FIG. 12.—Portion of Fig. 11 enlarged (Swift's obj. $\frac{1}{8}$). (*G*) Branch going to the vagal ganglion (*F*) and coursing through it.

I have already stated, Kölliker regards medullated fibres occurring in the distant visceral periphery as sensory. Both kinds, according to him, have free endings.

The relation of these fibres to *ganglion cells* and clusters of cells is of anatomical and physiological interest. While the general relation of the peripheral ganglion cell, as an anatomical entity, to nerve fibres may be well shown by Sihler's method, their more intimate relation to these, and to one another when occurring in groups, is probably best shown in successful Golgi preparations. Dogiel, however, has obtained very good results by his modification of Ehrlich's methylene blue method. To these I shall have to make a passing reference later.

Secretion being a peripheral process, maintained ultimately, like every other function of the body, by force passing centrifugally from the dominant centres, the nerves of secretion must be regarded as belonging to the efferent or motor rather than to the afferent or sensory group.

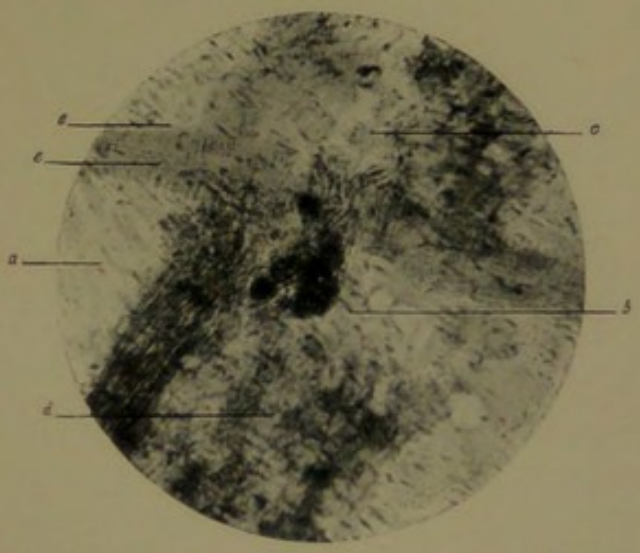

FIG. 13.—From the kidney of a mouse. (*a*) Nerve trunk; (*b*) ganglion cells; (*c*) nerve strand proceeding from cluster; (*d*) ditto. From (*c*) nerves arise which encircle the blood vessel (*e*), but are not shown in the photograph.

Sensation, on the other hand, being a central phenomenon, the current in nerves evincing sensibility must be, as we know it is, centripetal. Now, as the nerve fibres originating in peripheral ganglion cells have a centrifugal course and distribution, it follows that the ganglion cell itself must have a centrifugal function. It does *not*, however, follow from this, as seems to be too readily assumed, that the cell is a mere link in a chain of passive conduction.

The ganglion cell may occur isolated on a nerve or small strand of nerve tissue (Fig. 8), or embedded as it were in the heart of a considerable trunk (Fig. 9). A group of cells may also form a fusiform or irregular enlargement on the course of a nerve larger than the nerve itself, one end (the afferent end) being as it were lost in the fusiform enlargement, and a fresh trunk issuing from the other or efferent end; afferent and efferent in this sense being

used relatively to the fusiform ganglion, not to the central nervous system from which both, naturally, are efferent (Figs. 10, 11, and 12). Or, again, a cell or group of cells may lie outside a nerve trunk and have connections with *it* on the one hand, while on the other it distributes fibres in different but always centrifugal directions (Figs. 13 and 14). The ganglion cell may also apparently occupy a somewhat peculiar position in this wise. The cell or cells may be placed at a considerable distance from the nerve trunk, and send axis-cylinder processes into the latter, the ultimate destination of which it may not be possible to trace (Fig. 15).

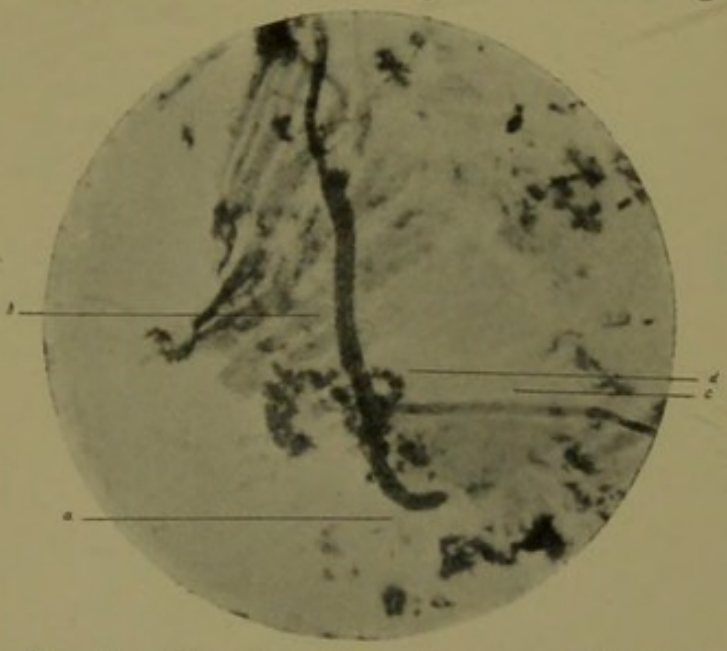

FIG. 14.—From the spleen of a mouse. (*a*) Nerve trunk; (*b*) ditto; (*c*) ditto; (*d*) crescent of ganglion cells.

Finally, the cells may form a congeries which appear to be placed at the junction of a peripheral centrifugal system (Fig. 8, *a*). These various relations of the peripheral ganglionic cell may be very distinctly seen in the illustrations.

FIG. 15.—From the spleen of a mouse. (*a*) Ganglion cells; (*b*) strand connecting (*a*) with the nerve trunk (*c*).

The relation of ganglion cells to one another is a matter of interest, but cannot at present be regarded as certainly determined.

Kölliker inclines to the prevailing belief, that the fine plexuses which surround the cells of peripheral ganglion cells are derived from cerebro-spinal motor fibres of the first class (that is, primary cerebro-spinal motor fibres), and not in any instance, as

Dogiel insists, from fibres arising from peripheral ganglion cells.[1]

The question is very difficult to decide on anatomical grounds, for the intertwining of the axis cylinder of one cell with the processes of another in the same group, easily induces the belief that the two have active touch of one another. This apparent connection is shown in a Golgi preparation, given to me by Professor Kölliker's curator, and which is reproduced in Fig. 16. Physiological arguments, on the other hand, intended to

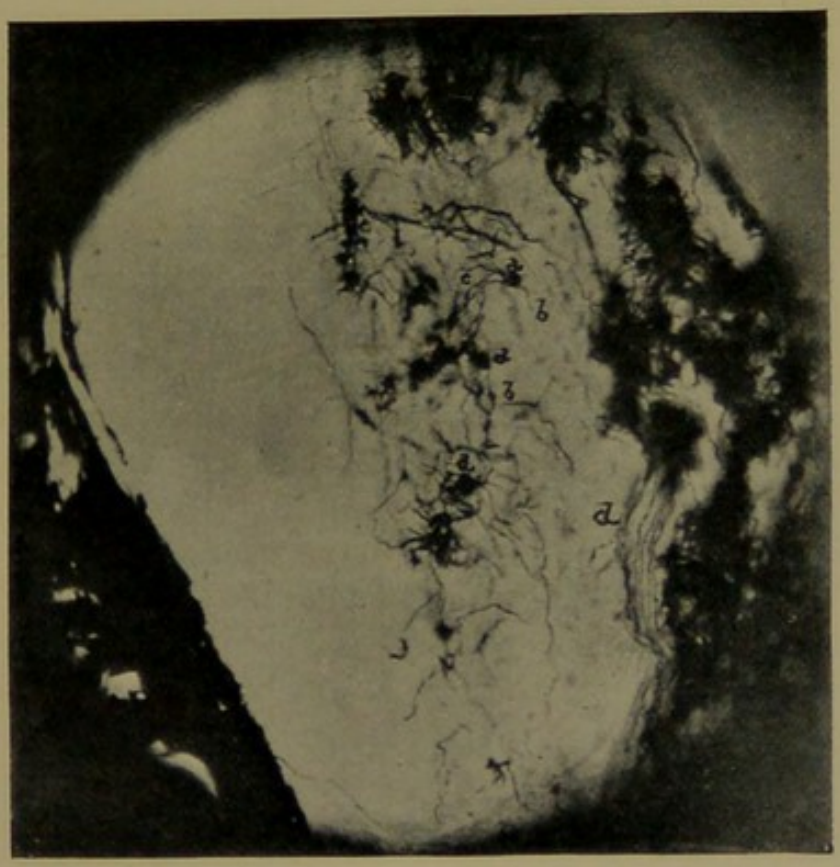

FIG. 16.—Cervical sympathetic ganglion of a calf. (*a a a*) Neurons; (*bb*) neuraxons; (*c*) neurodendrites; (*d*) varicose nerve fibrils.

solve this question, involve the production of so-called facts, which not only require the apprehension but also the comprehension of the recorder, that is, they require not only to be seen, but to be interpreted. The interpretation of all phenomena, and especially of experimental or artificial phenomena, is admittedly no easy task. Inasmuch, however, as the function of all efferent ganglia in a given stretch of peripheral nerve tissue is probably the same in kind, there does not appear to be any insuperable reason why a chain of relay structures should not be

[1] *Op. cit.*, S. 868 and 869.

in touch with one another, as Dogiel considers them to be. We do not, therefore, appear to be at present in a position to express more than a "pious opinion" upon the subject, and do well to avoid too positive a dogmatism.

The opinion of the individual, as a result of personal observation and reflection, may, however, be modestly expressed. The evidence adduced so far—anatomical, physiological, and, last but not least, clinical—inclines me to the belief that successive ganglia and their cells may be connected anatomically, and support one another in the execution of a common function, while they are at the same time incapable of executing independent reflex actions. Against the latter there is at present a general consensus of educated opinion.

Had the spiral fibre, noticed by Beale, in ganglia from various situations in the frog,[1] really arisen, as he thought, from the surface of the cell, while the straight companion fibre arose from its interior, it would have been still less conceivable than it is now, that the one was afferent and sensory, and the other efferent and motor, for a double function in a single cell cannot at present be regarded as possible. This cell has very frequently been reproduced. I have recently had an opportunity, through the kindness of Dr. Beale, of examining the original preparation from which the well-known drawing was made, and of which the latter is an accurate portrayal. The specimen has been preserved for thirty-five years in acidulated glycerine, and is still perfect. From the general arborisation of efferent fibres, on cells of the sympathetic system, a cellular reflex would seem more probable did the spiral fibre, so accurately described by Beale as being on the surface of the cell, really end there. This Arnold and Ehrlich, quoted by Kölliker, maintain it does,[2] and that it is probably of cerebro-spinal origin. The cerebro-spinal nature of the spiral fibre cannot, however, at present be accepted without question.

Could we regard the spiral fibre as a *sensory* arborisation, and the straight fibre as the motor exit of a cell in a continuous motor chain, a cellular reflex would no doubt be more conceivable under these circumstances than when Beale supposed the spiral fibre to have its origin in the cell. The fact, however, that motor as well as possible sensory fibres in the central nervous system arborise on and communicate their own impulse to other cells, casts a doubt upon the functional nature of the spiral or arborising fibre in

[1] *Phil. Trans.*, London, 1863.

[2] *Op. cit.*, S. 42.

peripheral ganglia. Physiological evidence has therefore to be sought to corroborate or refute a notion suggested by anatomical possibilities. Such evidence is at present against the existence of peripheral reflex action.

While Dogiel thus appears to stand alone, among working histologists of repute, in maintaining an arborisation of the axis cylinders of one sympathetic cell upon another of the same group, and from this fact, and his maintenance of the existence of end-nets and loops in the ultimate distribution of nerves, represents a view at one time generally if not universally accepted, there appears to be a more general consent that the dendrites of ganglionic cells in the sympathetic system touch and embrace other cells of the same series. Gustaf Retzius figures such,[1] and quotes Kölliker and Ramon y Cajal as having demonstrated this fact.

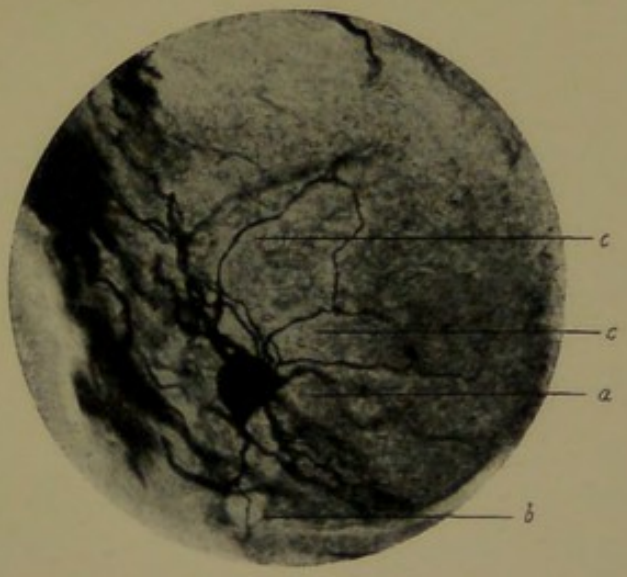

FIG. 17.—Würzburg Golgi preparation. Cell from the cervical sympathetic in a calf. (*a*) The neuron; (*b*) the neuraxon; (*c c*) neurodendrites.

What is the conclusion to which the last fact points? That these cells mutually nourish one another? Or is it that the cerebro-spinal nerve arborising on one cell, can through dendrites of neighbouring cells influence still others?

That dendrites, although they do not terminate in nerve fibres, may be conductors of nerve impulse, is admitted by Kölliker[2] and others; and in view of this fact, if fact it be, it is legitimate to conclude that one cerebro-spinal nerve may influence a number of peripheral ganglion cells, and through them a considerable territory of the organ to which they are distributed. This appears to be the view at present most generally accepted. Modern methods of staining, which have revealed the general multipolarity of peripheral ganglionic cells, render such a conclusion very reasonable (Fig. 17).

Before leaving the subject of peripheral ganglia, I wish to draw

[1] *Biol. Untersuch.*, Stockholm, pt. iv. S. 58.
[2] *Op. cit.*, Bd. ii. Hälfte 1, S. 39.

attention to a cell system of practical interest in connection with the heart.

It is possible in certain situations to distinguish between what appears to be small penultimate, if not ultimate, clusters of *sympathetic* ganglionic cells, and the ganglia which occurs in or near the efferent stream of the pneumogastric nerve.

The cells and groups of cells I refer to, have been met with by me in connection with the heart, and appear to be the same as those described by Vignal, who is quoted by J. Dogiel.[1] Groups of cells, from two or three to many more, may be met with in the

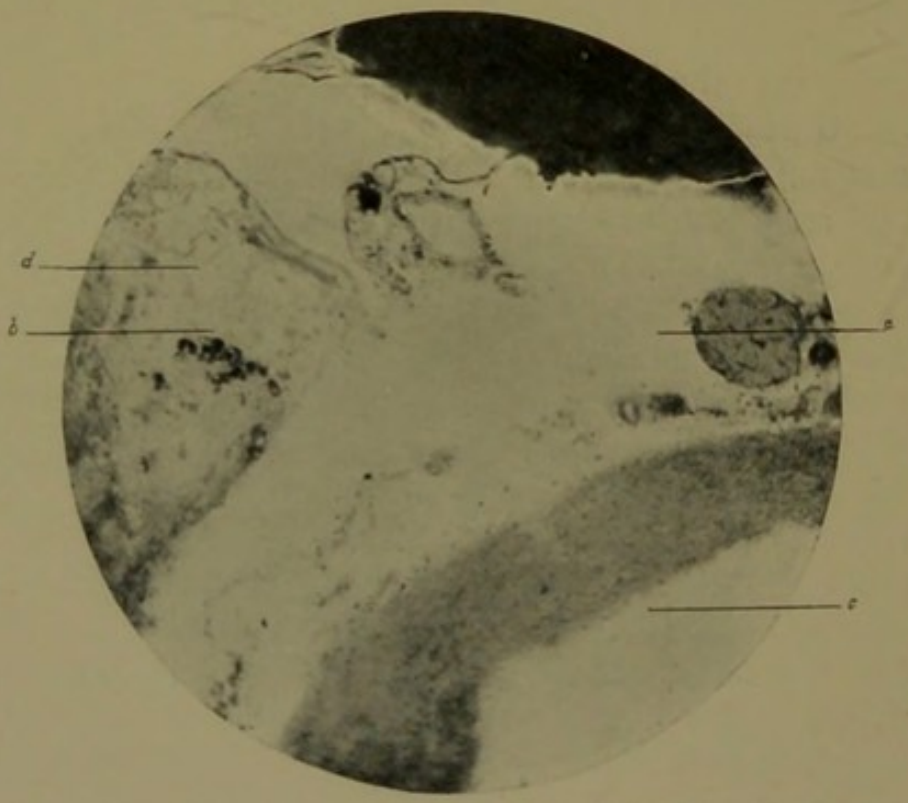

FIG. 18.—Transverse section of the base of the heart in a cat. (*a*) Vagus; (*b*) Sympathetic ganglion cells; (*c*) wall of aorta; (*d*) fat cells.

fatty tissue at the base of the heart, and traced in transverse sections into the subepicardium over the chambers. Occasionally they may be observed under the superficial strata of the cardiac muscle. They stain well by the Nissl method, and reveal the same configuration and characters as the ganglionic cells of the lateral and collateral sympathetic chains. They may also lie in proximity to subepicardial vessels and the larger nerves, but do not appear to be in direct connection with either. The appearances now described may be very distinctly seen in the

[1] *Loc. cit.*, S. 226.

illustrations (Figs. 10, 11, 12, 18 and 19). They may be easily distinguished, as I have said, from the ganglia on nerve trunks which I have already described, and of which I show good specimens for comparison with them, from the heart of a mouse, stained by Sihler's method. To the importance of this distinction, with reference to cardiac action, I shall have occasion to refer again.

In following the nerve stream still further upwards, and passing by other more or less peripheral trunks, cells, and clusters, we reach the more central collections of nerve elements—the so-called collateral and lateral chains. The relation of these, on the one hand, to the periphery, and, on the other, to the cerebro-spinal centre, is a matter of practical moment and scientific interest.

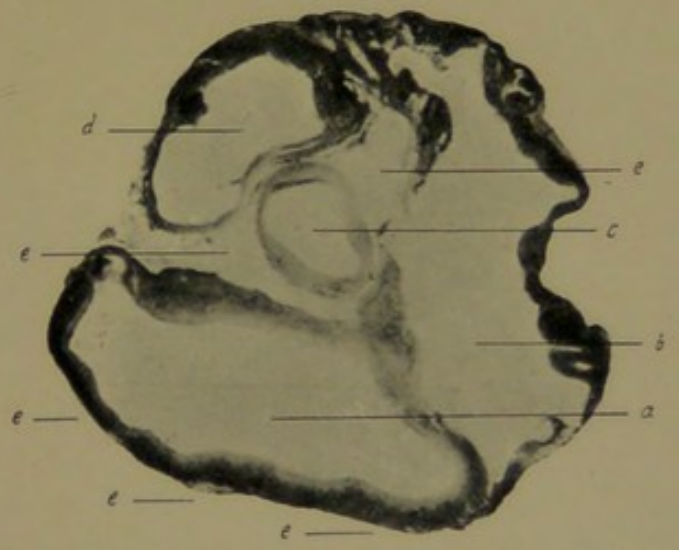

FIG. 19.—Transverse section of the heart of a cat. (*a*) The cavity of the left, and (*b*) of the right auricle; (*c*) the lumen of the aorta, and (*d*) of the pulmonary artery; (*eeeee*) the situations in which the sympathetic ganglion cells described in the text were found.

I have no desire to crush all observation into a Procrustean bed of what might be called triplicity, but, curiously enough, at this point also we have to deal in the main with a threefold state, namely, with nerve fibres which find their bourne in the ganglia, with those which arise in them, and with those which pass through or over them. I am, however, in good company in adopting this rule of three in classifying some points in sympathetic innervation. W. H. Gaskell of Cambridge, who wrote the first enlightening paper of practical interest on visceral control,[1] uses the threefold classification of nerves of vascular muscles, nerves of visceral muscles, and glandular nerves, and proceeds, moreover, to deduce the visceral nerves from three sources—the sacral, thoracic, and cervico-cranial—and to expose their behaviour or distribution from these points.

As regards nerve fibres which find their bourne in the lateral, collateral, or more distant ganglia, these reach the primary ganglia

[1] *Journ. Physiol.*, Cambridge and London, vol. vii.

by way of the white rami communicantes between the cerebro-spinal and sympathetic systems. The white ramus communicans, as we know, consists of the joint contribution of the anterior and posterior spinal roots. Gaskell has shown[1] that in transverse sections of the anterior-spinal root, osmic acid reveals large and small medullated fibres, and in certain regions a much larger number of small fibres are to be observed than in others. The chief of these lie between the second thoracic and the second lumbar nerves inclusively. Gaskell further demonstrated that transverse sections of the white ramus presented almost although not quite exclusively the medullated fibres of small calibre, and only a few of larger size. Finally, he also showed that osmic acid detected, in the grey ramus, a few medullated fibres of large size, and still fewer of small size, and that the mass of the grey ramus consisted of non-medullated material. I have copied some of Gaskell's drawings to illustrate these points.

It can, however, be easily understood how impossible it is to follow by continuous ocular observation with the microscope the course and destination of fibres through so tangled a web as a sympathetic ganglion. It is at this point that the valuable researches of Langley come to our aid.

Langley found that about 10 mgrms. of nicotine injected into a vein of a cat prevented for a time any passage of nerve impulses through a sympathetic or homologous cell. He found also that the duration of paralysis increased with the dose. He argues, therefore, thus: "Since nicotine does not prevent an impulse started peripherally of a nerve cell from producing its normal effect, it follows that by stimulating a nerve at various points of its course the place or places where it is connected with nerve cells can be determined."[2] By the nicotine method the course of pilo-motor nerves was determined by Langley, and also that of some nerves of secretion.

If, thus, a nerve in its course be only interrupted from conveying an impulse at certain cellular points upon it, it is evident that, at such points, some change in the anatomical and physiological continuity and character of the nerve must take place; the nerve, in short, may be assumed to arborise upon and terminate at the interrupting cell. Hence Langley's nomenclature of "preganglionic fibre" as applied to this portion of nerve, a term in place of which Kölliker suggests that of *precellular*. The latter seems the more correct, inasmuch as the

[1] *Loc. cit.* [2] *Journ. Physiol.*, Cambridge and London, 1893, vol. xv. p. 181.

ganglionic cell as an anatomical entity, not the ganglion as a conglomerate structure, is the essential point of interruption.

As, again, on the distal side of the interrupted point, the possibility of stimulation reasserts itself, it is evident that a "postganglionic" or "postcellular" fibre, springing from the paralysed cell, takes up the rôle of conductivity. Thus a motor fibre may be shown to terminate in a given ganglion, or to pass through it to end in another.

The mode of determining the course of sensory fibres in "dumb animals," rendered still more speechless by anæsthetics, must be on other lines. It is by the absence or presence of reflex action that the course of sensory fibres can be determined. The present position of the majority of anatomists, physiologists, and physicians is, that the sensory nerve fibres pass from the periphery, without arborising interruption, through intervening ganglia, and reach the spinal cord unbroken. This is the view taken by Kölliker. The sensory nerve is not even allowed by him the poor consolation of an occasional collateral, but is marched severely from the periphery to the centre, by way of the grey ramus communicans, without being permitted to look to the right or to the left. Whether it does so or not, nevertheless, in an unauthorised manner, like the course of Galileo's earth round the sun, remains still somewhat uncertain. It must be admitted, however, that such evidence as exists at present is in favour of the opinion of the hour, namely, that the sensory current goes straight to the centre without intermediate dispersion, and dealing, as we are in this case, with a central phenomenon, *sensation*, this seems *a priori* probable.

While peripheral sensory fibres are considered by Kölliker to reach the spinal cord by way of the grey ramus, this connection of the sympathetic ganglia contains also motor, *i.e.* efferent, fibres of ganglionic origin. These, although coursing towards the spinal cord, are none the less peripheral, when regard is had to their origin in an extraspinal ganglion. For having elucidated this point we are indebted to Gaskell.[1] His words are: "Putting together all the facts mentioned, the conclusion is evident that the grey rami communicantes spring from ganglia of the lateral chain, and pass peripherally to supply the corresponding spinal nerves, together with the vertebræ and spinal membranes. They are, in fact, peripheral nerves of the same kind as many others which arise from the chain of lateral ganglia."[2] To illustrate

[1] *Loc. cit.*, Reprint, p. 6.

[2] *Loc. cit.*

these points diagrammatically, I may be allowed to refer to an instructive diagram of Kölliker's,[1] with which I find myself in agreement, except, and I say so with the profoundest deference, with that portion of it dealing with the final point in the journey of the sensory stream to the cord. This must also, it appears to me, and chiefly, reach the cord by way of the contribution from the posterior root to the white ramus.

This point emphasises the importance of a knowledge of the embryology of the cerebro-spinal and sympathetic system in its bearing upon anatomical, physiological, and practical medicine.

Remak, whose sagacity time has vindicated in the matter of the local cellular origin of nerve fibres in ganglia, has more recently been supported in his views regarding an important point in the embryology of the sympathetic nervous system. Many modern embryologists, including F. M. Balfour,[2] have derived the sympathetic system from the epiblast, and Balfour describes the lateral ganglia as "at first simply swellings on the main branches of the spinal nerves." Remak believed the sympathetic chain arose separately in the mesoblast, and his position has been convincingly upheld by Professor A. M. Paterson in his well-known paper on the "Development of the Sympathetic Nervous System,"[3] in which, by a series of sections, which to all appearance can only be interpreted in one way, he has demonstrated that the lateral sympathetic chain arises as a series of isolated points, which ultimately become connected with the spinal nerves and with one another, and that the cervical and lumbar portions of the system must be regarded as outgrowths of the lateral chain.

In this connection, also, a point of especial interest to the visceral pathologist is the evolution of the medullary portion of the suprarenal bodies from the sympathetic chain. Paterson sums up his position in the following words:—"From these considerations it may be regarded as very possible that under the term 'sympathetic nervous system' are included two structures entirely independent in nature, origin, and function—the sympathetic system and the nervous system proper. Such a view would be entirely in harmony with the mode of development described above, and would render more intelligible than has

[1] *Op. cit.*, S. 862.
[2] "A Treatise on Comparative Embryology," 1881, p. 384.
[3] *Phil. Trans., B.*, London, 1890.

hitherto been possible, certain developmental peculiarities, such as a conversion of a part of the sympathetic system into suprarenal bodies."[1]

I have copied some of Paterson's illustrations to show these points.

These embryological conclusions, moreover, support Gaskell's general description of the origin of the visceral nerves,[2] which is in these words: "They issue from the central nervous system in definite sacral, thoracic, and cervico-cranial regions.

"From these regions they pass out into the ganglia of the visceral system.

"From the sacral region they pass out in a single stream to the ganglia of the collateral chain.

"From the thoracic region they pass out in a double stream, one to the ganglia of the lateral chain, and the other to the ganglia of the collateral chain.

"From the upper cervical region they pass out in a single stream to the ganglia of the main stems of the vagus and glosso-pharyngeal nerves."

We have now followed the stream of visceral innervation up to its central origin, and it only remains to emphasise a few points, so far as they are known, and they are still very imperfectly known, which have a bearing upon the interpretation of the clinical phenomena with which we shall be concerned in the second series of these lectures.

Even in the spinal relations of the visceral nerves we find we cannot rid ourselves of the incubus of a triple arrangement. Gaskell has pointed out the very remarkable coincidence in the range of the vesicular column of Clarke, and its two cognate centres in the sacral and cervical regions, with the outflow of nerves which we have learned to regard as visceral. He has also endeavoured to show, from a study of the spinal accessory nerve, that we may rationally regard the ramus visceralis as having its roots in the lateral horn, and in the column of Clarke. The spinal segment, according to him, thus consists of an anterior or somatic portion, a posterior portion, and a lateral, visceral, or splanchnic portion, which has its roots in the structures named.[3] As regards his views of the relation of the vesicular column to the visceral nerves, we shall learn that they are disputable.

It has been already shown that nerve fibres arising in the ganglia and coursing centrally, are to be regarded as peripheral

[1] *Loc. cit.* [2] *Loc. cit.*, Reprint, p. 11. [3] *Loc. cit.*

nerves. It is therefore only with the origin of the nerves which end in ganglia and with those that pass through them, namely, the sensory nerves, that we are concerned in discussing the central relations of the visceral nerves.

In Kölliker's diagram,[1] the sensory fibres of the viscera are made to return to the cord by way of the grey ramus communicans. But if the white ramus be an offshoot of the combined spinal nerve, as we know it is, it seems to be the more natural conclusion that most if not all sensory fibres must return by way of the contribution to the white ramus from the posterior or sensory spinal root. As Michael Foster[2] remarks on this point, even the revehent fibres, as he terms them, from the ganglia, which usually run in the grey ramus, seem to return at times in the white, for the very sufficient reason that the one is occasionally indistinguishable from the other. The grey ramus, moreover, cannot in any case be regarded as a true root of the splanchnic system, and Gaskell has shown how in the tortoise, and in the case of some nerves even in the dog, the whole visceral ramus issues from the ganglion on the posterior root of the spinal nerves.[3]

It is simpler, therefore, to conceive the stream of visceral sensibility to flow back to the cord by way of the white ramus, and thus to amalgamate the mechanism of visceral sensations, which we shall study in a subsequent lecture, with sensory phenomena in general.

Although, therefore, Gaskell's surmise, that the posterior root of the viscero-motor inflow is on the cells of Clarke's column, or on homologous cells, does not rest on anatomical demonstration (Kölliker, who quotes Galgi, Ramon y Cajal, and von Lenhossek as agreeing with him,[4] states that he is unable to support Gaskell's view from observed facts), it is generally admitted that a considerable portion of the sensory fibres of the posterior root do arborise on these cells. Sensory fibres, then, having arborised on cells of the vesicular column, at once from the latter strike the direct cerebellar tract, and thus reach the cerebellum, whence, by probable but not yet fully demonstrated paths, directly or indirectly, motor visceral impulses may be assumed to reach the small cells in the antero-lateral horn, from which the small-fibred medullated nerves arise which characterise the efferent stream of visceral innervation. Pain and other visceral sensations likewise prove that the ascending impulse reaches the cerebral cortex by the usual or some

[1] *Op. cit.*
[2] *Op. cit.*, 6th edition, p. 114.
[3] *Loc. cit.*, Reprint, p. 62.
[4] *Op. cit.*, Bd. ii. Hälfte 1, S. 125.

other tracks for ascending sensibility, and induce motor consequences by way of the ascertained paths for projective influences, or by paths still undiscovered, for there is still a lack of definite knowledge on the subject. The anatomical considerations I have mentioned in fully developed and embryological states, explain the opinion—at one time entertained by leading anatomists and physiologists, such as Bidder and Volkmann, Kölliker, and others of the older school of scientists—that there was an inherent independence (*Selbstabhängigkeit*) in the sympathetic system. Even now, in a strictly limited sense, we appear to be justified in assuming a measure of executive or motor independence in the innervation of visceral control, of which I shall say more when considering some physiological aspects of the question. But the commonly observed influence of mind on body, the pain, as I have stated, at times associated with visceral lesions, and the influence of corporeal conditions on the sense of well-being, go to prove that the so-called independence of the sympathetic nervous system is more apparent than real.

A histological examination of the cerebello-nuclear tract, moreover, reveals considerable morphological likeness between the cells in these regions and those of the one time quite detached and always outlying and subordinate sympathetic system. Gustaf Retzius alludes to the likeness of cells of the sympathetic to ganglion cells in the anterior cornua of the cord, and Paterson also[1] rests some of his argument upon the distinctive histological features of the nerve elements in the sympathetic. To myself this morphological likeness was first suggested on examining cells in the grey matter of the inferior cerebellar peduncle, and observing their resemblance to those of the posterior root ganglion. But the dominant cell elements in the cerebellum and its related structures generally, such as the olivary bodies, resemble the cells of the sympathetic system so much more than do those distinctive of the higher centres in the cerebrum, that one cannot avoid the conjecture that with this morphological likeness there is also associated a functional relationship of a somewhat close order, which will be rendered clearer by future research, but which is at present altogether denied.

The relations of the vago-glosso-pharyngeal and vagus accessory nerves.—To the vago-glosso-pharyngeal and its associated accessory nerve belong a mixed series of voluntary and involuntary actions. Physiological experiments ending in the definite and brilliant

[1] *Loc. cit.*

demonstrations of Horsley, Semon, and Risien Russell, have localised the cerebral centres for the muscles of phonation. No definite result, however, has yet been reached as regards the cerebral representation of the involuntary actions carried out by the par vagum. That these have intimate relations with the higher centres cannot, however, be questioned. It is not, moreover, in any way remarkable that the more direct tracts of voluntary motion should have been discovered more easily than those of visceral action, for the relations of the involuntary system to volition are much the more complex, and involve a consideration of the mechanism of all-embracing mind. The emotions which "stir the heart," to use a conventional and subjective phrase, not without physiological significance, may or may not find expression in words. We can control the latter, and the mechanism of the phonic element in speech is a comparatively simple matter. But the unexpressed influence of the emotions may be existent, operative, and beyond the power of men to control, until, in the grimly pathetic language of the epitaph composed by himself, over the remains of the talented and unfortunate Dean of St. Patrick's, they reach that bourne,

"Ubi sæva indignatio ulterius, cor lacerare nequit."

The central connections of such influences are as wide as their causes, and are not to be localised by so many punctures in the floor of the fourth ventricle, or revealed by an accommodating monkey, after removal of its calvarium.

The proximate centres of vago-visceral action, however, lie, as we know, in the medulla oblongata, and with these and their more evident connections we must in the meantime, as practical men, rest contented. The complex relations of the three assumed sources of the vago-glosso-pharyngeal and vagus accessory nerves have been a fruitful source of hypotheses; and the exercise of anatomical ingenuity, and hypotheses more or less ingenious, and observations more or less accurate, will still be offered and made, before the questions affecting this important subject are placed upon an incontrovertible basis.

An advance towards greater simplicity in our conceptions of the subject has, however, been made in the growing tendency to regard the ascending vago-glosso-pharyngeal root, or fasciculus solitarius of Lenhossek, as the true sensory root of those nerves, the nucleus ambiguus as a source or station of their motor fibres, and representing the highest medullary portion of the nerve

accessory to the vagus, and the so-called "sensory root" of the vago-glosso-pharyngeal nerve as a terminal rather than initial nucleus.

On the last point Kölliker[1] remarks: "The so-called sensory nucleus of the vago-glosso-pharyngeus is, as we now know, no place of origin of the fibres of these nerves, but a terminal nucleus (*Endkern*) in which they end free, while from its cells other fibres arise which bring about connections with other parts of the brain." These connections are still largely undetermined. As regards the apportionment of this nucleus between the glosso-pharyngeal and vagus nerves, Kölliker,[2] like Alexander Bruce,[3] whom I have the honour of following in this lectureship, allots the upper part to the former and the lower to the latter. The fasciculus solitarius, or, in transverse section, *rotundus*, regarded as the sensory root of the vago-glosso-pharyngeal nerve, has been traced downwards for a distance beyond the decussation of the pyramids not yet determined. Roller, quoted by Kölliker, regards this fasciculus and its grey matter as the sensory root of the glosso-pharyngeus alone, but Kölliker, judging from the proportion in size between the fasciculus and that nerve, inclines to the belief that it is likewise the source of the sensory fibres of the vagus. In this view he is supported on embryological grounds by His.[4] The relative position of these centres to one another and to neighbouring structures may be seen in many specimens.

[1] *Op. cit.*, S. 259. [2] *Op. cit.*, S. 240.
[3] "Illustrations of the Nerve-Tracts in the Mid and Hind Brain," p. 4.
[4] *Op. cit.*, S. 248.

LECTURE III.

THE PHYSIOLOGY OF VISCERAL INNERVATION.

In considering the relation of the nervous system to secretion, visceral motion, and excretion, I desire to touch upon some points in the more recent conceptions of physiologists which are at variance with the views of many of their predecessors, and which are still open to discussion. As regards secretion, for example, it may be permitted to inquire what a nerve of secretion is?

Secretion, like every other form of distal motion, being a peripheral, outgoing, or efferent event in its active phase, its immediately regulative nerves belong necessarily to the outgoing or executive series. They are motor nerves. Secretion, however, like every other peripheral activity, is not solely caused by influences entering or leaving a gland and its associated territory. The secreting cell, like the muscle cell, comes into being before, so far as we know at present, it is in touch with nerve elements. There is doubtless, therefore, an essential secretory irritability, as there is an essential motor irritability. But the length of time for which either secretion or motion could continue in an independent organism, when a given organ is severed from its nerve supply, is admittedly a limited period, and the actual length of this appears to be shorter in an inverse ratio to the complexity of the organism as a whole. Thus the reptile survives longer than the mammal when the main innervation of viscera essential to life is divided.

Every peripheral movement in an ordered mechanism, whether that mechanism be an animal, a plant, or a universe, has a regulating centre—an initial or necessary source of motion in general, or of vital motion, that is life, in particular, by which these properties are conditioned. To solve this mystery would be to solve the mystery of life or even of abstract being, a problem which has defied so far not only the physicist but also his bolder

brother the metaphysician, and appears likely to do so, until the finite contains the infinite, a somewhat remote prospect.

Without aspiring to be defined, as a learned judge is said to have defined the metaphysician, namely, as a blind man looking for a black hat in a dark room, the hat in question not being there, it is permissible to consider with caution, and with a just sense of our limitations, the centre or centres of energy in the animal economy, without reference to the manner in which force is produced or reproduced.

As sensibility, in one phase or another, precedes motion, in one form or another in more complex and fully developed animals, it may be assumed that the initiating centres of energy are in the sensory portion of the nervous system, and that it flows thence down the efferent stream of innervation. This position is opposed to that maintained by Bain,[1] but this is not the time to argue the point. The impulses which explode energy in such centres arise in the afferent system of sensory nerves in the case of peripheral actions, and the active factors in such explosions are stimuli applied to such nerves.

We have seen in the anatomical section that the afferent nerves pass, so far as can be ascertained, through the ganglia which intervene between the periphery and the centre, without the interruption of arborisation on intervening cells.

The exploded energy, on the other hand, travelling down the efferent nerves, encounters innumerable arborisations on intercepting ganglion cells, and, like the current of a stream flowing towards its outlet into the ocean, splits or may split into as many fresh channels as arise between the centre and periphery. These fresh channels arise, we have seen, from the innumerable ganglion cells which are formed on the trunk and branches of the efferent system of nerves, cells which transmit and are permeated by the outflowing energy. The question then is, What is the relation of these cells to this energy?

Of experiments, the object of which is to show the relation of the nervous system to peripheral action, whether secretory, viscero-motor, or vasomotor, we may take the well-known one dealing with the nervous mechanism of secretion in the submaxillary gland as a type. I base my description of it on Professor Foster's lucid narrative in the last edition of his text-book of Physiology.[2]

The submaxillary gland of an animal is exposed, a tube is

[1] "Emotions and the Will," p. 328.

[2] P. 420 *et seq.*

placed in the gland duct, and its nerve supply rendered accessible to stimulation. The efferent nerves which go to the gland are (1) a branch of the chorda tympani, in the course of which, as it approaches the gland, ganglion cells appear; and (2) branches of the sympathetic, coursing along the blood vessels. The afferent nerves are the lingual branch of the fifth and branches of the glosso-pharyngeal nerve. Stimulation of the lingual, or of the glosso-pharyngeal, causes a profuse secretion of saliva by reflex action. If the lingual nerve be divided at a point more central than that at which its companion chorda diverges from it, stimulation of the lingual very naturally produces no reflex secretion. If, however, the peripheral end of the divided chorda be stimulated, the efferent impulses thus generated produce a copious secretion for some time, accompanied by vaso-dilation. That vaso-dilation is not the essential cause of the secretion, moreover, is shown by the cessation of the latter, even in presence of the former, if the secretory function be placed in abeyance by the administration of atropine, and also when the dissevered head of an animal still retains the faculty of glandular secretion.

Similarly, stimulation of the sympathetic is associated with the production of a more viscid, scantier, but more potent secretion, accompanied by vaso-constriction. In this case, atropine is said to have less influence in restraining secretion.

My excuse for relating these well-known facts on this occasion is, that they are of interest in connection with a parallel which I intend to draw, and which Professor Foster likewise suggests, between the action of different *efferent* channels of glandular innervation and those regulating the action of the heart.

The rôle of the peripheral ganglionic cell in this process interests us most at this moment.

When Langley, by the general and local use of nicotine,[1] showed that, after paralysis of ganglionic cells, stimulation of post-cellular fibres could still induce peripheral results, he in no way indicated all the functions of the paralysed cell. The question of a peripheral reflex from these cells may, it is true, be regarded as answered in the meantime in a negative sense by physiologists; but the question of a possible *storage* of *peripheral energy* in efferent ganglia is not settled by the disproval of a *true nerve reflex* at the periphery.

These cells, we have seen, are acknowledged to have the power of producing axis cylinders, that is nerve fibres, but are denied other

[1] *Loc. cit.*

properties than a vague nutritive quality, and the function of distributing a nerve supply over a wider area than would be possible to the cerebro-spinal fibres alone, which enter the ganglion.

The eviscerated heart which, when pricked, contracts, does so in the light of the fully resuscitated Hallerian theory of nerveless rhythmicality, by the explosion of non-neural energy in the muscle fibre. But this is surely an absolute assumption. The assertion, moreover, that this phenomenon can be induced in muscle, assumed likewise to be devoid of nerve supply, must also, we have seen, be regarded with more than scepticism, because such nerveless territories have in more than one instance been shown by improved methods of staining to be well supplied with nerves. Krehl and Romberg, for example, quoted by Dogiel,[1] thought there were no nerves in the apex of the heart of a frog, but Dogiel and others have proved the contrary. Even in the assumed absence of ganglionic cells, which would be a large assumption, it is possible that nerve plexuses, with distributing points, such as were shown when dealing with the anatomy of the subject (Figs. 2 and 3), may retain an irritability capable of farther provocation, by the various artificial expedients used to rouse the energy of the eviscerated heart, or of portions of it. There is naturally no question here of true reflex action, but merely of the possible stimulation of efferent nerves, regulating by an acquired automatism the contraction of the muscles which they supply.

The conclusion, therefore, seems warrantable, until indubitable proof to the contrary has been adduced, that at least in the fully developed organs of more complex animals, *persistent* rhythmicality has its proximate and always subordinate centres in the efferent stream of innervation. No one, it appears to me, who has seen the perfect consecutive contraction of the auricles and ventricles in a recently killed animal, can avoid the belief that no theory of mere inherent rhythmicality can fully account for this phenomenon. The same lesson appears to be taught by the disorders of rhythmical action observed by the clinician, and with which we shall be concerned in a subsequent lecture.

What I have said with regard to cardiac rhythmical action seems to me to apply equally to viscero-motor and vasomotor action elsewhere. The relation of peripheral ganglia to the efferent nerves in such a rhythmical organ as the spleen, for example, has been shown in the anatomical portion of these lectures to be such, that these nerve-producing centres may, with-

[1] *Arch. f. mikr. Anat.*, Bonn, 1894, Bd. xliii. S. 225.

out the exercise of much imagination, be considered as store-houses, in a subsidiary sense, of the outflowing energy, and as capable of playing a part in the automatic contractions evinced by that organ, when separated from its grosser nervous connections.

Among rhythmically contracting organs we must also include the arteries and some veins; and the extra-neural situation of ganglia on nerve trunks regulating the vascular supply of such an excretory organ as the kidney, seems likewise to suggest that a subsidiary storage of energy in these nerve-producing cells is not incompatible with the trophic power more generally conceded to them.

To return to the analogy between secretory and viscero-motor innervation, it will be remembered that I described two kinds of ganglia in connection with the heart, namely, those on the trunks of efferent nerves, and those which lie in the intervascular fat at the base of the heart and under the epicardium, it may be close to such efferent trunks, but apparently unconnected with them. They also occasionally lie, as has been stated, in close relation to blood vessels. The latter kind appear to be the distal ganglia of the sympathetic system, and probably differ in function, as they do in anatomical character, from the ganglia of the vagal stream.

The deeper relations of these varieties of ganglia to one another are not easy to determine, but it is as improbable that they should lose their individuality, as it is unlikely that the fibres of their respective nerves should anastomose at the periphery. They doubtless each supply nerves which have a common destination, namely, the muscle cells of the heart, and of the vascular system pervading it.

In explanation of the varying rate of the heart's action, I was at one time disposed to believe with Schmiedeberg (quoted by Brunton),[1] on purely hypothetical grounds, that the ganglion cell was a mid-point between the nerves slowing and those quickening the heart's action, and that this cell played in some measure the part of regulator. I now consider it more probable that the term common to the two streams of innervation, which both contain sensory and motor elements, is the muscle cell itself, and that the stimulus which calls the one or the other system into predominant activity is physico-chemical in nature, and due to cross stimulation of the two sets of nerves. By cross stimulation I mean the stimulation of one set of nerves by the products of the activity of the other. The chemical stimuli, if chemical they be,

[1] "Pharmacology, Therapeutics, and Materia Medica," London, 1893.

would, I presume, be termed by Gaskell anabolic or katabolic according as they were the result of retardation or of acceleration of muscular action.

The cross action is probably reflex in character, the anabolic products of retardation stimulating the accelerant sensory nerves, while the katabolic products of acceleration excite the afferent sensory fibres of the vagus.

I am aware that these remarks are based upon anatomical facts and clinical interpretation, rather than upon physiological observation, the result of experiment.

I have no desire to dogmatise on so obscure a theme, and remember, in a chastened mood, the numerous instances in which an apparent finality in scientific opinion has proved but the point at which a reversal of preconceived notions has taken place. For this reason also, as a humble opponent of the rampant Hallerism of the hour, I await with some curiosity, not unmixed with a measure of confidence, some modification in the views of anatomists and physiologists as regards the nerve supply and functions of the "ganglion free apex," which at present bulks so largely in the discussion of rhythmical muscular action.

Yielding all over the body to the perpetual encroachments of its predominant partner, the cerebro-spinal nervous system, the last refuge of the sympathetic vainly struggling to be free, was what has come to be known as the hypogastric reflex. This may be observed when the inferior mesenteric ganglion is separated from all its connections with the spinal cord, and when, in addition, one of the hypogastric nerves issuing from it to supply the bladder is divided. Stimulation of the central end of the latter by electricity is observed in some cases to be followed by muscular contraction of the bladder.

To account for such a phenomenon, on the assumed residual integrity of some portion of the connections of the ganglion with the cord, does not appear to be quite necessary. Electricity will be conducted by a continuity of conductive material in various directions; and the simplest explanation seems to me to be, the mechanical stimulation of structures storing and conveying efferent energy, that is, of the ganglionic cells and their centrifugal fibres in the ganglion in question.

Before leaving the subject of the efferent passage of energy into the viscera, I desire to make a few remarks upon the question, as to whether there is any reason to suppose that the

progress of the efferent current is influenced by the anatomical character of the chain it traverses. If Kölliker be correct in his belief, that the visceral afferent fibres reach the centre, without arborising on intervening ganglion cells, except in so far as they arise from the cells of the ganglion on the posterior root, while it is admitted that the whole efferent stream of visceral innervation undergoes the interruption or complication of cellular arborisation before ultimate distribution, it might, *a priori*, be supposed that such an anatomical difference implied some distinction, other than the broad one known to exist between these currents, namely, the sensory nature of the one and the motor nature of the other.

As regards the sensibility of the viscera, the experience of the physiologist, of the surgeon, and of the physician alike, serve to show that its conditions are peculiar.

As Foster states[1]: "In respect to all structures other than the skin and nerves—to such structures, namely, as muscles, tendons, ligaments, bones, and viscera generally—there is a large amount of experimental and clinical evidence, showing that, so long as these are in a normal condition, experimental stimulation does not give rise to any distinct change of consciousness; a muscle or tendon, the intestine, the liver, or the heart, may be handled, pinched, cut or cauterised, without any pain or indeed any sensation at all being felt, or any sign of consciousness given. Nevertheless, when the parts are in an abnormal condition, even slight stimulation may produce a very marked effect in consciousness."

When we arrive at the clinical portion of these lectures, this question will meet us again. My object in referring to these points at present is, to emphasise the fact that our perception of pain, arising from visceral causes, may be as acute as any capable of being generated elsewhere, and that the nature of sensibility, except in the skin, does not differ appreciably in the somatic and splanchnic divisions of the nervous systems.

On the other hand, be the condition of the viscera what it may, our voluntary control over the *efferent* stream of innervation flowing towards them is equally small. The channel *to* our perceptions, in other words, from the viscera to the brain, is potentially quite open; the channel *for our will* is, somehow, blocked between the brain and the viscera.

The *emotions*, however, affect the viscera as easily as they do

[1] *Op. cit.*, p. 1420.

the parts supplied by the somatic nerves. The difference, one is tempted to say, between the emotions or feelings and the will is the difference between the afferent and efferent sections of the nervous system, the emotions, or "feelings," being sensory, the volitions sensori-motor. It is more correct, however, to say that the stations for emotional reflex stop short of the nervous centres of will.

The *genius loci* urges one at this point to make a digression into metaphysics in the city of Dugald Stewart, of Thomas Brown, and of Sir William Hamilton. But we must remember the pitying smile with which the conventional physiologist would regard us, did we do so in the course of a physiological lecture, and leave to a more convenient season that wrestling with the transcendental for which our countrymen are famous the world over, and which has contributed in no small measure to their success in more material spheres. For your transcendentalist can, on occasion, be an exceedingly practical person, as the Afghan discovered who was charged by Rudyard Kipling's Highlander, after the latter had philosophically commented upon the unfortunate necessity involved in the occasional use of the bayonet! The difference between the power of emotion and of will to affect the viscera is nevertheless worthy of comment.

The emotion which arrests the heart's action or checks digestion appears to be a descending inhibition, liberating, on the theory advanced, products which, under normal conditions of the muscle and secretory cell, provide sooner or later a cross stimulation of the complementary sympathetic visceral nerves, and hurry the heart into katabolic activity. Whether this holds good also in the case of the gastric and other secretions, and a complementary sympathetic juice comes to the aid of the inhibited vagal secretion, we cannot, so far as I know, positively assert at present. But such experimental evidence as we possess does not appear to contradict such a notion. On the principle, moreover, of compromise, adaptation, equipoise, or, as Herbert Spencer terms it, "equilibration" in nature, which pervades and knits the everchanging but indestructible whole, such a process would seem very reasonable.

On the other hand, notwithstanding the oft-quoted case of "the Honourable Colonel Townshend,"[1] who is stated to have

[1] Cheyne's English malady, quoted by Guy and Ferrier ("Forensic Medicine," p. 239).

been able to arrest his heart's action at will, no effect upon the viscera, brought about by volition, is in any way comparable to that constantly exercised by the emotions upon these organs. None such is conceivable or known.

The rehabilitation of the scientific reputation of ancient worthies in the sphere of splanchnic physiology is a noteworthy phenomenon. Haller has many supporters of his theory of nerveless rhythmicality in the present day. Remak's accuracy has been vindicated by Paterson in his embryological study of the sympathetic system. I also venture to recall the name of an almost forgotten physician, whose views appear to me to contain an element of truth, which has not been altogether discredited by subsequent research.

Dr. James Johnstone, in his "Essay on the Ganglions of Nerves," published at Shrewsbury in 1771, maintained some theses which cannot be supported with our present knowledge of the subject. But in regarding ganglia as "checks to the process of volition" (p. 22), and if we restrict our meaning to ganglia of the efferent stream, it appears to me that these structures, in their histological condition and physiological behaviour, support Dr. Johnstone's opinion.[1]

Did the *efferent* stream pass through the peripheral ganglia, without arborising on nerve-producing cells, as Kölliker considers the *afferent* stream does, it is highly probable that our voluntary control of the viscera, if spasmodic, would in any case be as

[1] James Johnstone was born in 1730, at Annan in Dumfriesshire. It was inevitable, therefore, that one or other of his descendants should unsuccessfully claim the dormant Marquisate of Annandale. This one of them did some years ago. Johnstone studied under Whytt, whose portrait hangs on these walls, and graduated as doctor of medicine at the University of Edinburgh in 1750. He is not to be confused with his son James, who also graduated in Edinburgh in 1773. Johnstone, after studying in Paris, settled in practice at Kidderminster, and later at Worcester, where he died in 1802. His first essay on "The Use of the Ganglions of Nerves" was published at Shrewsbury in 1771, and in 1795 again formed the most important part of his "Medical Essays and Observations." His employment as a disinfectant in typhus, of "the thick white steam of muriatic acid, set free by pouring small quantities of vitriol from time to time upon common salt, heated in a chafing-dish of coals," was recommended for use by a committee of the House of Commons in 1802. These facts, together with his publication of an essay containing a scheme for the abolition of slavery, show him to have been a many-sided and ingenious man. Further particulars concerning him are to be found in the "Dictionary of National Biography," from which some of the facts mentioned were gathered.

As I have stated, there is no question of the adoption of his views concerning the functions of ganglia, as a whole, but his essay contains suggestions well worthy of consideration even in the present day.

decided as our perception of pain under certain circumstances, when the *afferent* stimulus is originated in the vegetative organs of the body.

It is, moreover, not maintained that the motor cells and processes of the cerebral cortex reach the periphery without arborisation on intervening motor cells, in the central nervous system; nor can it be argued that secondary motor cells are impotent to generate efferent force, and transmute sensibility into motion. The whole physiology of the spinal reflex disproves this.

It may, indeed, be contended that physiologists believe they have shown that energy, to rouse motor cells in any and every part of the body, must *always* arise *de novo* in some portion of the sensory system. But a motor nerve will induce contraction in a muscle, when electrical stimulation is applied directly to its trunk; and we have seen that the secretory nerve, severed from its central connection, may still be made to exercise its function, by similar stimulation of its peripheral portion.

To this it may doubtless be replied, that these effects are the result of stimulation of the inherent irritability of the ultimate structures, namely, the muscle cell, or secreting cell, as the case may be. To prove this, however, two conditions are necessary—(1) That these ultimate structures should be made to manifest their properties on the direct application of the stimulus to them, as is *apparently* easy enough in the case of muscle; and (2) that the parts locally stimulated should be shown to be free from nerve elements. Now, the "ganglion free apex," which is at present the sole hope of the Hallerists, still appears to stand, to use an expressive German idiom, "on weak feet." The contention, therefore, that all manifestations of peripheral motor energy must arise *de novo* in the sensory system, cannot be regarded at present as indisputable. It is thus premature to conclude that there is no dormant energy in motor cells and processes, capable of explosion by other means than by transmitted sensory impulse. The effects of electrical stimulation, indeed, appear to disprove this, for no one confuses vital nerve impulse with electricity. The pin-prick or slap which rouses the eviscerated heart to contraction is probably electrical in nature, but neither these nor the current of a battery are any more nerve force than is the match, which may be the immediate cause of the blowing up of a powder magazine, gunpowder. The slap, the match, and the nervous impulse alike, liberate latent energy in the explosive substance,

one of the constituents of which in the animal body is nervous material.

Why, then, should the ganglion cells on the efferent splanchnic stream be excluded from every other function than the production and nourishment of fibres, and the property of conductivity? These very qualities appear to me to argue the probability of the peripheral storage of secondary energy by them, and the innumerable arborisations of outgoing fibres in the tangled net of intervening ganglia some impediment to the efferent impulses of the will.

Some support, finally, appears to be given to this view, by the peculiar behaviour of visceral muscle under electrical stimulation, as manifested by the delayed response to such stimulation, or the "refractory period," as it has been called, the disproportion between cause and effect, and the phenomenon of the "staircase" or cumulation of viscero-motor contractions, observed and related by various physiologists.

With Dr. James Johnstone, I therefore venture to consider it probable that these ganglia may be regarded as checks to volition, and that they are just as important factors for consideration, in accounting for involuntary muscular action and secretion, as are either the anatomical character of peripheral, mobile, and secretory structures, or the essential irritability, whether rhythmical, secretory, or excretory, which is proper to all living matter.

In having, with, I trust, becoming diffidence, expressed myself thus, I have no desire to assume the irrational attitude of a special pleader in physiology. I hold no brief for the splanchnic nervous system. The client of the natural philosopher, in the widest sense of the term, is Truth, and anything which falsely masquerades in that guise is sooner or later denounced and renounced in physics, although for a time it may hold us in bondage, clad as an angel of light. I merely maintain that those who would reduce the viscero-motor nervous system to the passivity of a telegraph wire have not yet proved their case.

In a discussion, preliminary to the consideration of the relation of the nervous system to visceral disease and disorder, it is necessary to refer to the connection between the manifested force which we call "mind," and the non-cogitative functions which we term "body."

It will be remembered that in examining the sources of the vago-glosso-pharyngeal nerve in the medulla, that view was

adopted of the nature of the nucleus, usually regarded as the sensory root of this important nerve stream, which considers it to be a gathering point for afferent fibres of the vagal system, whence they are connected with other nerves and with more remote portions of the encephalon. The very general terms I employ in making this statement, are a measure of our present ignorance as to particular knowledge on this point. We appear, however, to be justified in regarding the opinion expressed as correct. Ramon y Cajal has described and figured a direct connection between fibres of the vagus and the ascending root of the fifth nerve; and it is very reasonable to expect that continued investigation of this region, and of the paths whereby sensory impulses pass from the cord to the cortex cerebri, by staining methods and induced degeneration, will prove still more certainly that intimate connection between visceral innervation and the higher nerve centres, which we know, on physiological grounds, to be quite unquestionable.

It is necessary, therefore, in connection with our present theme, to inquire shortly into the nature of those encephalic influences and stimuli which such lines of neural conductivity bring to bear upon the viscera, and by which the viscera also influence the activity of the higher centres.

Were we to be guided by Professor Bain's definition of a definition, namely, that "a definition should itself be intelligible, and composed of terms not standing in need of farther definition,[1] it would be hazardous to proffer any definition of *mind*. Inasmuch, however, as we as physicians must have some more or less definite conception of the forces with which we have to deal, we may be pardoned if we attempt to formulate to ourselves, in the generation in which we live, some proximately adequate verbal equivalent for so wide and mysterious a force, even though our mental grasp should embrace but a very small portion of it.

With this apology, our present knowledge appears to warrant our regarding mind *as a mode of vital motion manifested by some cells of the cerebral cortex, and as the more or less permanent product or effect of such motion, which we call memory.*

When we examine so instructive and beautiful a diagram as that with which Sir John Batty Tuke illustrated his lecture in this hall, on the cerebral convolution regarded as an organ,[2] and which I have had reproduced as a lantern slide, and when we consider,

[1] "The Senses and Intellect," p. 2.

[2] *Edin. Med. Journ.*, 1894.

moreover, the results of experimental physiology and of diseases affecting the brain, particularly those associated with aphasia, we cannot avoid the conclusion that, whatever the mind may represent to the speculative philosopher, to us as physicians it must be regarded as a product of cellular activity, however we may define it. Nor need such a conclusion carry with it a materialistic conviction, in the philosophic sense. If evidence for the existence of a more permanent soul be not found in the collective history of the joys and the sorrows, the aspirations, the defeats and the triumphs of our race, it is scarcely probable that it will be discovered in the crucible of the chemist, or in the workroom of the physiologist.

The constructive school of modern physiologists who have busied themselves with the origin of life, will in all probability for æons of æons, if their patience endure so long, remain like the pedant Wagner at their task in the manufacture of their *homunculus*. That sprite, when he appears as the embodiment of finite life evolved by finite ingenuity, will probably greet his triumphant maker, from the romantic depths of the flask, in the words of Goethe's famous creation:—

"Nun Väterchen! Wie stehts? Es war kein scherz!
Komm, drücke mich recht zärtlich an Dein herz!
Doch nicht *zu* fest, damit das glas nicht springe."

Ah, Pápa! how then goes it? 'Twas no joke!
Come, press me gently to thy parent heart!
But not *too* fondly, lest thou break the bottle.

With the mystery and incomprehensibility of life and its various manifestations, including mind, we are not, however, at present concerned. Our business is with the product man, and with so much of him as is more or less comprehensible. Averting our eyes, therefore, like Faust from the endless macrocosm of life in the abstract,[1] we must, less ambitiously, direct our attention to the sufficiently large microcosm of *human* life, and endeavour to understand in some measure its manifestations in the sphere of thought.

Every form of functional activity alters the conditions of the structure manifesting it. This is true of the secreting cell throughout the body. It is no less true of the cells whose activity results in the manifestation of mind. On a former

[1] "Welch' Schauspiel, aber ach ein Schauspiel-nur,
Wo fass, I dich, unendliche Natur!"

occasion, Sir John Tuke interestingly described the changes which have been observed to result from the normal and artificial stimulation of nerve cells (their obscuration and irregularity induced by wakefulness and work, and their restoration of contour and original character by sleep and rest); brain cells, and the cells of the spinal centres, thus, like digestive or salivary cells, manifest changes indicative of work and non-work. When, however, we come to the question of the registration of impressions, without apparent anatomical change of parts, we arrive at a theme which must still be treated entirely hypothetically, but changes associated with which must, nevertheless, be regarded as existent. Whether the registration of memory be *in* the cell, or merely rendered possible through the instrumentality *of* the cell, we cannot now say, and possibly never shall be in a position to assert positively; but that it would be impossible *without* the cell, and that the passage of impressions *through* the cell influences the organic conditions of the latter, may be assumed to be so probable as to carry with it the assurance of certainty. Every possible explanation of the nature and seat of mind in its various manifestations, which the ingenuity of man, from pre-Platonic down to post-Cartesian times, could devise, has long ago been given. The operations of the mind can be described more or less interestingly by metaphysicians, but they cannot explain them any more than the child can the flight of an eagle as it soars into the empyrean, although it has the power to follow it with its eye for a short distance.

Our inability to explain memory and many other elements of mind does not, however, shake our conviction that all these are the results of cellular activity, and upon the physical basis of mental acts and stored experiences I shall make some comment in the last lecture of the next series.

On this point, also, with a clearness of statement and an elegance in diction characteristic of his writing, Dr. Maudsley remarks: "Of no mental act can we say that it is 'writ in water'; something remains from it, whereby its recurrence is facilitated. Every impression of sense upon the brain, every cerebral reaction which passes into muscular movement, leaves behind it some modification of the nerve elements concerned in its function, some after effect, or, so to speak, memory of itself in them, which renders its reproduction an easier matter, the more easy the more often it has been repeated, and makes it impossible to say that, however trivial, it shall not under some circumstances recur. Let

the excitation take place in one of two nerve cells lying side by side, and between which there was not any original specific difference, there will be afterwards a difference between them. This physiological process, whatever be its nature, is the physical basis of memory, and it is the foundation of the development of all our mental functions."[1]

I am not aware that now, twenty years after these words were written, any more can be said upon the subject. For us as physicians, and in connection with our present theme, it is enough that no manifestation of mind can occur without cellular excitation, and that such cells are portions of an organism which is one and indivisible, however various the functions of its several organs, or of portions of the latter, which I shall refer to again as organules.

These cellular activities and persistent impressions are proper to all animal life, and are capable of influencing the organism manifesting them for good or for evil. In the microcosm of man, however, we have to deal with a development of ideation as peculiar to him as the maintenance of the erect position. When Mephistopheles wrote in the album of the young student, "Eritis sicut Deus, scientes bonum et malum," that profound judge of human nature added, as the awestruck boy withdrew, and with something as nearly approaching a sigh as His Highness was capable of, "A *weary* man thy likeness to the gods will make of thee." This likeness to the gods, however indistinct at times that image may become, the physician has to bear in mind in every department of the healing art, outside the sphere of veterinary medicine. For, while the first impulse of every living creature is to *live*, the desire of an ideational creature is to live in accordance with that which makes life precious to it, and which is not always of the most Godlike nature. These are self-evident conditions, which do not admit of argument. The suicide terminates his existence, when his brain is *not* disorganised, and sometimes probably when it *is*, not because he has ceased to desire life, but because he cannot live the life he desires. Even when he has no thought of laying violent hands upon himself, circumstances, whether they favour the attainment of his ideal or no, act upon his cogitative cells *so* as to generate stimuli of an invigorating or depressing character, as Dr. William Falconer of Bath, writing from his knowledge of the long experience of man, rather than from physiological investigation, pointed out more than a century

[1] "The Physiology of Mind," 1876, p. 27.

ago in the first Fothergillian prize essay.[1] Such stimuli by efferent channels act in promoting the health and life or disease and death of the viscera, and of the body of which they are a part. Physical disorders, on the other hand, which impair the nutrition of the centres of vital force, directly or indirectly produce similar results, in various ways, with varying rapidity, and in varying measure.

How often, for example, do we encounter cases in practice, in which the weariness of life causes the patient to desire death, when the actual cause of disturbed health or happiness appears to us quite inadequate to account for so much distress. And, again, how frequently do we observe the desire to live strong in those, the cessation of whose discomfort can only coincide with the termination of life. This despondency in some cases, this unquenchable hope of recovery on the brink of dissolution in others, as also the anxious, or calm and herioc, struggle for life in yet others, are noteworthy phenomena, and reveal to us how complex a creature we have to deal with in man. Could we explain more fully the organic relations of the *tædium vitæ*, of the *spes vivere*, and of that *magna quies*, that grand composure manifested in face of the still greater quietude of death, we should have made a considerable advance in our knowledge of the relation of the nervous system to visceral disease and disorder. These subjects are, moreover, germane to the topics discussed in a lectureship on mental diseases—that is, on the mental symptomatology of cerebral disorders. As Maudsley has eloquently remarked, in his "Goulstonian Lectures on Body and Mind" (p. 102): "The mental effects of perverted sensation afford a promising field of future research; when better understood, it cannot be doubted that they will explain many phenomena in the pathology of mind, that now quite baffle explanation. It behoves us to clearly realise the broad fact, which has most wide-reaching consequences in mental physiology and pathology, that all parts of the body, the highest and the lowest, have a sympathy with one another, more intelligent than conscious intelligence can get, or perhaps ever will, conceive; that there is not an organic motion, visible or invisible, sensible or insensible, ministrant to the noblest or to the most humble purposes, which does not work its appointed effect in the complex recesses of the mind; that the mind, as the crowning achievement of organisation, and the consummation and outcome of all its energies, really comprehends the bodily life." To a study

[1] "Memoirs of John Fothergill," by Lettsom, 1786.

among others of some such points in the pathology of visceral control, and the clinical phenomena observed when such control is impaired, I purpose devoting the remainder of these lectures, appreciating full well the difficulty of the subject, and also my own inability to do it justice.

LECTURE IV.

THE PATHOLOGY OF VISCERAL INNERVATION.

WHEN the founder of this lectureship first conceived the intention of proposing its establishment, which was, I believe, many years before that actually took place, there were, I understand, few if any systematic courses on psychological medicine in this country. I have seen it stated, indeed, that he was himself at one time the only systematic and special lecturer on the subject in Great Britain; and although he had large opportunities for teaching the subject practically, I understand he evoked a very tepid enthusiasm in the matter, and that his classes were never so large as the importance of the subject and the prevalent ignorance of it, at that time, would have rendered desirable. Novel subjects in a curriculum only attract the more prescient students. It is of interest to know that the late veteran head of our profession, Sir William Jenner, was one of the few students who attended the lectures in question.

As, therefore, this lectureship was originally intended to supply in a measure the want of systematic teaching, it was agreed that a considerable number (six) lectures should be delivered annually. Now, however, that psychological medicine is more generally taught, and has acquired an acknowledged importance, which is but an adumbration of its future pre-eminence as a branch of medicine, the *raison d'être* of this lectureship is not quite the same. It has become, like some cognate foundations elsewhere, a means of bringing before the profession the work of individual lecturers, and what is newest and most important in the work of others in connection with the theme proper to the foundation. But original or new work is an exhaustible quantity, and to spread it over a prescribed number of lectures might be difficult, perhaps tedious, especially to the audience, and certainly unnecessary. The delivery of a smaller number of lectures

annually, therefore, than was originally contemplated, would seem to be to the advantage of all concerned. I think I am correct in assuming that this is the conclusion at which the College has arrived as regards the character of this lectureship and the duration of the individual courses.

In selecting, therefore, so large a subject as the relation of the nervous system to visceral disease and disorder, I need scarcely state that I had not the presumption, in view of the audience I should have the honour of addressing, to entertain any intention of an exhaustive treatment of material, concerning which many of my hearers would be in a position to be, as some of them possibly have already been, my teachers; but rather to indicate, so far as I could, guiding points in a subject of increasing interest and importance; to endeavour, in short, to discover principles—*principia*—those light rays of the dawn, the first perception of which, in obscure surroundings, is one of the most exalted pleasures of which the human mind is capable.

In considering some features in the anatomy and physiology of the visceral nervous system, in this place last year, the method pursued was centripetal,—we examined the subject from the so-called peripheral nerve-endings in organs to their known or surmised origin in the intermediate or central portions of the nervous system. In referring to some points in the pathology or pathological physiology of the same structures, I propose following the same course.

The pathology of the visceral nerve-ending may be frankly stated to be unknown, although it may legitimately be assumed to participate in the disintegrative changes which may affect visceral nerve trunks, and to which I shall presently refer. We have seen how difficult it is in many cases, and under the most favourable circumstances as to freshness of tissue, to detect the nerve-endings in the viscera, anatomically; and when we remember that some of our best histological methods, such as the chrome-silver methods, are not at present well adapted for pathological work, and that such investigations themselves require an amount of time which is not at the disposal of many general pathologists, it need not surprise us that the pathological changes in the nervous periphery are still in great measure a *terra incognita*. The recent tendency of physiological thought, moreover, to rob the peripheral nervous system of the very modest amount of subordinate autonomy claimed for it, is calculated to delay active research in this direction. When,

however, the inevitable period of reaction against too narrow a Hallerism sets in, and our histological methods for pathological purposes are extended, we may expect the same new life to be infused into the investigation of the peripheral nervous system, which a better knowledge of the fine anatomy of the nerve cell has already called forth in the examination of the obscurer changes in the cell protoplasm of the central nervous system.

The visceral nerve trunks, as we determined on a previous occasion, are spinal or sympathetic and vagal or non-sympathetic; although the root and trunk ganglia of the par vagum appear to constitute a compromise between the character of the non-visceral or somatic and the visceral spinal nerves.

The disintegrative changes in the visceral nerve trunks may be broadly regarded as of an active and passive kind, the former being due to organic or inorganic poisons, and the latter to slow or rapid solutions of continuity by pressure or grosser traumatism. The organic poison playing the part of a morbific agent may be introduced, or of home growth; it may be heter-intoxicant or aut-intoxicant. The heter-intoxicant organic poisons most frequently operative are alcohol and the infectious or contagious fevers, especially diphtheria; the aut-intoxicant, some form of caco-metabolism, such as diabetes or gout. The most common inorganic poisons which are of necessity introduced and heter-intoxicant are lead, phosphorus, arsenic, and mercury.

The specific effect which these poisons have upon the peripheral nervous system is to cause a proliferation of the connective tissue of the sheaths and of the nerves themselves, and thus, apparently by the accumulation of adventitious products, to disturb the nutrition, impede the conductivity, excite in sensory nerves the sensibility, and ultimately to destroy the continuity of the axis cylinders of the affected structures. This process produces, in short, an acute tumour, which rapidly invades the structure, eliciting in some cases its responsive properties, and finally abolishing the latter. Fortunately, the cessation or withdrawal of the morbific agent, and the reparative power of nerve tissue drawing its life from a higher source, serve, on the removal of the proliferant and disintegrative blockage, to restore the nerve in many cases to its pristine activity or to a state of sufficient functional power.

These well-known features of peripheral neuritis in general have also been found to apply to the visceral nerves; although, having to deal in this case with structures differing largely in

important anatomical particulars from the somatic series, there would appear to be some modification of the process in the internal organs, and the whole subject still constitutes one of the fruitful fields of future pathological research.

Paul Meyer,[1] in his account of one of the most carefully examined cases of diphtheritic paralysis with which I am acquainted, found the degenerative changes referred to well marked only in the coronary of all the visceral plexuses. The pulmonary and gastric plexuses were doubtfully implicated, and the semilunar ganglion and sympathetic system generally showed no distinctly pathological alterations. He concluded that the fibres involved in the coronary plexus were probably of vagal origin. The clinical visceral phenomena of diphtheritic poisoning, although in their most tragic form frequently associated with cardiac failure, are not, however, as we know, restricted to that organ, and it is probable that like changes occur especially in the medullated nerves of other viscera. The severe pain of lead colic, which Ross[2] considers neuralgic, as well as the agonising enteralgia associated with specific and old malarial poisoning in some cases, point to an irritative neuritis of sensory visceral fibres.

The difficulty of detecting changes in the sympathetic system, as a whole, is doubtless due, as some have remarked, to the preponderantly non-medullated character of the nerves in question. The sensory nerves in the distant periphery are, however, according to Kölliker, usually medullated,[3] and in these the alterations attendant upon degeneration ought to be capable of detection.

The more gradual pressure exerted upon nerves by morbid growths, while it is conceivable that in some cases it may induce neuritic changes, similar to those already referred to, may, by the slow obliteration of nerve-paths, produce a disintegration more allied to the well-known consequences of nerve section, in which the disintegration of the medullary sheath is more general and associated with a minimum of thecal proliferation. Martius, in his monograph on tachycardia,[4] refers to a case of Hayem's, in which pressure by a sarcomatous tumour in the mediastinum induced atrophy, with fatty granular degeneration of the myelin sheath in both vagi, and likewise mentions a case of Billroth's, published by Kappler,[5] in which that distinguished surgeon excised a portion

[1] *Virchow's Archiv*, Bd. lxxxv. S. 181 *et seq.*
[2] "Diseases of the Nervous System," vol. i. p. 738.
[3] Gewebelehre, Bd. ii.
[4] "Tachycardie, Eine klin.-Studie," 1895, S. 68.
[5] *Arch. d. Heilk.*, Leipzig, 1864, S. 271.

of the right vagus nerve in a man, without permanent effect upon his heart's action, but with persistent paralysis of the laryngeal muscles innervated by the cut nerve, which doubtless exhibited the sectional disintegration of which mention has been made.

Such processes destroy the activity of visceral nerves, and are distinctly destructive, death-dealing, or pathological. The increased demand made upon the functional activity of an organ, from break-down in a system of which it is part, such as the demand made upon the muscular power of the heart when the circulation is from any cause rendered more difficult of maintenance, may, however, be regarded as constructive, life-giving, and physiological, although the organ manifesting compensatory power cannot be regarded as a typically normal one.

It has appeared to me to be permissible and a matter of sufficient interest to again examine a question which has already occupied the attention of some whose names will ever be held in honour by us. I refer to the relation of an hypertrophied organ to its nerve supply. A study of affections of the heart has impressed upon me the importance of this subject, and I have chosen the uterus as the organ manifesting greatest variation in physiological bulk, as that best calculated to furnish data for the determination of the question, although, as I shall remark later, both this organ and the heart have intrinsic peculiarities not altogether shared by organs which do not possess the same range of rhythmical variation in capacity.

William Hunter appears to have been the first to "suspect"[1] that the nerves of the gravid uterus were enlarged in proportion to the vessels. John Hunter[2] disputed this assertion, and declared himself an unfaltering Hallerist, so far as the nerves were concerned. "The uterus in time of pregnancy," he writes, "increases in substance and size probably fifty times beyond what it naturally is; and the increase is made up of living matter which is capable of action within itself. I think we may suppose its action more than double, for the action of every part of this viscus at this period is much increased, even beyond its increase of size, and yet we find that the nerves of the part are not in the smallest degree increased. This shows that the nerves and brain have nothing to do with the action of the part."

The matter seems to have been regarded as more or less debat-

[1] "Anatomical Description of the Human Gravid Uterus," London, 1794, p. 21.
[2] "Works," Palmer's edition, vol. iii. p. 117.

able, until the acceptance, by a considerable number of leading men, of the published results of Robert Lee's work.[1]

Lee, who asserts that William Hunter never dissected the non-gravid uterus, maintained from his own dissections that these "prove that the human gravid uterus possesses a great system of nerves, which enlarges with the coats, blood vessels, and absorbents during pregnancy, and which returns after parturition to its original condition before conception takes place." As we know, a very bitter controversy took place over this question, and called forth a flood of private correspondence, much of which Lee published. In one of these letters, Robert Knox, the Edinburgh anatomist, while agreeing with Lee as to the nature of the structures in dispute, considers that the question of the increase of the nerves in size had been exaggerated.

In more recent gynæcological literature the matter is not referred to very frequently, but Galabin's position may probably be regarded as that of the majority of authorities in that department of medicine. "It is now established," he writes, "that, as might have been expected, growth does takes place in the nerves, including the so-called 'ganglion cervicale uteri,' to fit the uterus for the process of labour, in which both reflex action and periodic centric discharge of nervous energy play important parts."[2]

The question, it will be gathered, was one not easy of determination, and also eminently calculated to be embarrassed by the influence of preconceived notions. Lee himself showed how, by laboriously picking off all connective tissue surrounding the nerves, their apparent size could be greatly reduced; and, valuable as his work was in many respects, it is probable that he rather overestimated the increase in the size of the nerves in the physiologically active organ.

As I have already stated, Lee asserts that William Hunter never dissected the non-gravid uterus, and could not therefore have been in a position to institute a comparison. That great man, however, as I have also stated, merely expressed a suspicion. The method of Lee, moreover, was open to fallacy. The ganglion cervicale uteri is not an unyielding structure, and a good deal of adventitious tissue surrounds extra-organic nerve trunks. Nerves and ganglia may be flattened without notable intrinsic overgrowth.

To avoid these sources of fallacy, I resolved to examine the nerves of the uterus at various stages of pregnancy, by transverse

[1] *Phil. Trans.*, London, 1842, pt. ii.

[2] "A Manual of Midwifery," London, 1886, p. 97.

sections of its lower segment where the nerves are largest, and by longitudinal section and other means, the body of the organ where the nerves naturally are diminished in size and less easy of detection and comparative measurement on transverse section. Sections of the lower segment were stained with hæmatoxylin in the usual way, while the nerves of the upper portion were examined by Sihler's method, which I described last year. The animal used was the cat; and as I altogether failed to discover an adult animal which was not more or less pregnant, one was kept for twenty-two days after parturition, to allow of the uterus regaining its non-pregnant size, and was accepted as the type of that condition. The animals were killed before examination by chloroform, hydrocyanic acid, and by drowning, after having been anæsthetised.

In gauging the size of the nerves at a given level, the largest nerve visible was sought as that most easy of detection and least liable to erroneous observation.

A large number of sections were made and examined more or less carefully. The general impression conveyed by these to my mind is reproduced in the micromillimetric measurements actually made, as shown in the following table:—

Advanced Pregnancy.	Cervix.	Level of Bicornu.	Body.
Fœtus nearly fully grown.	8-10 microm.	5–10 microm.	6 microm.
Early Pregnancy.			
Fœtus measured 1·5 mm.	8–12 ,,	10–12 ,,	3–4 ,,
Twenty-two days post-partum.	7–10 ,,	5–7 ,,	5 ,,

As I have stated, only the largest measurements were taken. Below these, every size of nerve, down to the terminal fibrils and penultimate plexuses, were observed, and to peculiarities of the latter I shall have to return when discussing visceral pain in the next lecture. The present observations on the relation of size of nerve to hypertrophous organ were indeed made *en passant*, the research being directed more to the elucidation of the local causes of visceral pain, with a view to the discussion of the etiology of angina pectoris. In estimating the value of the measurements given, three questions have to be answered—(1) Were the animals

the same size? (2) Were all the measurements taken from uterine nerves proper? (3) Do the comparative sizes given in the three animals represent corresponding levels?

The first and second of these questions I answer in the affirmative. The third requires some explanation as to the diameter of the nerve from the body of the uterus post-partum. The body of the uterus in this condition being smaller than in early pregnancy, and much smaller than in advanced pregnancy, the whole of it was inadvertently sliced with Cathcart's freezing microtome prior to staining; and it is possible that the nerve of comparatively large diameter, noted as the largest seen in this case, may have been obtained from the body of the uterus at rather a lower level than the mid-body—the portion examined in the other cases—and thus be somewhat of an over-estimate for the non-pregnant state.

An examination, however, of the diameter of nerves in the cervical portion of the uterus leads to the conclusion that, while there is practically no difference between the size of the uterine nerves in advanced and early pregnancy, there is a certain increase of size to be noted in these conditions, as compared with those in the quiescent uterus twenty-two days post-partum; and it may therefore be validly assumed that what is true of one part of the organ is true also of the whole, and that some increase in the apparent size of the nerves in the gravid as compared with the non-gravid uterus may be conceded. The increase is, however, I believe, apparent rather than real, for a closer examination of the individual fibres constituting the nerve trunks reveals no increase in them, either in size or numbers. What may, however, be observed is, a somewhat greater pliability and looseness or succulence of texture; the bearing of this upon the remarkable condition I shall presently refer to will be apparent. It may therefore be safely asserted that, if any increase takes place in the size of the nerves of the gravid uterus, it is in no sense proportionate to that which is by common consent met with in the case of the vessels, muscular fibre, and connective tissue constituting the organ.

Lee states that John Hunter left no preparations of the uterine nerves, in support of his assertion that there is no increase in the size of the nerves of the gravid uterus. That matchless observer, however, left a positive assertion of an observable condition, and it requires some boldness to call in question the accuracy of his observation. Personally, I respectfully tender my

adhesion, with the qualifications already stated, to John Hunter's statement as regards the condition of these nerves in pregnancy. But the difference between a statement of facts in an observable condition, and the expression of an opinion, however positively made, which is not covered by those facts, is very considerable. Science knows no *ex cathedrâ* utterances, and the humblest who can draw from the bosom of nature an indubitable fact, which contravenes the opinion of the most exalted, not based upon such, adduces a more mighty argument for his position than volumes of hypotheses backed by the sign manual of sacrosanct authority.

John Hunter said that the uterus might be fifty times as large in pregnancy as in non-pregnancy; that all the textures of the organ are increased in size except the nerves; and that therefore the nerves have nothing to do with the action of the enormously overgrown organ. Hunter was not much of a casuist, or he might have been more careful on this occasion.

If, however, the uterus be fifty times as large when gravid as when not gravid, and the muscular fibres of the organ can be shown to be innervated like all other muscular tissue, somatic and splanchnic, what becomes of the innervation of the uterine muscle most distant from the point of entrance of the nerves at the cervix, if these nerves do not enlarge? Do they snap in the stretching? To ask the question is to insult nature. Is there, then, any provision for the adequate innervation of the gravid uterus without an anatomical increase in the size of the nerves in that state? There is; and a provision which to my mind is one of the most remarkable, as it is one of the most simple conceivable. It is a trite remark, that the great and the simple are often convertible terms, and nature is ever great; and could we but always hear its dominant note, even in apparently complex operations, I believe we should find it to be essentially as simple as it is great, strong, omnipotent.

The simple and sufficient expedient adopted by nature, under the conditions discussed, is one which was unknown to me when I undertook this investigation, and I am not aware that it has been described before.

Tortuosity in the blood vessels of the uterus, from their notable increase in size, is more apparent in the gravid than in the non-gravid organ. Tortuosity of the uterine nerves is, I believe, inversely as the size of the organ. Tortüosity of nerve trunks may indeed be seen in the fully gravid uterus; but in none of the sections of the organ at term, which I have examined, have I

observed by any means the same degree of tortuosity and coiling as in the nerves of the uterus in early pregnancy or post-partum. This coiling may indeed be such (as in one specimen which I show) (Fig. 20) as to suggest the figurative parallel of paying out a coil of rope to an object which is increasing its distance from a point of attachment.

In the facts I have mentioned, and the specimens I show, I believe I have grounds for maintaining that it is by this grandly

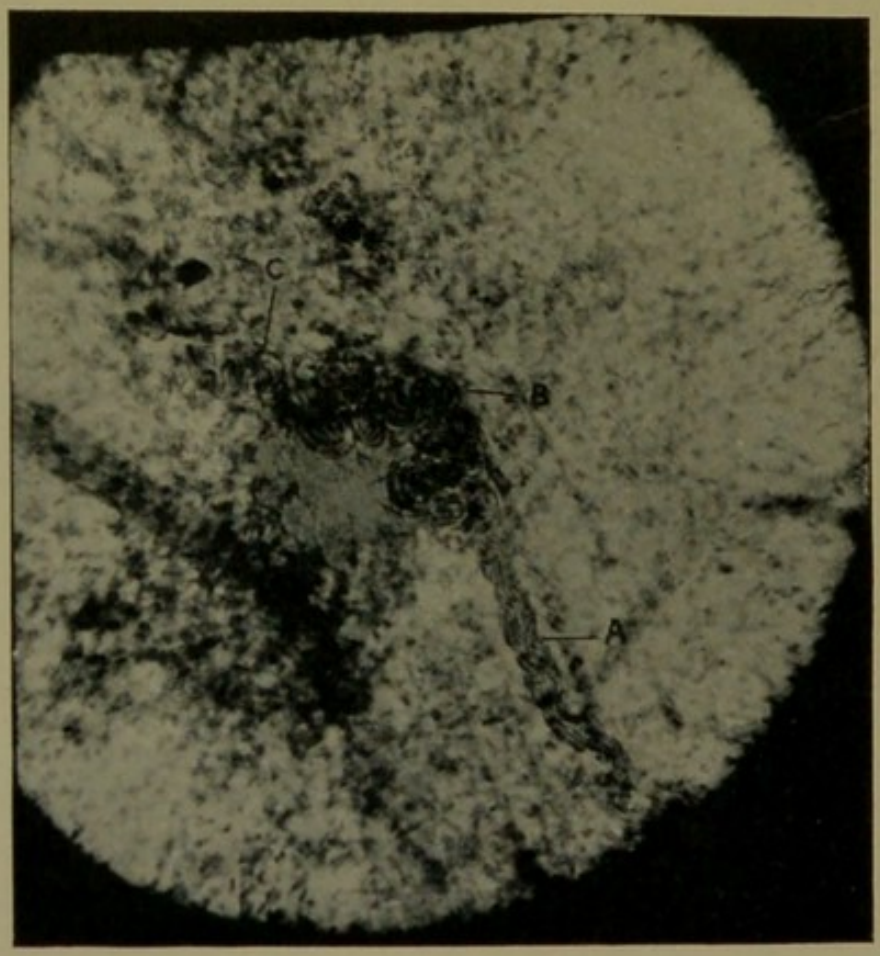

FIG. 20.—Coil of nerve from the uterus of a cat in early pregnancy. Swift's obj. $\frac{1}{6}$. Eye-piece out.

simple expedient that the nerve supply of an organ, intended to vary in size, is adapted to these varying circumstances. The apparent increase in the size of the nerves, their more open texture, their more succulent appearance, are but adjuvant conditions which promote the paying out of the nerve-rope to the lengthening organ. When we come to examine the relation of the cardiac nerves to angina pectoris, in the next lecture, the bearing of these facts upon a wider range of physical conditions will be more apparent. The nerve-coil is, however, but an

emphasising of that wavy elasticity, which the longitudinal section of any nerve with a considerable range of extensibility, such for example as the pneumogastric nerve, will show.

On the trunks of nerves in the substance of the uterus, I do not happen to have observed ganglion cells. I shall not, however, take upon myself to assert that they do not exist. Had they been common, I think I should have encountered them.

The conclusion, therefore, to be drawn from the facts I have stated, as regards the anatomical relations of the nervous system, in a physiologically hypertrophous organ, possessing a considerable range of normal variation in size, is, that there is no essential increase in the proportions of such nerves to such organ, but that anatomical and physiological changes occur in the nerves, which enable them to adapt themselves to the organ they supply, and in a measure control. The statement that the nerves in a measure control the organ, requires some explanation, although to enter into a fuller discussion of the subject would be foreign to our present purpose.

As Galabin states in the passage I have quoted, "both reflex action and periodic centric discharge of nervous energy play important parts" in the process of labour. With essentially centric conditions I am not at present concerned. They stand in need of much elucidation still, and will doubtless in time, by a minute anatomical and physiological investigation of the sensory and motor cells which regulate uterine rhythmical action, be more or less satisfactorily explained. My present purpose is to suggest that one of the factors, in evoking reflex action at term, and in inducing those contractions, associated with pain, referred to the active viscus, under these circumstances, is the fact of the enlarged organ having reached at a certain period the full tether of its intrinsic nervous system. The rope has been paid out to its full convenient stretch, and the note is sounded for a return of the organ to more moderate dimensions. The admitted prematurity of labour, moreover, in many cases of twin pregnancy and hydramnion is, I would suggest, quite as valid an argument in favour of the theory I have suggested, as for the premature provocation of rhythmical uterine action without nervous influence. There is a crudeness about the suggestion, I admit, which at first repels one; but, having carefully thought the matter over, and without wishing to impute an unduly prominent rôle to this factor in the production of labour, I can come to no other conclusion. The predisposition to centric discharges, as Galabin calls it, is doubtless induced, *pari passu*, with the changes I have

indicated, but I do not think that the factor named can be eliminated. As I shall argue again, a study of visceral pain in other organs appears to me to support my contention.

Robert Lee[1] maintained the same theses in connection with the nerves of the heart, when the organ is hypertrophied, as he did in the case of the gravid uterus. His words are: "The ganglia and nerves of the heart enlarge like those of the gravid uterus, when the walls of the ventricles are affected with hypertrophy." Cloetta, quoted by Walshe,[2] partly agreed with Lee, but could not decide whether the apparent increase in the size of the nerves was due to an increase in the connective tissue sheath or to actual increase in the nerve fibres. These assertions have not, so far as I know, stood the test of time, although I am unaware of any systematic examination of the question. In view of the facts I have stated in connection with the innervation of the gravid uterus, and which are opposed in great measure to Lee's conclusions, I should, *a priori*, dispute the correctness of his views as regards the innervation of the enlarged heart. There is, as I shall endeavour to point out in my next lecture, a special provision in the nervous anatomy of the heart, the same in principle as that met with in the uterus, and to which I have referred, for allowing the nerves of that organ, which varies so much in size during action, to adapt themselves to such variation. This provision, as we shall see, is less marked in organs such as the spleen and the kidney, with a smaller range of normal variation in size; and even in the heart, tortuosity is more apparent in the smaller than in the larger nerve trunks.

Leaving nerve trunks, I pass now to some mention of the pathology of the ganglion and the ganglion cell in the visceral nervous system.

Death, that universal law which organised matter must obey, and which has been suitably defined in scientific language on the tomb of Bacon, at St. Albans, as the command, "Let compounds be dissolved," induces changes in such compounds, whether they be individual cells, or those larger aggregates of cells, which have at one time constituted a considerable part of Lords Chancellor of England and of more humble persons—changes observable, and yet not truly pathological, as we usually understand the term, but which may be mistaken for such. The criteria for their satisfactory

[1] "History of the Discoveries of the Circulation of the Blood, and of the Ganglia and Nerves, and of the Action of the Heart," 1865, p. 28.

[2] "Diseases of the Heart," 4th edition, p. 281.

discrimination from pathological changes, cannot yet be said to have been determined. To grow old is, in a manner, partially to die; to be enfeebled, is likewise a retrograde change. Advance in life, however, is not pathological—enfeeblement is; and yet changes may be met with post-mortem in the cells of old and young alike, which are at times difficult to distinguish the one from the other, which have both the common property of death, and death in the child is nearly always pathological. In some cases, in the aged, it can scarcely be regarded as such. This confusion between dead, young, and old tissue, is not, however, I think, frequently possible. Collateral conditions serve to distinguish the one infallibly from the other. The features of senile degeneration in ganglion cells, mentioned in one of the most recent and reliable works on diseases of the nervous system,[1] are a certain diminution in size and number of cells, and well-marked pigmentation, such pigmentation not being associated with notable disorder of function. This general statement must, however, be regarded comparatively, for the ganglion cells of a man who is "young," and whose blood is "warm within him," cannot but differ in appearance and functional activity from those of his "great-grandsire," virtually "cut in alabaster," though possibly still in the flesh, and whether the cells of the latter be pigmented or non-pigmented. When changes normal to senility are found in youthful cells, it is highly probable that the latter have been rendered functionally old by disease, and that the change must be regarded as pathological.

In writing of the changes met with in the cardiac ganglia, Ott[2] states that two kinds of pathological change occur in them, the one progressive and consisting of hyperplasia of connective tissue, and the other retrogressive and consisting of parenchymatous degeneration of new cells. The former he met with in congestion and hypertrophy of the heart; the latter he found associated with qualitative blood changes, such as uræmia and pyæmia. Ott does not remark upon the influence of these changes upon cardiac activity, but the association of parenchymatous changes in the cells in profound blood dyscrasiæ is a suggestive one, because it is just under these circumstances that degeneration of the visceral muscle is most frequently observed.

The proliferation of connective tissue in a visceral sympathetic

[1] Leyden and Goldscheider, "Erkrangungen d. Rückenmarkes," Wein, 1897, S. 102.

[2] *Ztschr. f. Heilk.*, Bd. ix. No. 45, and quoted by Balint, *Deutsche med. Wchnschr.*, Leipzig, 1892, No. 1, S. 2.

ganglion may, however, be of a more active type, as was shown by Lancereaux's case,[1] which so long reigned alone as an instance of cardiac neural pathology. In this case, the cardiac plexus participated in an extremely rich abnormal vascularisation at the root of the aorta, and showed microscopically a round-celled infiltration between the nerve fibres of the ganglion which compressed the former. These conditions were associated with *angina pectoris*.

But the progressive and retrogressive changes may be met with in the same case. A ganglionic structure may participate in a general interstitial proliferation, such as that met with in granular kidney. Although it may be difficult to decide whether the parenchymatous change in the nerve cell be due to such interstitial hyperplasia, or both it and the latter be the expression of a blood dyscrasia causal of each, the influence of interstitial cirrhosis, as interfering with the due nutrition of a nerve centre, cannot, I think, be altogether excluded, and may even be causal in some measure of the changes in question. Such changes need not, however, place the cell out of action, although it is highly probable that the functional activity of such a cell is subnormal.

This combination was well shown in a posterior root ganglion which I examined last year, and which I obtained from Dr. Risien Russell, Pathologist to the National Hospital for Paralysis and Epilepsy, in Queen's Square. The case had been under the care of Dr. Hughlings Jackson, to whom I am indebted for permission to refer to it on this occasion.

A male, æt. 65, presented weakness and rigidity of the right arm; he could, however, move the arm and also the hand slightly. The left arm was normal. Both legs were weak and somewhat rigid, but the patient could get out of and into bed. There was some history of a fall a year previously. There was no facial weakness, except a slight difficulty in pursing the lips and whistling. The tongue was protruded rather to the right. There was no apparent difficulty in swallowing. The palate moved fairly. Articulation was much affected, and the voice was thick and harsh. The face was suggestive of a bulbar condition.

The knee-jerks were exaggerated; the right more than the left. Radial and ulnar reflexes were also exaggerated, and the plantar reflex was present. The sphincters were normal. The specific gravity of the urine was 1006, and it contained neither albumin nor sugar.

The autopsy took place *six* hours after death. The nervous

[1] *Gaz. méd. de Paris*, 1864, p. 432.

system revealed nothing abnormal beyond an atrophic state of the convolutions of the hemispheres generally, and the cerebral vessels were atheromatous.

The kidneys presented the typical contracted granular appearance associated with the changes of interstitial nephritis, and the heart the corresponding condition of concentric hypertrophy.

A posterior root ganglion, which I examined by various methods, showed well-marked interstitial hyperplasia, like that characteristic of the general state of the body, and parenchymatous change in a large number of the nerve cells. This change would, I presume, be termed pigmentary, but as the degenerated portion stained very darkly after exposure to bichromate of potash, osmic acid, and nitrate of silver, which had no effect upon the rest of the cell substance, a fatty degenerative change would appear to have been present. To compare with such atrophic and proliferant conditions, I may refer to the state of a posterior root ganglion from the body of a female, 18 years of age, who died in Queen's Square Hospital, of double pneumonia from mastoid disease, without central nervous complications. The case was under the care of Sir William Gowers, and the ganglion examined was given me by Dr. Risien Russell. The differences between the old degenerate ganglion associated with arterio-sclerosis and general interstitial hyperplasia, and the normal organ of a young person who practically died an accidental death, are very striking. The large, better differentiated cells, with little parenchymatous and no interstitial change in the young and normal ganglion, are easily distinguished from the ganglionic cirrhosis and degenerated cells of the decrepit old man. Nevertheless, as the history tells, the sensory conductivity of the cirrhotic ganglia does not seem to have been notably impaired. Leyden and Goldscheider,[1] however, basing their remarks upon the researches of Hale White, appear to consider that degeneration of the posterior root ganglion is a more important condition than a similar change in the semilunar and superior cervical ganglia of the sympathetic.

It is only necessary to refer to two other conditions of the posterior root ganglion, those, namely, associated with herpes zoster and dorsal tabes.

Atrophy and induration have been found in posterior root ganglia, related to territories of skin affected by herpes, the

[1] *Op. cit.*, S. 104.

agonising pain of many cases of which affection is so well recognised a clinical fact; while in dorsal tabes an inflammatory process, chiefly affecting the proximal and central portions of the posterior root ganglion and the posterior root itself, has of recent years attracted growing interest and attention. These changes are described by Leyden and Goldscheider as atrophic,[1] and affecting the nerve fibres. The connective tissue is also said to be increased, but the question of a change in the nerve cells is left undecided. The admitted alterations are, however, of interest in connection with the sensory disorders of the viscera, with which we shall be engaged in the next lecture, and particularly with the visceral crises of tabes, which have so pernicious an effect upon the course of the disease.

Our knowledge of the course of visceral fibres in the central nervous system is still so limited, that a discussion of the pathological lesions associated with general trophic degradation would not at present be useful. It is a very remarkable fact, how little most central lesions outside the bulbar area are accompanied by such general atrophy. The two factors in chronic diseases of the central nervous system which appear to bring about malnutrition most rapidly, are pain and mental anxiety; and the latter may be regarded as pain in the intellectorium, just as the condition we conventionally call pain is a reaction in the sensorium, to use old terms, largely and perhaps prematurely discarded. Inasmuch as physical degradation will be brought about by these conditions, in the absence of central lesion, we cannot well gauge the influence of the latter, but it is rational to think that their presence hastens and emphasises the malign influence of pain and mental distress. The absence, indeed, of marked interstitial or trophic changes—that is, splanchno-motor changes—in disease of the central nervous system, and the evil influence of pain and mental distress, appear to me, on the lines of our anatomical discussion of last year, to be an argument in favour of the subordinate automatism of visceral motion. The avenues for viscero-sensation are, as we ascertained, more direct and open than the cumulative blockage of the efferent visceral nerves.

It will thus be observed how rudimentary our knowledge of the pathology of the visceral nervous system still is. There are, however, already hopeful evidences of light-giving work in this obscure field; and I cannot close this lecture without a passing reference to those histo-physiological investigations which have

[1] *Op. cit.*, S. 512.

disclosed most interesting facts as regards the behaviour of nerve cells cut adrift from peripheral organs with which they are normally associated. The changes, although purely physiological, appear to point to a method of research which may lead to knowledge of pathological change in cells, whose touch of the organs they innervate may be loosened by disease general and local. Although I have myself undertaken some work on these lines, my work is still incomplete; and for the information on which my few present remarks are based, I am indebted in great measure to Van Gehuchten's exhaustive paper on the fine anatomy of the nerve cell,[1] in which also full references to the very interesting literature of the subject will be found.

It would seem to be essential to the maintenance of healthy structure in the nerve cell, not only that it should itself be undamaged, but that the organ its axis cylinder more or less innervates should also be in a condition healthily to exercise its function. This is surely a very suggestive fact as regards the relation of body and mind, the subjective recognition of which is at least as old as Juvenal, who associated the sound mind with the healthy body. The functional unit, in short, as we shall argue again, is not one but triune—peripheral organic cell—central nerve cell—blood. Our knowledge of the general effect upon the central nervous system of the severance of the periphery from the centre is as old as the researches of Berard, Vulpian, and Dickenson (1829–1868), quoted by Leyden and Goldscheider,[2] who studied the effect upon the cord of the amputation of limbs; but our more exact knowledge of details in the process is much more recent, and due in great measure to the method of staining nerve cells introduced by Nissl, and which has already been fruitfully applied to the examination of normal and abnormal conditions of cells in the cerebral cortex.

Van Gehuchten's observations were made upon the hypoglossal and pneumogastric nerves of the rabbit, the latter nerve being divided below the plexiform ganglion.

The changes noted in the medullary nuclei of both nerves were—(1) A chromatolysis, during which the chromatic granules in the cell protoplasm were dispersed towards the periphery of the cell, the protoplasm staining soon afterwards a uniform blue; (2) a centrifugal displacement of the nucleus, which may proceed to its

[1] *Cellule*, Liege and Louvain, tome xiii. fasc. 2, p. 315 *et seq.*

[2] *Op. cit.*, S. 89.

extrusion and the consequent sacrifice of the cell; (3) in the case of motor cells, a gradual recovery, at least for the time, to their original chromatic or "pyknomorphic" condition was noted, while the sensory cells in great numbers disappeared absolutely. In illustration of these facts, Van Gehuchten gives carefully executed drawings. More recently, Goldscheider and Flatau[1] have studied changes induced in cells by various poisons of an organic and inorganic nature. Their results, with the use of tetanus toxin, are particularly interesting, as also are the effects they have observed to follow the exposure of animals to high temperatures. There appears to be a very noticeable enlargement of the cell nucleus in tetanus, and a complete chromatolysis seems to be induced by excessive temperatures. Interesting, however, as these researches are, we are not yet in a position, as these authors confess, to draw very certain conclusions from them.

This sketch of the changes, pathological and experimental, met with in the visceral innervation, shows how little is, as yet, positively known of the alterations which underlie neuro-visceral disorders; but it likewise declares plainly that the night is past, and that daylight, more or less clear, cannot be very long delayed.

[1] "Norm. u. pathologische Anatomie der Nervenzellen," Berlin, 1898.

LECTURE V.

THE DISORDERS OF VISCERAL SENSIBILITY.

It may be remembered that, while discussing some points in the physiology of the visceral nervous system last year, I drew a parallel between viscero-motor actions in general and cardio-motor action in particular, arguing that, while the products of such motions differed with the organs which were the seat of motion, the mechanism of such action, whether anabolic or katabolic, was essentially the same. It is possible in Protean nature to push a parallel too far, and I have no desire to become too general in discussion. But it appears to me that it will be convenient, in considering the relation of the nervous system to disease and disorder in the viscera, to divide these into two large categories, namely, into disorders of sensibility or sensation, and into disorders of motility or motion.

The brain could no doubt be thus considered collectively with the other viscera, but there is a certain difference between the former and the latter which, together with the special character of this lectureship, renders it desirable that that viscus should receive separate treatment. The distinction consists in the fact that, whereas the control of the viscera generally by the brain is through the agency of nerves, structures continuous with it, and inseparable from it, the influence exerted upon the brain by the rest of the body is not only by way of the sensory channels which come to it embryologically, although they leave it physiologically, but also by means of the blood which in great measure goes from it. There is indeed throughout the body, as there is in every organ, a functional unity, which might be more accurately termed a tri-unity, due to the consentaneous operation for the production of a common result of the peripheral organic cell, whether in brain or muscle, a central regulating cell and its nerve

channels, and the bond of union between the two, namely, the blood with its stimulating and life-giving properties.

Recent physiological thought appears rather to have dissociated this essential unity, and much ingenuity has been exerted to show how very well the organs can get on without the nervous system. The question of non-neural cardiac rhythmicality we touched upon last year, and traced the controversy from the now untenable assertion of an absence of nerves in general in the cardiac apex, to that of an absence of ganglion cells in particular in that portion of the organ.

Personally, I endorse Henry J. Berkley's physiological standpoint, although I cannot agree with his description of the cardiac ganglion. His words are—"Cajal, in portraying the Auerbach plexus by the vital blue method, gives a picture that is not entirely dissimilar to our cardiac nerve-plexus with the neural enlargements and nerve-cells. Though in the cardiac plexus the nerve-cells are vastly inferior in number, different in appearance, and do not occur in clusters, yet the general likeness is sufficient to allow of some comparison being drawn between the two."[1] This is fairly correct as regards the lower third of the heart which Berkley examined, and I shall show some of these ganglia of the apex which agree in great measure with this description. But in applying his words to cardiac ganglia generally, Berkley's description is not correct. As I demonstrated last year, the cardiac ganglia of the vagal system, as I take them to be, may consist of very large clusters of cells, such as the fine specimen which was figured in the *Edinburgh Medical Journal* last year (Figs. 11 and 12). My reason for regarding such ganglia as pertaining to the vagal system is, that they bear much the same relation to the peripheral distribution of the nerve that the plexiform ganglion does to it at its origin, and they are to be met with in many of the organs to which the vagus is distributed. The important point, however, is that, character apart, the apex of the heart, although not profusely, is nevertheless sufficiently ganglionated, and the Hallerist must look for some other support than his anatomical argument. Physiology affords more scope to the imagination. But we saw that the presence or absence of ganglionic cells was, after all, a matter of small moment to the Hallerist. They were nutrient or something else. In any case they had little to do with motion in any organ. You cut a vagus and the heart does not feel it long. You detach an organ and stimulate it, and the

[1] *Johns Hopkins Hosp. Rep.*, Baltimore, 1894, p. 89.

functional result is there. It has been shown, however, that if you cut both vagi the staying power of the heart is seriously compromised. Balint[1] has shown that if aortic regurgitation be artificially established, and one vagus cut, the action of the heart is not materially interfered with; the compensated organ continues to act efficiently. But that if both vagi be divided, the heart, even although it has undergone compensatory hypertrophy, soon gives out, and the animal dies in about a week with well-marked evidences of retrograde stasis. I have already mentioned a case in which Billroth accidentally excised a portion of one vagus during an operation in the neck, with only temporary disturbance of the heart's action; and my colleague, Mr. Watson Cheyne, has recently mentioned to me another case not yet published, and which he has kindly permitted me to refer to on this occasion. During an operation for malignant disease involving the larynx, he found it necessary to excise a considerable portion of one vagus. The immediate consequence of this appeared to be an arrhythmical action of the heart which subsided in a few days; but the stability of the organ has apparently been more permanently impaired, because slight emotional excitement re-induces the condition, which was not present prior to the operation. Survival after the division of one nerve is probably the result of what may be termed incomplete peripheral decussation in the organic plexus, a subject, as it appears to me, of much practical interest, and one which I have examined somewhat, but my results are still too rudimentary for publication. The nerve from one side probably sends fibres to both sides in such unified organs as the heart, while division of both nerves naturally destroys such a nerve supply and saps the fountains of persistent rhythmicality.

Inasmuch, however, as anatomy lies at the foundation of our knowledge of all forms of organic activity, it would have been a difficult matter for the adherents of a neural theory of sustained motion to have defended their position, had it been possible to point indubitably to mobile structures which continued efficiently to act for a lifetime without such endowment. The conception of such a condition would *a priori* seem unreasonable, but as the unexpected does occasionally happen, it was just possible that such a fact might conveniently come to the aid of the distressed Hallerist. This was supposed to be so in the case of the intracranial vessels. Some of the peculiarities of the intracranial circulation certainly appear, at first sight, to lend probability to

[1] *Deutsche med. Wchnschr.*, Leipzig, 1898, Nos. 1 and 2.

the occurrence of an exceptional condition in this sphere. The resistant skull-cap, Alexander Monro the second's suggestion of the full bottle held upside down without spilling its contents, Kellie's well-known experiments, and much argument founded thereon, suggested that vasomotor nerves had little to do with the intracranial circulation. Some, like Hill and Bayliss,[1] argued that nerves were absent because they had not been found, and for the purposes of their theory it was necessary to assume such absence.

In my ignorance I had assumed that these vessels were innervated, until Sir John Tuke informed me last year that they were supposed not to be. Were this so, I felt that I was standing upon somewhat thin ice in much that I had to say, and found it advisable to proceed somewhat a-tiptoe until I felt more secure, although I suppose walking a-tiptoe does not materially lessen your weight, but it may avoid the clumsy kick which would bring about a sudden and ridiculous immersion. I therefore determined to investigate the point at an early stage of animal life, when the tissues appear to be, as a rule, most amenable to staining methods. As I have related in the *Edinburgh Medical Journal* for November 1898, I selected the fully-grown fœtus of a cat for the purpose, and was fortunate enough to find not only that the pial vessels were fully innervated by an ample plexus, but also that branches of nerve might be found in close relation to blood vessels which bore fully developed and permanent ganglion cells.[2]

As I owed it to Sir John Tuke that I had undertaken the research at all, I considered it my duty to inform him first of the result, which I did while he was at Aix-les-Bains last June. I have since discovered that Obersteiner found some such nerves on an old-gold preparation in 1897, and understand that Dr. Gulland also found the intracranial vessels to be innervated in July 1898.

Thus, then, another non-neural persistent rhythmicality has found its way to the limbo of many an ingenious hypothesis. The preparations under the microscope show these structures, the relation of which to sleep and cerebral activity must be a very important one.

Assuming, therefore, that the nervous system bears an important relation to splanchnic as well as somatic motion in health, I assume also that that relation is quite as important in the case of disordered visceral sensibility and motion.

Having argued that motion, whether sensory or mobile, to use

[1] *Journ. Physiol.*, Cambridge and London, 1895. [2] Appendix, p. 124.

a convenient although tautological expression, is one in kind in all organs, although modified by the functional nature of the organ manifesting it, I shall take as the type of disordered sensibility and motion abnormal conditions of the heart, for fuller discussion, as those with which circumstances have rendered me most familiar, and shall apply the lessons they seem to point as rationally as I can to disordered sensibility and motion in other organs.

On the threshold of such a discussion it seems necessary to inquire what the local elements in visceral or referred pain are. It occurred to me that the uterus might be taken as the best physiological type of visceral pain, and that an examination of the finer innervation of that organ might throw some light upon the general question. This I have accordingly done; and should I in the course of my anatomical remarks relate facts known to others and discovered by others without due acknowledgment, I must plead ignorance of such previous work, and can therefore disavow any intentional plagiarism.

A lateral branch from a large nerve in the uterus is given off, so that the portions chiefly constituting it appear to run in opposite directions in the outer strands of the parent nerve, and within its adventitious sheath. This will be evident from an examination of the specimen (Fig. 2). Fibres may also cross over the trunk from the opposite side to join the branch, and likewise from the side from which the branch springs, and between the two diverging strands referred to. The explanation of this divergence is not an easy matter. As the branch increases its distance from the main stem, its division for distribution takes place, as one would expect, by gradual subdivision, which naturally diminishes the size of the parent branch. On examining the mode of distribution of a small branch or twig, and noting its relation to blood vessels, we find that some of the smaller subdivisions tend to follow the course of the vessel, and others cross it for final distribution to individual muscle fibres. The branches following the vessels form a plexus around them, a sort of plexal tube or sheath, through which the vessel runs, and by twigs from which it is innervated.

Before distribution to the organic muscle, tri-radiate nuclear points of dispersion may be observed, as in other structures, such as the pial membrane and the pelvis of the kidney; and nuclei strengthening fine fibrils may be observed in the uterus, as elsewhere. But I have also noticed a peculiar relation of some neural swellings or nuclear points on the uterine fibrils which I have not

seen elsewhere, but which may nevertheless quite possibly occur. A rounded nucleus may be placed quite laterally to the fibril, so as to constitute a rounded knot or excrescence upon it, and which is so rounded and displaced laterally as to convey at first sight the idea of a small ganglionic cell, but which, on examination by high power ($\frac{1}{12}$ immersion), reveals nothing more than an irregularly stained nuclear body, somewhat resembling a small Pacinian corpuscle, but without the characteristic striation of the latter.

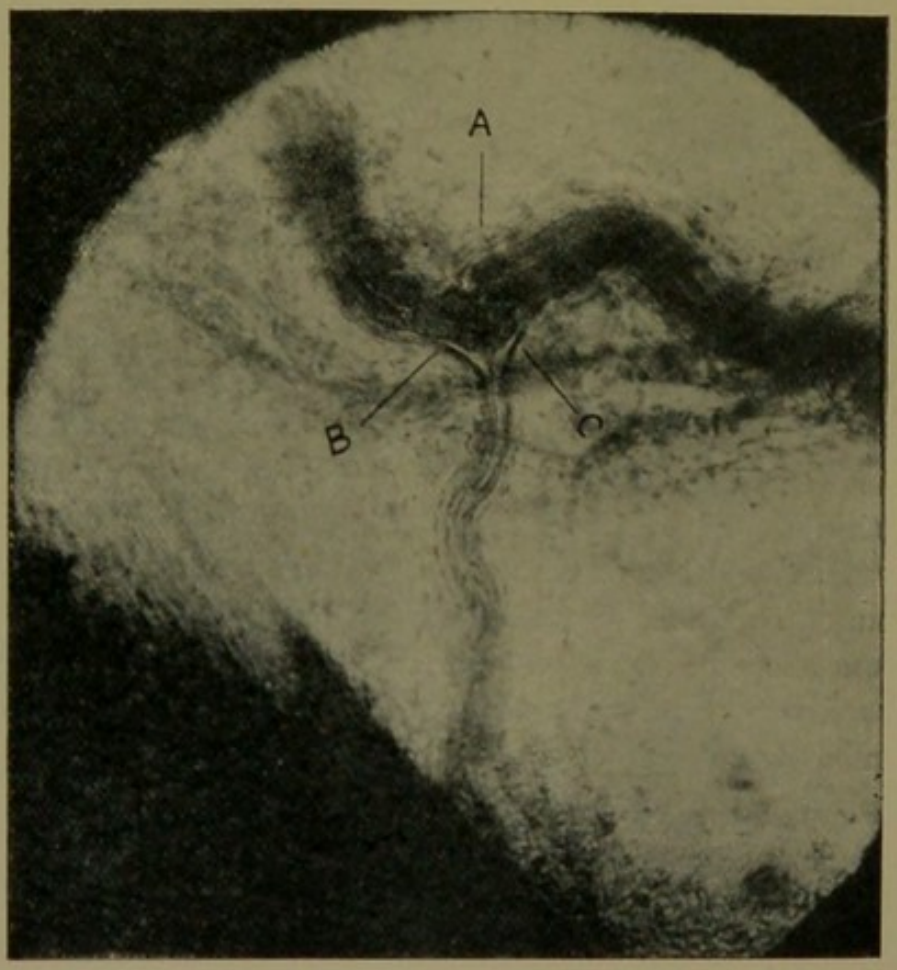

FIG. 21.—Divergent radicles B C of the branch of a nerve A, from the uterus of a cat in advanced pregnancy. Swift's obj. $\frac{1}{3}$. Eye-piece out.

These peculiarities may be seen under the microscope and on the screen. As we have already seen, the trunks and branches of the uterine nerves have a more or less tortuous course, a tortuosity which, in the case of the larger nerves, I believe to be in inverse proportion to the stage of pregnancy or size of the womb.

The local causes of pain in the parturient organ, which may for convenience be termed visceral pain, are uterine and extra-uterine. By extra-uterine pain I mean such as is caused by

pressure upon surrounding textures, including those innervated by purely somatic nerves as the uterine contents are extruded. With such pain I am not at present concerned, although it perhaps constitutes a great, if not the greater, portion of the pain incidental to labour, taken as a whole. The total pain is, however, undoubtedly commensurate with the degree of uterine contraction, and some of it appears to be localisable in the uterus itself, for pain is present before extra-uterine pressure is a considerable factor in the situation, and also after labour is over, when coagulated blood or other residuum has to be extruded. Such essentially uterine or visceral pain must, it appears to me, be caused by intramural pressure upon sensory nerve structures distributed to the muscle, and although I have not found any indubitable Pacinian corpuscles, the lateral rounded nuclei to which I have referred, if they be sensory in character, may be among those structures the intramural squeezing of which, during contraction of a certain degree of severity, is a local cause of pain, and the points to which the sensorium refers the centrally experienced sensation, and of necessity the sites of peripheral sensory stimulation. Spasm, for example, in the calf of the leg may give rise to severe pain, and the pain is proportionate to the severity of the tetanic contraction. We know from the researches of Sherrington and Batten, to which I referred last year, that there are good grounds for regarding the muscle spindles as sensory organs, and doubtless, if they be so, they must likewise be the chief seat of referred pain attending somatic muscular cramp. On the same principle, the tetanic squeezing of visceral muscle (and we know from experimental physiology that visceral muscle is apt to develop a cumulative contraction out of proportion to the stimulus applied) may be the local stimulus inducing the pain which is referred by the sensorium to its place of origin.

The absence, however, of visceral pain under circumstances in which we might *a priori* expect it to be present, is a striking clinical fact. As we saw last year, the visceral nerves, in the absence of inflammatory states, are so little sensitive, that organs may be freely manipulated, and even injured, without the evident production of painful sensation. Nodules of malignant disease may also stud a viscus, and cause little pain. Cysts may rupture into the pericardium and elsewhere, causing death, of the presence of which there was no sensory or other evidence during life. On the other hand, it is commonly observed that in certain situations, and without inflammatory lesions, visceral pain may be as well

marked in the splanchnic as in the somatic nervous system. Large calculi may lie in a gall-bladder for a lifetime without causing pain, but even a small one under the peristaltic grip of the bile duct may cause an agony which, from its very intensity, may prove fatal. The same is true of renal calculus. The stone, once engaged in the ureter, may jeopardise life, and even cause death from collapse due to the severity of the pain, while very little and it may be no pain may attend its presence in the pelvis of the kidney, which we have seen is richly endowed with nerves having the anatomical character of peripheral sensory nerves. Slight causes may, moreover, provoke great visceral pain, such as the colic, which is due to very moderately irritating material in the alimentary canal.

It would appear, therefore, that visceral pain, in the absence of inflammatory conditions, may be of direct and indirect origin, and that it has some relation to the degree of pressure exercised upon sensory nerve-endings, either directly by such action as the passage of a calculus through a narrow peristaltic tube, or the indirect spasm induced, it may be, by slight causes in the visceral muscle. It is therefore the implication in disease of orifices having contractile cavities behind them, which are most calculated to make pain a prominent feature in clinical histories. Thus the strictly local ravages of disease in a viscus may be painless, but the provocation by it of tetanic muscular action or cumulative peripheral pressure may cause much suffering.

Finally, visceral pain may be the peripheral expression of a central lesion. That pain should be referred to a locality where the original stimulus is situated, as it must of necessity be somewhere, does not seem in any way remarkable. It is but a form of touch, a painful touch, and the whole utility of touch, whether painful or otherwise, is to indicate locality and the character of the circumstances surrounding a sentient being. Pain may, indeed, in some measure be regarded as a beneficial provision for the preservation of the individual. But the experience of pain not at the site of its cause is somewhat remarkable. The surgeon is familiar with the pain of vesical calculus referred to the end of the penis, and with the knee pain of hip-joint disease. In like manner do the visceral crises of tabes appear to be caused by a peripheral projection of sensory irritation from structures in process of sclerosis, to which I shall refer again, as I also shall to the somatic projection of pains having their site of stimulation in the viscera, and to the stimulation of one viscus by another.

With this introduction I pass to the consideration of cardiac pain as a type of disordered visceral sensibility.

The natural provision made for safeguarding from undue mechanical stimulation the nerves entering and permeating an organ, is nowhere better seen than in the heart. If the heart of an animal be taken which has died in systole, and be fixed in that tetanic state forthwith by being placed in alcohol, microscopic sections show well the means adopted by nature to protect both

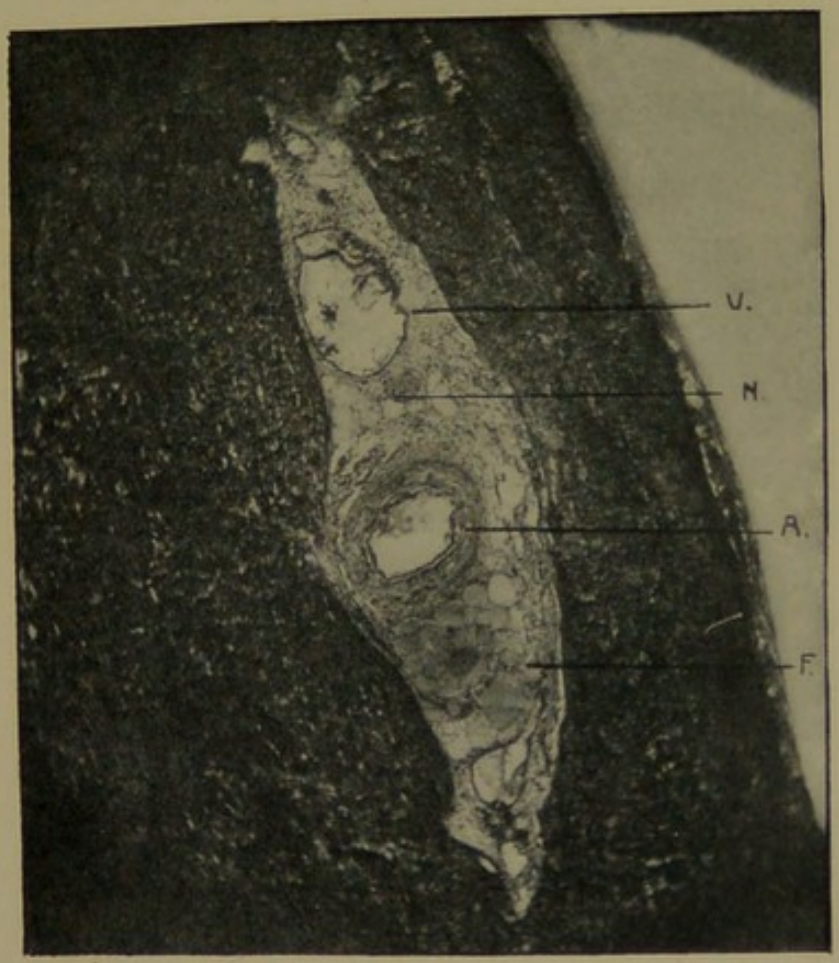

FIG. 22.—Transverse section of a neuro-vascular atrium near the apex of the heart in a sheep which died in systole. A, artery; V, vein; N, nerve; F, fat.

vessels and nerves from undue squeezing by the close-grained organ. The specimen I describe is from the apex of a sheep's heart prepared in the manner stated. The largest nerves may be seen to be situated nearer the vein than the artery, as they enter the organ at its surface, while the neuro-vascular atrium is also well padded with fat. The whole constitutes a perfect contrivance for obviating undue pressure from the surrounding muscle, which may be observed to be in a state of systolic contraction. The same perfect adaptation to circum-

stances which we see at the surface obtains as we follow the nerve trunks into the organ, the vessels and nerves coursing largely together, and being protected in more open situations by associated fat cells. The heart being, like the uterus, an organ having a wide range of contractile variability, if the suggestion I have made in explanation of the tortuosity of the uterine nerves hold good, we should expect a somewhat similar provision to exist in the heart also, and we find that it is so. Coils, such as are met with in the uterus, are not found, for sufficient reasons, which need not be discussed further than by pointing out that the return

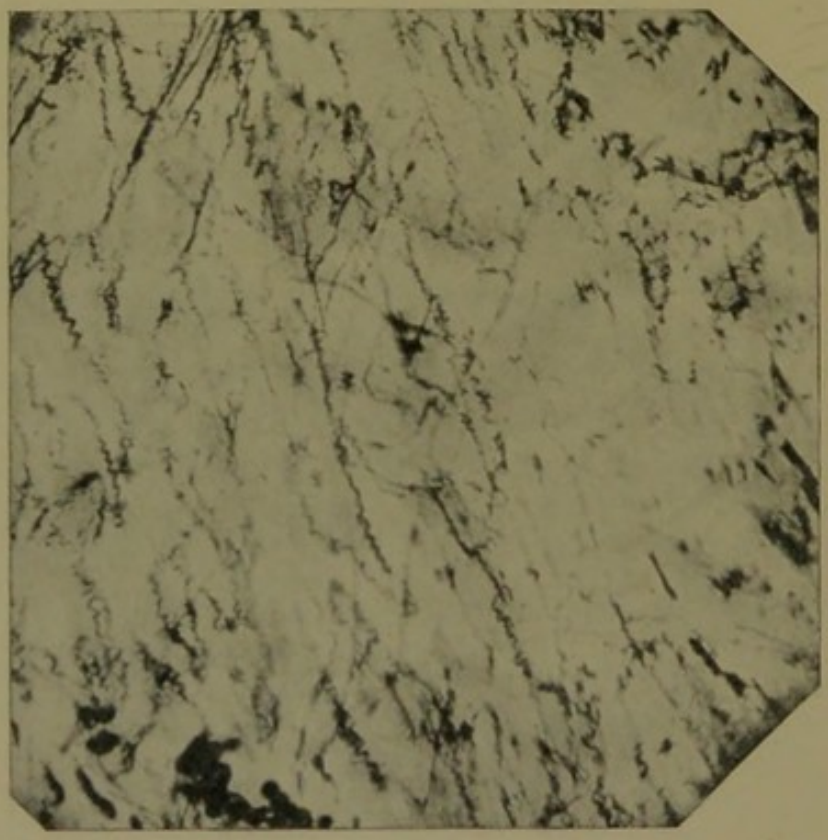

FIG. 23.—Golgi preparation. Tortuous nerves in the lower third of the heart of a cat.

of the organ to smaller size is but momentary in the case of the heart, and the difference between the maximum and minimum less than in the case of the uterus. Berkley[1] refers to the "wavy" nature of the nerves passing through the cardiac muscle. My preparations, like his, were made from the lower third of the ventricle, and include, of course, the absolute apex. The rich innervation of the part is well seen in the specimens, which I stained by the quick Golgi-Cajal method. The specimens are from the heart of a cat in advanced pregnancy, which was killed

[1] *Johns Hopkins Hosp. Rep.*, Baltimore, 1898.

by being anæsthetised and then drowned. The heart was thus in an uncontracted condition when first placed in the reagent, and this may account in a measure for the satisfactory results obtained. This, however, is not quite certain, for the capriciousness of the Golgi method, which yields such superb results when successful, is not yet altogether explicable. It will be observed that waviness is a very mild term to express the almost corkscrew tortuosity of some of the nerve trunks depicted. One can readily conceive the perfect adaptation of such a contrivance for suiting the altering state of the organ in systole and diastole. In the systolic organ, as in the non-gravid uterus, the threads of the screw, so to speak, are approximated, while in the diastolic organ, as in the gravid uterus, they are extended.

Now, dilatation of the heart is in a sense a partial and persistent diastole, a condition in which the threads of the neural screw must be somewhat extended, and it is conceivable that such extension may be associated with a degree of sensory stimulation, having in its train various degrees of motor consequence, to which reference will be made in their proper place. At present we are concerned with sensory phenomena, and we know that the sensory incentive to motion—a reflex—need not be experienced as a sensation unless the resultant motion be of a type to induce sufficient peripheral stimulation to cause a degree of pain. This, I believe, it may do. Then, one of the forms, the indirect form, of angina pectoris is the result. Stimulation of the cardiac nerves on this principle, which is not provocative of visceral spasm, may cause various irregularities of rhythm, to which also I shall refer later, as well as various degrees of sensory discomfort not amounting to angina which cardiac patients frequently experience.

We have seen that the cardiac nerves, in penetrating the heart, are more or less intimately associated with blood vessels, and in the case of the larger vessels this association may be seen very distinctly in some of the specimens I show. The nerves, in fact, on transverse section, may be seen to crown the arteries as the arteries themselves crown the heart. On longitudinal section, they may be seen to course with and around the vessels. We can understand, under these circumstances, in the event of a hardening and irregularity of the arteries, such as we meet with in advanced stages of arteriosclerosis with calcareous degeneration, when associated, as it frequently is, with a cognate change in the interstitial tissues of the organ, and in the interspaces along which the vessels and

nerves find their way, how actual frictional contact with irritation of nerve trunks may induce frequent and ultimately fatal attacks of cardiac pain. Angina pectoris, thus originated, may be regarded as the direct type of angina or visceral pain, like the pain caused by the passage of a calculus along the bile or urinary ducts.

It has been cogently objected to this theory of angina pectoris, that, were it true, angina should be more constantly associated with the conditions mentioned than it is found to be. Atheromatous arteries are frequently met with after death, which do not appear during life to have caused cardiac pain.

I trust I may not be thought to assume too dogmatic a tone in the presence of some whom I regard as the chief authorities upon the subject I am discussing, when I express my belief that the association of angina with calcareous degeneration of the coronary arteries and hyperplasia of interstitial cardiac tissue, is dependent in a great measure upon the degree of change in the vessels and in the channels in which they run, associated, it may be, in some cases, with a certain amount of visceral neuritis which, as we know, would be calculated greatly to increase the sensibility of the nerves involved.

Dealing as we are with the relation of the nervous system to visceral disease and disorder, I shall not be expected to enter fully into the discussion of alternative theories of angina pectoris. I do not deny that concurrent circumstances not strictly neural may so exalt the sensibility of the organism, local and general, as to render some cases more prone to visceral pain than others; but pain is a property of the nervous system, and I do not think that much will be gained by emphasising remote causes, and by overlooking those which are evidently more direct. As George Balfour remarks in the last edition of his classical work,[1] "angina is a nerve pain, a neuralgia of the heart; but it is something more, it is a neuralgia only developed on a sudden call for exertion. . . . Whenever, from any emotional cause, or from the slight exertion of ascending an acclivity, or from a sudden rise of blood pressure from reflex or other causes, the augmentor nerve has to make a call upon the heart for increased action, to which it is unable to respond because of long-continued imperfect metabolism, . . . the call for increased katabolic action is at once followed by exhaustion revealed as agonising pain shooting along some or all of those sensitive spinal nerves with which the katabolic nerve is embryologically connected."

[1] "Diseases of the Heart and Aorta," pp. 318 and 319.

To this lucid description I can add nothing, except that, for the general term "exhaustion" in the above etiology, I should read more or less dilatation, and assign the subsequent neural stimulation to physical provocation from alterations in the tension and action of the cardiac wall.

There are those who have described an anatomical sensitisation of the endocardium, and if they be correct, it is conceivable that the incentive to angina from increased blood pressure within the chambers of the heart may be due to stimulation of such endocardial innervation. Clifford Allbutt also ascribes great influence to intra-aortic tension as an etiological factor in angina pectoris. For myself, however, I am more disposed to regard intramural and intra-aortic stimulation of nerves as the cause of those reflex muscular changes which induce visceral pain, just as I attribute to similar causes the essentially visceral pains associated with a uterus in rhythmical action of a certain intensity. Such conditions as favour a dynamic dilatability of the chambers of the heart, whether from local disease or general debility, are calculated to induce such stimulation and reaction as I have referred to, and which are most calculated to result in angina, when, to the indirect influences I have mentioned, there are added local causes of intramural stimulation of the cardiac nerves.

Under the microscope and on the screen I have placed preparations from the heart of a man, aged 53, who was under my care at the Great Northern Central Hospital, with almost constant angina pectoris for eleven months, and who ultimately died during an attack of cardiac pain. The preparations are from the apical portion of the heart, as I wished to obtain tissue from the same neighbourhood as that from which I stained the nerves shown. The vascular, circumvascular, and intermuscular sclerosis is well seen, and is very suggestive of the possibility of that direct irritation of the concurrent nerves which I believe to be one of the causes of angina pectoris. It is a neural form of that extramural or exocardial variety of angina pectoris which Sir William Gairdner has described as being associated with the pressure of small aneurysms at the base of the heart upon sensory nerves in their immediate neighbourhood.[1] On the screen I have also thrown a delineation of the interior of the aorta in this case, and of the coronary artery. The first shows some occlusion of the coronary orifices, with dilatation of the pouches

[1] Reynolds's "System of Medicine."

of Valsalva, which is indicative of excess of intra-aortic pressure, such as that which Clifford Allbutt regards as causal of angina in many cases, and the second exhibits the hard thickened lumen of the coronary vessels which crowned the heart in its most sensitive portion like a chaplet of thorns. This case has been published at greater length.[1]

So-called pseudo-angina is of two kinds, and in only one of these is the qualifying adjective appropriate. In a certain proportion of these cases I agree with Clifford Allbutt and others, that the condition is in reality a variety of intercostal neuralgia. The angina may be real enough, but the organ affected is not the heart. In others, again, the neuralgia dependent, it may be, on the ordinary causes of neuralgia, such as anæmia, occurring in predisposed or neurotic subjects, the seat of the disorder appears to be the heart itself, inasmuch as the præcordial distress may be associated with inhibitory phenomena in that organ. These cannot be regarded as false but as true anginæ.

Painful affections of the heart may, as is well known, be associated with somatic points, areas, and radiations of pain, and Walshe has described the opposite process of peripheral aura resulting in central cardiac distress.[2] In the case which Walshe refers to, the pain began in the hand and spread up the arm to the chest. This must, of course, merely be regarded as the peripheral projection of a central stimulation such as the shoulder pain associated with some hepatic conditions, and other well-known somatic manifestations of visceral stimulation. For the local cardiac origin of angina is to my mind indubitable, and this conclusion has been impressed upon me by the situation of the anginoid pain in a rare case of dextral valvular disease of the heart, which I have published.[3] The specimen is in possession of this college, and I throw on the screen a copy of the drawing I made shortly after the autopsy. The hugely distorted and diseased pulmonary valves, as well as the diseased tricuspid orifice, ultimately induced a dyspnœa which was associated with præcordial pain of sufficient severity to cause radiation down the right arm; just as in the majority of cases of valvular disease which are sinistral, the painful radiations, when not of sufficient severity to become general on that side, or even bilateral, are

[1] *Treatment*, London, October 1897.

[2] "Diseases of the Heart and Aorta," 4th edition, p. 198.

[3] *Trans. Path. Soc. London*, 1876.

restricted to the left arm, and most usually to the course of the intercosto-humeral nerve, owing to its origin from the second intercostal, which itself arises from the second dorsal nerve, which also, as we know, supplies visceral branches to the heart.

It does not follow, however, that cardiac pain may not have a truly extra-cardiac origin. Less frequently than in the case of some of the other viscera, the painful crises of dorsal tabes may affect the region of the heart, as is stated by von Leyden and Goldscheider,[1] who quote other authorities for the same fact. The attacks may have the severity of *angina vera*, and even threaten life. The pulse is described as being small, weak, and irregular. It is known, moreover, that cardiac may be superadded to the more common gastric crises of tabes. Assuming that in a given case the crisis induces cardiac and not *intercostal* pain mistaken for it, the site of stimulation in the majority of cases is probably that affection of the posterior root ganglion to which I referred in the last lecture, and the depressor phenomena which may ensue, due to an implication of the pneumogastric system by that cross-stimulation which causes retardation to follow acceleration and depression to modify augmentation, and *vice versâ*. Whether the sensory phenomena of such crises may originate, as some have supposed, in the pneumogastric system, may be left an open question. That the pneumogastric does not play the important part in the painful symptoms of visceral crises which was at one time assigned to it, is fairly certain in view of our present knowledge of the pathology of the disease. In some cases, however, there appear to be grounds for associating such cases with central pneumogastric irritation; for although the nerve has a largely trophic influence, its spinal sensory fibres, coming as they probably do from the far-reaching solitary fascicular strand, may be regarded as quite as efficient channels for sensibility as the lower spinal nerves and posterior root ganglion.

In 1878 I published in the March number of the *Edinburgh Medical Journal* the case of a man who had glycosuria, with partial left hemiplegia, and well-marked left hemiparæsthesia. He had had syphilis thirty years before coming under my care. He died in an attack of angina pectoris. The anginal attacks only developed shortly before the fatal issue. Permission was only obtained to open the head. The value of the case is not, therefore, great for

[1] *Op. cit.*, p. 544.

determining the question of a central causation of angina, but some of the intracranial conditions were well marked, and might be argued to have some bearing upon the short but persistent angina which killed the patient. At the autopsy, some convolutions, not definitely noted, were found to be softened. There were two small cystic cavities in the upper and posterior part of the right optic thalamus. There was also a well-marked granular gelatinoid degeneration of the floor of the fourth ventricle, which was most marked in the lower and left portion of that space. The acoustic striæ were obliterated by gelatinoid material in this situation. It is conceivable that in such a case as this the origin of cardiac pain might be in the higher centres or in the sensory nucleus of the pneumogastric nerve, and I have mentioned the case that I might not appear to emphasise the lower spinal etiology of angina pectoris too much. All the phenomena of sensory localisation and radiation, however, in cases of visceral angina, whether cardiac, hepatic, or renal, indicate the spinal rather than the cranial nerve supply of the heart as the chief territory of objective pain. This point would appear to have been first emphasised by Allen Sturge.[1] Ross[2] appears to have come to the same conclusion independently. Clifford Allbutt made a similar suggestion in his Goulstonian Lectures in 1884; and, while laying more emphasis than Sturge did on peripheral excitation, essentially the same conclusion impressed itself on me before I was aware of his valuable paper on the subject. No doubt others have and will come to a like conclusion without knowing anything of the work of any of us. The human mind, considering more or less carefully the same phenomena with an average knowledge of the underlying conditions, draws like conclusions, just as the eye, travelling with the same care over the same landscape as others, observes the same features as they have done. The petty little differences about priority in scientific matters, therefore, which some of our most distinguished men have indulged in, and which posterity reads with more amusement than sympathy, seem rather beside the mark. There is much truth in the comment which Mephistopheles made on the exultant self-complacency of the young graduate in the second *Faust*, once the modest student whom we encountered last year, and which has been well done into English by Dr. Anster—

[1] *Brain*, London, Jan. 1883, vol. v. p. 492.
[2] *Ibid.*, vol. x. p. 354.

"Original! move onward in your pride,
Oh! how the spirit would sink mortified,
Could you but know that long ago,
All thoughts whatever, dull or clever,
That cross the twilight of your brain,
Have been o'er and o'er again
Occupying other men."

The inimitable playwright adds that the younger portion of the audience did not applaud.

It is considered by some physiologists that tactile and muscle sense sensations travel up the cord to the brain by way of the vesicular column and the gracile and cuneate nuclei, while sensations of heat and cold pass up through the grey matter to the optic thalamus. If this be so, it may explain the alterations in the temperature sense in lesions of the cord involving the grey matter, such as syringomyelia, but the degree to which such lesions influence the temperature sense in the viscera is for many reasons difficult to determine. It is difficult indeed to test the temperature sense in syringomyelia, even of the stomach, much beyond its cardiac end, and even here we have the complicating condition of nerve supply from another source above the seat of lesion. The temperature of hot and cold drinks may be appreciated in the stomach, but beyond it, the warmth of the body in the case of cold drinks, natural loss of temperature in the case of hot drinks, and the comparative and normal insensibility of viscera generally, soon seem to render the temperature indifferent, and its perception impossible. It may be shown, however, in syringomyelia, that while the surface exhibits abnormalities and loss of temperature sensation, the temperature of imbibed material is still felt by the stomach, and this retention of sensibility is probably due in some cases to the pneumogastric innervation of the viscera. In the record of such cases, however, I have not been able to discover that the internal temperature sense has been investigated with the same care as the external, and the point seems worthy of more attention.

The association of cephalic paræsthesia with visceral disorders is a subject of interest. The situation and characters of such sensitiveness have been carefully studied by Head,[1] who has been the most recent observer to point out the situation of hyperæsthesiæ on the surface of the head in connection with visceral disorder, and has given anatomical reasons for the con-

[1] *Brain*, London, 1893–94.

current implication of the sensory nerves of the scalp. Such sensory points in connection with visceral disorder undoubtedly occur, as also do hyperæsthetic points on the thorax and trunk in connection with cardiac and other visceral disease and disorder, but in a large proportion of headaches, chest-aches, and trunk-aches, pain with little or no tactile hyperæsthesia, or hyperæsthesia difficult to detect and delimit, is, so far as my experience goes, the rule. This association of visceral disorder with cephalic pain has long been known, and some forms of it carefully described. Robert Whytt of Bennochy, sometime President of this College, and Professor of Medicine in the University, was as good a judge of a headache as his late representative, the amiable author of "Katerfelto," was of a horse. In discussing the causes of periodical headaches, Whytt writes[1] among these of "Sympathy with the stomach, by which the nerves chiefly of the fore part of the head suffer; and the small vessels to which they are distributed are either affected with a continued spasm, or agitated with alternate contractions and relaxations, in consequence of which the patient feels a pain, straitness, fulness, and pulsation about the forehead and temples." This excellent description of migraine, now 130 years old, emphasises the vasomotor and neuralgic elements in these visceral headaches, a certain proportion of which are probably meningeal, not cutaneous, and from their intracranial situation not accessible to tactile investigation, and therefore not objectively hyperæsthetic.

While searching for the innervation of the pial vessels, I likewise investigated the innervation of the pia mater, and found that the nerves which have long been known to course through it end in it by plexus, as I have stated elsewhere.[2] Some headaches, therefore, and the pain of meningitis, are explicable by the copious innervation of the membranes of the brain, and the neural pathology of the investment of that organ is thus brought into line with painful affections of the pleura and peritoneum. The severe headache of tertiary specific disease may in some cases be meningeal; but as the brain differs from other organs in being the seat of perception and the focus for the sensory channels of the body, it is probable that in the case of this viscus, disease implicating the structure of its centres and nerves may cause pain in a manner in which a similar lesion would not do in the case of other viscera. The determining factor for local pain in the latter I have argued is a

[1] "Observations on the Nature, Causes, and Cure of those Disorders which have been commonly called Nervous, Hypochondriac, etc.," Edinburgh, 1767, p. 298.

[2] *Edin. Med. Journ.*, 1898, N.S., vol. iv. p. 413; and Appendix, p. 124.

simultaneous tension which increases the force or degree of impression, and in the case of visceral muscle a reflex cramp which squeezes nervous end-organs.

In speaking of the general trophic influence of disease of the central nervous system, it was pointed out that pain and mental anxiety were the chief determining factors under these circumstances, and that mental anxiety might be regarded as having the same relation to the intellectorium that pain had to the sensorium. That they were, in short, both painful emotions. Laycock, indeed, called mental anxiety phrenalgia, and considered depression of spirits and hypochondriasis varieties of that species of pain.[1] As the brain, moreover, is compact of many organs, or, as I shall term them later, organules, which concur to produce that multi-unity the mind, which can distinguish the effects of the exercise or want of exercise of one organ or centre from those of another, such as the different effect of the various special sense centres, so it is probable that the direct effect of the disorder of one viscus may impress the mind differently from the disorder of another, the harmonious and painless operation of all being necessary for that unconsciousness of the existence of a particular viscus which is characteristic of vigour and health. Some organs, moreover, like the liver and kidney, the functional activity of which influences the character of the nutrient fluid for the whole body, have when diseased a more depressant general influence than disorders or diseases in those organs which are chiefly mechanical or more limited in function and effect. The attitude of the patient to disease is also, no doubt, modified in a measure by the condition of the mental organ itself. The naturally blunt and stupid, who fail to appreciate the general gravity of their situation, have also probably a minor power for the appreciation of discomfort, and may exhibit a callousness in physical distress only attained in the more sensitive and gifted after a philosophical estimate of their general relation to things and time. But, putting aside stupidity and philosophy, the hope to live or desire to die as influenced by disease or disorder of particular organs is largely dependent upon the circumstances, whether such disease or disorder saps energy or produces pain beyond a certain point, which is open to individual variation. A pronounced and protracted sense of feebleness is little if at all more endurable than actual pain, and disease which engenders such induces a mental depression and despair of vigorous life more certainly than many more serious diseases which have

[1] "Medical Observation and Research," 2nd edition, p. 352.

not that specific effect. The suicide of the so-called convalescent from influenza—not an uncommon event—is an instance of this; and prolonged enfeeblement in general from any cause, with its concomitant discomforts and disillusionments, is productive of a misery which the serious disorder of a particular organ which does not rapidly and profoundly enfeeble or cause pain to a certain degree does not induce. Thus the cardiac sufferer, whose natural vigour is good, and whose diseased heart is well developed and has been well compensated, may evince much less and experience less distress than the patient who has experienced angina vera for the first time. Nothing has struck me as being more pathognomonic than the expression and general attitude of some patients on their first experiencing that form of cardiac anguish. It is like "a bolt from the blue" in their lives; they have never experienced anything similar before; the cloud-curtains of the unknown seem suddenly about to be raised, and it fills them with an anxious astonishment which frequently, on a repetition of the phenomenon, plunges them into an acute despair; until the innate bravery of man at his best enables them to face that, as any other contingency, with indifference, and with such aid as it is the privilege of the physician to be able to render.

Chronic dyspeptics again, with their minor but constant dysæsthesiæ with periodical exacerbations and imperfect hæmopoiesis, frequently develop a mental habit which renders them, like one of the most distinguished of them, to whom we can forgive much, "gey ill to live wi'."

On the other hand, chronic disease which attacks youth, is not associated with much pain, and only deteriorates vigour so that the perceptive power of the individual does not appreciate great differences in this respect, may be coupled with all the sanguineness and natural expectation of life and usefulness which is proper to that period. The expectation of recovery of the phthisical, even in the last stages of the disease, is so well known and common a phenomenon as to have become stereotyped in clinical language.

There is no doubt, under all these circumstances, except in the case of the stupid, a so-called metaphysical element in the manner in which the mind is affected by organic disease, but it may, I think, be regarded as based upon clinical facts, that the mind appreciates the necessity for the exercise of philosophy least readily, as is most reasonable, when visceral pain and rapid enfeeblement are not dominant characteristics of the type of disease from which a given patient is suffering. This conclusion

may appear after all a "surface-worm" to dig up, and the labour of finding it rather incommensurate with the value of the result, but the subject has appeared to me of some interest in its bearing upon the relation of visceral disease to mental emotion, and I trust I may not seem to have laboured the point too tediously.

LECTURE VI.

THE DISORDERS OF VISCERAL MOTION.

THE separation of sensation from motion is relatively to the mind a distinction in what may be termed objective consciousness. We feel pain and can localise it, and we can observe movement. The separation of sensibility from motility is a finer distinction, and is largely in what we may term subjective consciousness or reasoning. Essentially, the transmutation of one form of motion into another merely emphasises the common property by which a living universe is conditioned. Clinically, the distinction is convenient, and no circumstance reveals more instructively the relation of the nervous system to visceral motion than the influence one organ has upon another. The displaced or twisted kidney which induces a tachycardia, the diminished thyroid secretion which causes a cardiac stagger or a bradycardia, the retained excretion, or the peripheral excitation which induces a convulsion, or the functional inactivity generally which disturbs metabolism, all show how intimately one form of motion is related to another; and when we emphasise motility in a given clinical condition, we might rationally regard it in some instances as the motor feature of an essentially sensory and causal disorder.

In touching upon some points illustrative of the relation of the nervous system to viscero-motor disease and disorder, I shall follow the plan already adopted in discussing sensory disorders, and take as the type of disordered visceral motion abnormalities in the action of the heart, making reference incidentally to analogous conditions in other organs.

The motor innervation of the heart, we know, is accelerant and augmentor-motor, inhibitory and depressor-motor, and trophic or pneumogastric proper, all these movements having necessarily their sensory concomitants or equivalents. Gaskell and his successors, anatomical and physiological, have revolutionised, as

we learned last year, our conceptions of the visceral nervous outflow in general, including the innervation of the heart. For whereas we formerly regarded the pneumogastric as a primary, and the cervical sympathetic as a secondary source of cardio-motor innervation, we now believe that the pneumogastric is a secondary and the cervical sympathetic a tertiary source of such innervation.

Whether all the suprathoracic vasomotor outflow originates as low down as the second dorsal spinal nerve, appears still to be somewhat doubtful.

Hill and Bayliss[1] failed to evoke vasomotor action in the intracranial circulation by electrical stimulation from this region, but in the performance of their experiment they split the thorax and sewed it up again. Whether in doing so they disturbed the intracranial circulatory conditions by affecting the power of thoracic aspiration, which I endeavoured on clinical and anatomical grounds to show, in a paper on the treatment of aortic valvular disease read before the British Medical Association in 1896, has an important influence in maintaining the intracranial circulation, I cannot say. In any case, they failed to evoke the anticipated result. The source of the nerves in question, therefore, still appears to be doubtful, and it may be that their origin is somewhat higher.

Without the aid of experimental physiology, and merely using the microscope for anatomical research, I have met with conditions bearing on this point. It will be seen that what appear to be the sources both of the pia matral and pia vascular innervation are certain tassel-shaped bodies which are arranged centripetally to the vessels, and of which I gave a short account in the *Edinburgh Medical Journal*,[2] and which has been reprinted as an appendix to this volume. The precise locality of these vessels I have not yet had an opportunity of determining, but they appear to me to be sufficiently characteristic in design to be capable of identification by injected specimens. Thus identified, the position of the bodies in question, whether they be the source of vasomotor nerves or no, should also be determinable.[3] In the meantime we may assume, notwithstanding Hill's and Bayliss's failure to elicit response, that the outflow of the indubitably existent vasomotor nerves in the pia

[1] *Journ. Physiol.*, Cambridge and London, 1895. [2] *Loc. cit.*

[3] Since writing this, I have examined these peculiar bodies with some friends, one of whom, an expert microscopist, for whose opinion I have much regard, disputed their neural nature, and considered some ganglion cells in connection with similar structures to be from another source. On careful consideration of the point, however, I feel myself justified in maintaining the view I have already expressed.

mater is from the same region as the general vasomotor outflow, that is, below the level of the first dorsal nerve, and thus bring the vasomotor phenomena of all the viscera, including the brain, into line.

Cardiac motion, like secretory and other motion, may be average or normal and plus or minus. A mid-point or equilibrium is a balance of extremes, and vital equilibrium is maintained by a certain variation around a centre of equipoise. Acceleration and retardation, augmentation and depression, constantly correct one another with the sensitiveness of a species of tentacula to surrounding circumstances, these tentacles being the nerves and the properties with which they are endowed.

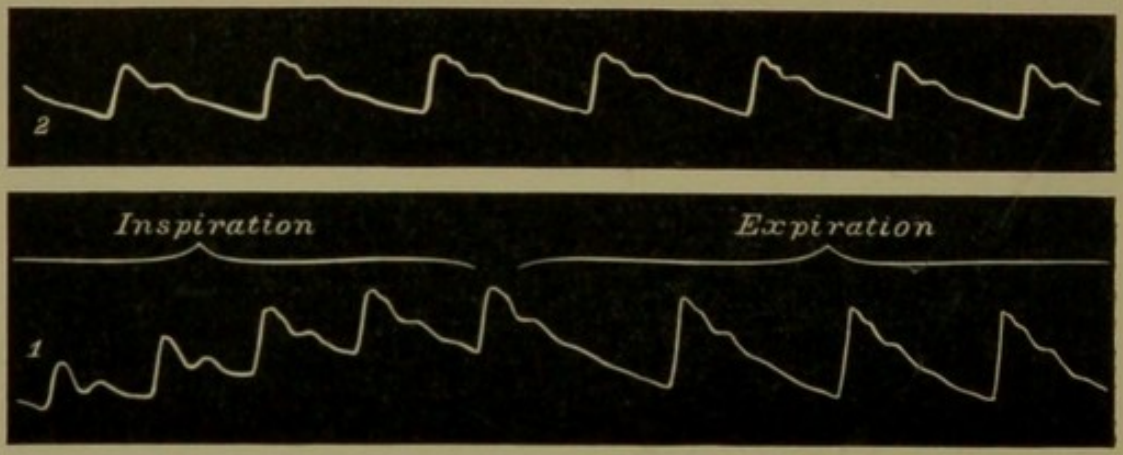

FIG. 24, Tracing 1.—Sphygmogram showing the influence of forced respiration upon the radial pulse wave. Tracing 2.—Sphygmogram of the same pulse during quiet breathing.

This is well exemplified by the influence of respiration on the character and rate of the radial pulsation. The sphygmogram (Fig. 24, Tracing 1) shows the small waves of forced inspiration on the ascending portion of the curve, followed by the large waves of prolonged expiration on the descending portion. These are no more the evidences of a mere pneumatic suction and propulsion than the cerebral circulation is the passive arterio-venous balance which Monro and his disciples conceived it to be. The pneumatic conditions play a part in the one, as the comparative resistance to atmospheric pressure does in the other, but the character and rate of the waves in the two portions of the curve indicate a vasomotor regulation, the peripheral incentive to which is, I believe, to be found in the increased pressure in the dextral chambers of the heart and pulmonary circuit during inspiration. For comparison with the tracing of forced respiration, I show one of the pulse of the same subject taken at the same time during quiet breathing,

in which the pneumatic factor is conspicuous by its absence, although in a minor degree doubtless still operative (Fig. 24, Tracing 2).

The antagonistic action of the accelerant and retardant nerves of the heart has been disputed. Retardation can be induced when artificial acceleration is in progress. It is none the less true that the safety of an abnormally inhibited heart consists in some acceleration of cardiac pulsation; and, as was mentioned last year, in the sphere of secretory motion, there appears to be a certain compensatory independence in the secretory influence of the cranial and sympathetic nerves of the sub-maxillary gland. It is probable that the same rule applies to other forms of vital motion. William Hunter,[1] referring to the fact that intense and even fatal jaundice may rapidly follow emotional shock, accounts for the phenomenon by suggesting a spasm or reversed peristalsis of the bile ducts while the bile is in full flood, as the probable cause. He admits, however (p. 81), that diminished quantity and increased viscidity of bile may be a cause of its absorption. The viscidity he attributes to catarrh of the bile ducts. Can a more directly neurotic hypothesis be advanced?

The main secretory nerve of the liver is the pneumogastric, and its sympathetic endowment is from the splanchnic nerve, while vasomotor nerves for the portal vein are derived, according to Bayliss and Starling, quoted by Halliburton,[2] from nerves ranging from the third to the eleventh dorsal. It appears possible, therefore, that the sequence of events may be somewhat as follows:—In sudden, severe, and mental cases, shock is followed by pneumogastric inhibition and arrest of its secretory-motor function. This entails an attempt on the part of the sympathetic to come to the rescue, which it does by producing a more potent but also a more viscid bile—the nature of such potency not being at present to the point—which, like a blundering but well-meaning friend, stands in the way, just when the pneumogastric, having recovered from its inhibition, throws out by augmented activity too large an amount of bile for rapid escape, hence absorption and rapid toxæmia in some cases, and slow poisoning in others. I do not for a moment presume to indicate this solution as correct, but it appears to me as probable as other theories suggested, and brings the motor activities of the liver

[1] Allbutt, "System of Medicine," vol. iv. p. 68 *et seq.*

[2] *Op. cit.*, p. 670.

into line with those of the heart, which it is my present purpose to maintain.

Again, the striking phenomena, on the one hand, of Graves' disease, which I prefer on this occasion to call Begbie's disease, and, on the other, of myxœdema, appear to suggest a parallel on similar lines. The thyroid gland is innervated by the pneumogastric and visceral nerves which reach it by way of the inferior and middle ganglia of the cervical sympathetic. Of these its most active secretory nerve is probably the pneumogastric, although I am not aware that the fact has been experimentally proved. If we regard Begbie's disease as in the first instance a cardio-vascular neurosis, to employ a term expressive of our ignorance, we can conceive an increased though ineffectual effort upon the part of the pneumogastric system, that is, of motor fibres probably derived from the spinal accessory nerve and running in the pneumogastric, to restrain the cardio-vascular organs in excessive visceral motion, and although unsuccessful in that effort, so stimulated by it as to provoke increased activity in its own secretory motor fibres. This would result in an excessive secretion, among others, of the thyroid juice, the effect of which upon the circulation is to accelerate it. Thus the increased activity of that gland may add fuel to the fire which burns so lustily as vasomotor commotion under the circumstances in question. This secretory increase, as we know, is at present regarded as one of the most probable causes of excessive pulsation in Begbie's disease, the etiology of which, however, is not yet by any means clear.

It is conceivable, moreover, that a period of persistent hypersecretion may result in one of hyposecretion, the retardant influence of which may be slow in showing itself, for the following reason:—The sympathetic system, besides its general vasomotor over-action, may also induce a supplementary sympathetic juice as in the case of the submaxillary gland, and thus maintain for a time the waning accelerant influence of pneumogastric secretion. We know, however, that ultimately in a large number of cases the excessive excitement of the cardio-vascular system subsides more or less, that in some cases bradycardia succeeds tachycardia, and that in yet others myxœdema takes the place of Begbie's disease. The neuro-motor activity of the gland, in short, and its associated organs, is worn out, and we may expect some day to have demonstrable pathological changes in the controlling centres, which, together with peripheral degeneration, would account

satisfactorily for the striking complex of symptoms referred to, and still unexplained. Action and supplementary action, endeavour and support, overaction and reaction, error and correction, seem to be general laws of life, and there does not seem to be any just reason why they should not apply also to the life manifest in visceral motion in its various forms.

To study the matter a little more closely, and taking cardiac action as the type, let us examine the motor effects of shock upon the heart, and in the first instance of the shock of physical pain, with which Laycock's "phenalgia" must necessarily be associated, and often is in a high degree.

As has already been remarked in a previous section, pain or excessive sensibility in any organ may influence the heart's action in association with various degrees of concomitant mental emotion, proportionately to the amount of the stimulus. The tachycardia associated with a displaced kidney may be present without much associated pain, and therefore without great mental distress. With more pain the same conditions will be emphasised. The reflex effects of nephroptosis may affect many organs besides the heart, and the severity of these secondary motor disturbances is not proportionate, as Macalister has stated, to the amount of mere displacement.[1]

Calculi, we have seen, may induce an extreme of agony which may terminate in collapse and death, the associated cardio-vascular phenomena being those of rapid and enfeebled action of the heart and a general vaso-paresis accompanied by profuse perspiration and depression of temperature. These extreme phenomena differ from those associated with angina pectoris chiefly in the situation of referred pain and in the uninterrupted duration of the agony. With this distinction these cases might be termed cases of angina pectoris hepatica, renalis, *et hæ species omnes.*

The first effect of sudden visceral pain, whether cardiac or general, on the movement of the heart is to arrest its action, and probably, could we at the moment of the onset of pain auscultate that organ, we should detect an inhibition. This, however, like peripheral spasm, which is usually regarded as the cause of angina pectoris, is so early a phenomenon that it must very rarely be indubitably observed, and when observed and present it is not necessarily the essential cause of the general complex of

[1] Allbutt, "System of Medicine," vol. iv. p. 344.

symptoms. The conditions usually first observed by the ear and hand are the phenomena of depression which follow inhibition, associated in many cases, shortly afterwards, with those of a rescuing augmentation and acceleration of the heart's beat.

Lauder Brunton, whose many-sided scientific activity has recently been recognised by his and our Alma Mater, and with whose name one of the most beneficent agents in the treatment of angina pectoris is indissolubly associated, was the first, so far as I know, to note graphically the cardio-vascular movements connected with valvular angina. He published a case[1] of aortic valvular disease with sphygmograms, in which he showed the quick small pulse of the agony and the larger and slower pulse of the interval free from pain. Brunton considered the pulse of the agony to indicate peripheral spasm, and was at a loss to reconcile its rate with its assumed condition. Since Brunton's original observations, however, opinion has modified a good deal on this point, and there are those who feel more disposed to regard the peripheral signs usually observed as those of empty collapse rather than of active spasm—of profound collapse—in other words, such as might be caused by other visceral and even somatic pain of a certain degree of severity.

Sir Richard Douglas Powell, however, in his recent Lumleian Lectures before the Royal College of Physicians, London,[2] also describing what he terms vasomotor angina in the case of a young man suffering from aortic regurgitation, spoke as follows: "It was curious to note the absolute extinction of all the aortic characters in the pulse, which became contracted to a small hard pulsating thread; whilst, as the patient sat forward, leaning against a chair in great pain, the bed shook with the violence of the cardiac beats, and his neck and subclavian vessels could be seen pulsating with responsive violence. A dose of trinitrine quickly brought back the aortic features of the pulse and dissolved the painful scene. One could not observe the labouring beat of the heart, the strongly pulsating large vessels contrasted with the almost effaced small vessels, without appreciating the power of vasomotor contraction to cause cramp or paralysis of a healthy ventricle; yet there are physicians who still doubt the efficacy of vasomotor spasm in the mechanism of angina."

I presume it is because of the humane desire not to disturb unnecessarily the patient in the throes of cardiac agony, that we

[1] *Trans. Clin. Soc. London*, vol. iii.

[2] *Lancet*, London, March 26, 1898.

find more frequent record of the condition of the radial pulse in these cases, than of the heart itself. If, however, the heart of such a patient be examined, it will be found that the extinction of "aortic character," which Powell noted in the radial pulse, is also very distinctly appreciable at the aortic orifice itself. The usually very considerably hypertrophied left ventricle will be found to pulsate with increased frequency, the bruits significant of the valvular defect being almost or quite hushed, and increased tension in the pulmonary circuit indicated by a well-marked accentuation of the second sound at the pulmonary arterial orifice. There is repletion of the ventricular cavity, and comparative emptiness of the extra-cardiac systemic arteries. The full and hypertrophied heart labours violently to rid itself of the residual, stimulating, and dilative burden of blood, not because it cannot jerk some of its contents into the larger comparatively empty vessels with more than "aortic" emphasis, but because its own intrinsic and momentary failure has cast upon it a paralysing weight which must be rapidly reduced if the organ is not to come to a standstill. The small peripheral pulse which is associated with such valvular angina during the period of cardiac failure, is not on this showing one of spastic narrowing, but of empty collapse. The following sphygmograms (Figs. 25–28), which I published to illustrate a paper on the blood pressure in angina pectoris,[1] may render my meaning clearer. The first shows the attack at its height, with a lowering of the predicrotic wave and a flat drag in the diastolic interval, meaning, as I think, that the collapsed and comparatively empty artery has failed to reach the lever of the instrument. In the next the cardiac force is increasing, its action becoming slower, and, although blood still fails to reach the periphery in normal abundance, there is a rise in the position of the predicrotic wave and an indication of dicrotism; pain is still present under these circumstances, but the patient is easier. The next sphygmogram represents the refilled and retarded pulse and the cessation of pain. The fourth and last tracing shows the typical aortic regurgitant pulse of the patient during a period of temporarily re-established compensation. The tracings also show the influence of respiration upon the circulation. Dyspnœa, at its acme in the first, shows the rising curve of preponderant inspiration, the line falling to the expiratory and equable type as the attack subsides. With these tracings, those given on p. 94 may be compared.

[1] *Edin. Hosp. Rep.*, 1895, vol. iii.

The conditions are somewhat different in the angina of arterio-sclerosis without valvular disease, and also in those mainly associated with fatty degeneration of the heart. In the former, while the initial conditions of the attack are to my mind indubitably central, not peripheral, there may at times be noted a short period of simultaneous arterial hardening in association with a quickly pulsating heart. How much of this is spasm, and how much the

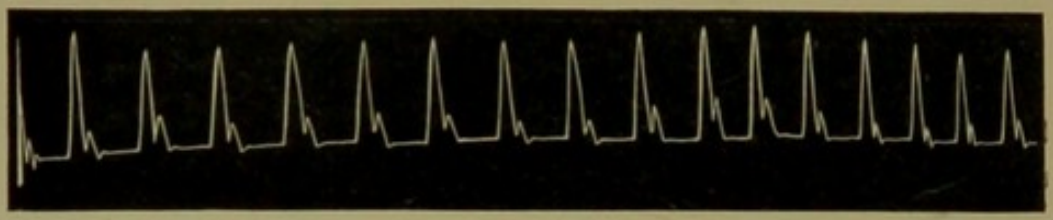

FIG. 25.

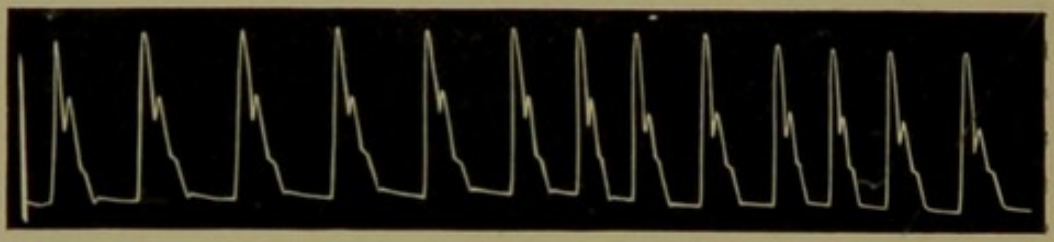

FIG. 26.

FIG. 27.

FIG. 28.

induration of an arterio-sclerotic and imperfectly filled vessel, I have not been able, so far, to convince myself.

The angina of the fatty heart, again, may be associated with a slow, full, and soft pulse without suspicion of spasticity, the irresponsive and degenerated ventricle throwing its contents into the systemic arteries with bradycardial sluggishness, and in imminent danger of that syncope which so frequently overtakes it.

It has been mentioned that shock which so markedly affects cardio-vascular movement may likewise influence secretory motion, and I have suggested the presence of a supplementary or balancing secretion in such cases. Shock to the liver may, indeed, prove fatal to hepatic motion, as shock to the heart may to cardiac motion, but it is probable, for the reasons stated, that minor degrees of shock may have their consequences averted by a supplementary mechanism in such a way as would not be possible but for that double innervation which is a fact in the anatomy of the viscera, and but for that bilateral and double innervation which appears to play an important part in the innervation of unified or single viscera such as the liver and heart. This bilateral action is probably secured by an incomplete peripheral and plexal decussation which has not yet been demonstrated anatomically, but of which there is good experimental evidence. Thus, as has been stated, section of one pneumogastric nerve has little effect upon cardiac action, while section of both nerves permanently disables it, just as a similar lesion abolishes the glycogenic function of the liver.[1]

In addition to the transient phenomena of disturbed or excited, but not necessarily disordered, cardiac action, to which I have referred in connection with angina pectoris, changes of cardiac rhythm of a more persistent character may be met with, and on the nervous relations of these, taken as a type of viscero-motor irregularity in general, I desire to comment very briefly.

I trust, however, that enough has been said to justify the thesis that in the regulation and maintenance of sustained visceral motion the nervous system always plays an important part. Its regulating faculty is more generally conceded than its sustaining power. I assume, therefore, for the reasons stated, that in this respect also it plays essentially as important a part as the blood and the inherent irritability of the cell manifesting any particular form of motion. As I have stated, the functional unit is not one but triune in every form of visceral motion,—mobile, secretory, metabolic, and excretory,—and that, differ as these may from one another in details of manifestation, they are subject to essentially the same order or regularity of action, and to the same disorder or irregularity of action, as the more obviously mobile form which we associate most readily with muscular tissue. With this, perhaps unnecessary, reiteration I proceed to say a few words concerning abnormal variations in cardiac action and their relation

[1] Halliburton, *op. cit.*, p. 670.

to the nervous system, regarding such as typical of other forms of disordered visceral motion.

The heart's action, undisturbed by forced respiration, bodily exertion, or mental emotion, is, normally, quite regular. The eviscerated heart of an animal recently killed is also usually quite regular. Auricular systole precedes ventricular systole with automatic precision. Circumstances, in other words, which induce variation in stimulation are removed, and rhythmical cellular action, one of the factors in the triune partnership, for a short period, alone or assisted by some residual storage of nervous energy, or some remnant of stimulation by blood, continues to act with the unvarying rhythm which blood, nerve, and muscle in common contribute towards during life, when the persistently isochronic and isodynamic organ is undisturbed by extraneous stimulation. The first observable departure from this isochronia and isodynamia is a variation in rate rather than in force. The heart beats are all complete in themselves, and if, when more rapid, they are individually less powerful than a single slower beat, they collectively carry on the circulation with much the same efficiency as when the heart's action is more regular, provided no call be made upon the heart for additional exertion. This condition, when not due to mental excitement, as it may be (in which case it may be characterised either by augmentation or by depression, or by both these states alternately), is usually due to variation in the stimulation of the cardio-vascular nervous system caused by variation in the tone of the chambers of the heart, and in the amount of their contents. This simplest form of abnormality may be termed anisochronia, as variation in rate is more easily appreciable than variation in power. If the condition be present for any length of time, the variation in force becomes more noticeable, and to irregularity in rate is added irregularity in the size of the pulse wave. The systole may have half its normal force or less than half, a condition which may in general terms be called hyposystole. Now, inasmuch as the empty and eviscerated heart may have a perfectly regular rate and amount of systole, this hyposystolic condition (Fig. 30, Tracing 6) cannot be attributed to the amount of blood in the chambers of the heart. It must therefore be due either to the muscular or neural factor. The muscular factor, we have seen, with the nervous and hæmic factor at a minimum, may act perfectly regularly, and irregular post mortem tremor of muscular tissue is most frequently observed in somatic, not in visceral, muscle. On the other hand, there is abundant

evidence, clinical, physiological, and pharmaceutical, to prove that stimulation of the nervous system may profoundly influence the action of visceral muscle in augmenting or depressing it, and in hastening or retarding it. It seems, therefore, rational to conclude that variations in cardiac action during life, whatever the special character of the rhythm, must be largely, although not altogether, due to the combined or alternate and always associable play of the nervous mechanism we have examined. Such nervous action, even under abnormal circumstances, may be rhythmically or arrhythmically exerted.

Reduplication of the second sound of the heart may at present be excluded from discussion, as it may be wholly due to hydraulic variation in the pulmonary artery and aorta. Triplication, however, otherwise termed *bruit de galop*, cantering rhythm and reduplication of the first sound of the heart, while it is capable of being influenced by gravitational conditions and modified by posture, is essentially a retarded systole, or in some cases a systole followed by a very small supplementary systole, which for definiteness may be termed a hypo-hemisystole, or something less than a hemisystole. Like variation induced in the pulse wave by respiration, the neural factor is necessary to its production, as we may convince ourselves comparatively satisfactorily by a study of the more pronounced condition to which it is related, namely, quadruplication, or one of the forms of rhythmically dropped beat. Reduplication of the first sound has been variously accounted for. Sibson[1] considered it to be due to asynchronous action of the two ventricles, and his disciple, Sir William Broadbent, has recently expressed the same opinion.[2] Physiologists, however, such as François Franck,[3] dispute the possibility of dissociated ventricular action, and clinical examination and sphygmography appear to me to support the physiologists. Two ventricular systoles would, of course, mean two diastoles, and reduplication of the first sound in Sibson's hypothesis should usually be associated with a reduplication of the second sound, which is not the case. But were the double systole situated in the left ventricle, it would not necessarily imply an audible reduplication of the second sound. Now, sphygmography shows that cases of quadruple pulsation consist of a long systole followed by a short diastole, and this by a short systole followed by a long diastole. Systole, in other words, is followed by

[1] *Lancet*, London, 1874.
[2] "Heart Disease," London, 1897, p. 34.
[3] *Arch. de physiol. norm. et path.*, Paris, 1895, No. 3.

hemi-diastole, this by hemi-systole, and this finally by a long diastolic pause. The tracings emphasise these points (Fig. 29, Tracing 1 and 2, and Fig. 30, Tracing 2). It has been observed that digitalis induces this rhythm in some cases, and this fact, I think, supports a neural view of its causation. When the beat is triple, and the first sound reduplicated, these events are crowded up, the first short diastole is omitted, and the triple rhythm with anacrotism results (Fig. 29, Tracing 3). Instead of the bigeminal pulse of quadruplication, a trigeminal pulse may be present which consists of three systoles and two diastoles (Fig. 30, Tracing 5). It is a quintuplication. In all these varieties the ventricles act together, not apart, and the regulating factor in the rhythm is, I believe, neural. The cardiac cycle may, we know, be altogether or almost suppressed, and this acyclia, it may fairly be argued, is a variety of inhibition, and probably not only neural but more precisely pneumogastric in origin, and due to local cardiac or distant reflex stimuli (Fig. 30, Tracing 7).

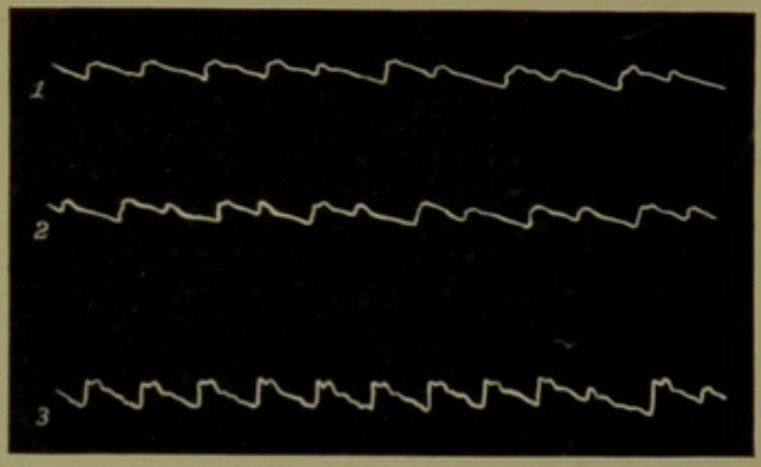

FIG. 29, Tracings 1 and 2.—Sphygmograms of dropped beat, with quadruplication of the heart sounds best marked in 2, when the patient was recumbent. Tracing 3.—Sphygmogram from the same case standing, when the quadruplication by change of rate was converted into triplication, the anacrotic summit being the representative of the hemisystole in Tracing 2.

Some of the varieties of abnormal cardiac rhythm mentioned may be of long duration, but they are essentially an adaptation of the organ to certain circumstances, with a view to carrying on the circulation; and while they may at times be significant of cardiac failure, they are not necessarily so, and cannot therefore be regarded as pathological. It is not so in some cases of persistent *bradycardia* and *tachycardia*. In the former, as we know, the heart's action is abnormally retarded, the neural cause of such retardation being, it would appear, either *in* the heart or *outside* the heart (Fig. 30, Tracing 1). Dehio showed[1] that extracardial bradycardia could be accelerated by the administration of atropine,

[1] *St. Petersb. med. Wchnschr.*, 1892, No. 1.

and that what he terms cardial bradycardia could not be so affected. It is the latter kind which constitutes the graver danger to life. The precise neural mechanism of the condition can only be surmised, not having yet been demonstrated. Retardation should normally provoke acceleration; and as it does not do so, it would appear, in

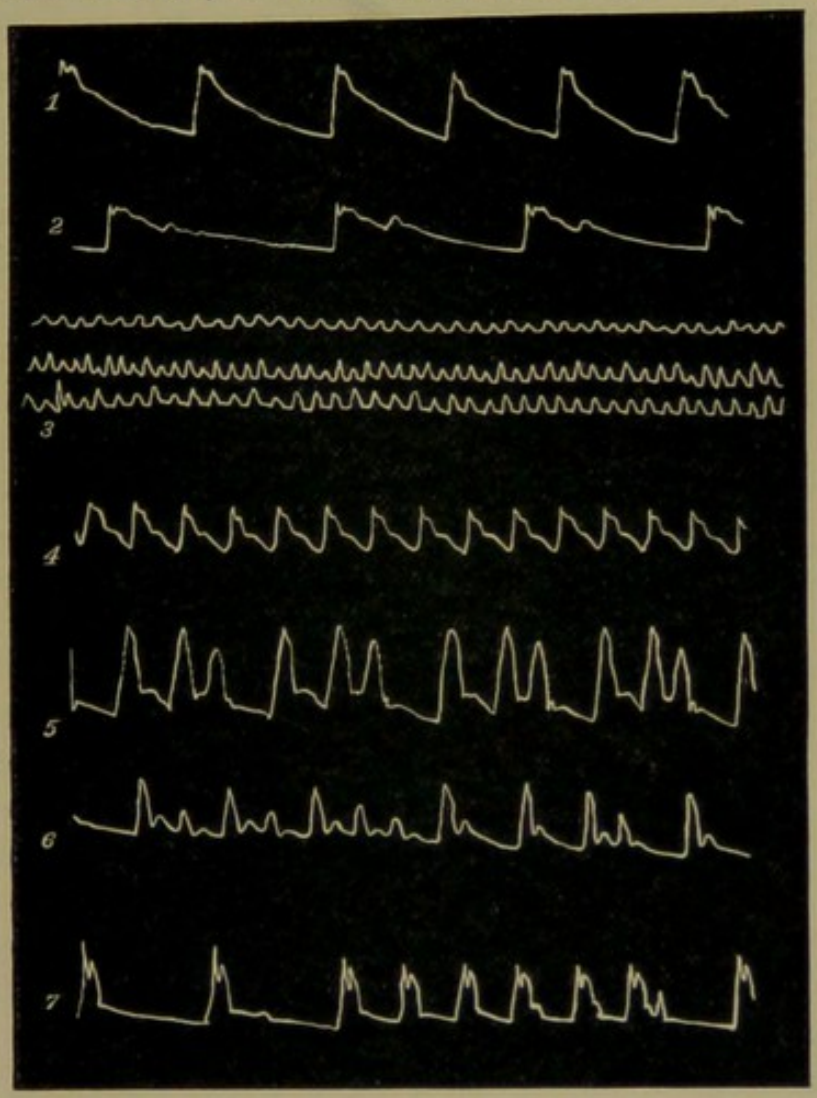

FIG. 30, Tracing 1.—Sphygmogram of persistent bradycardia. Tracing 2.—Sphygmogram of bradycardia with dropped beat. Tracing 3.—Sphygmograms of paroxysmal tachycardia. Tracing 4.—Sphygmogram from the same case of paroxysmal tachycardia, after subsidence of the attack. Tracing 5.—Sphygmogram from a case of quintuplication of the heart sounds in aortic valvular disease. Tracing 6.—Irregularity of the pulse, with hyposystole from a case of double mitral disease. Tracing 7.—Acyclia, with complete and partial intermission of the pulse.

the absence of myocardial degeneration, or some general depressant, such as a poison, whether auto- or heterogenetic, that the seat of the disorder is in the spinal visceral innervation of the heart, an examination of which will probably ultimately reward the labour of some one. The transient bradycardia which follows fevers such

as pneumonia may be attributable to exhaustion of the spinal visceral nerves, and Goldscheider and Flatau[1] have recently shown that high temperature has a very distinct effect upon the appearance of central nerve-cells. We know, however, as little, positively, about the essential neural causes of bradycardia at present as we do of those of persistent *tachycardia*. These very terms reveal our ignorance. There is some reason to believe, however, that persistent tachycardia, like bradycardia, may be of cardial and extracardial origin. My former colleague at the Great Northern Central Hospital—Mr. Spencer Watson—cured a case of persistent tachycardia by the removal of post-nasal growths. Martius also, in his monograph, has collected a number of cases in which a degree of persistent tachycardia was associated with disease of the pneumogastric nerve or nerves. I have already suggested that in some cases of cardiac dilatation, associated with persistent tachycardia, a neural stimulation of the rich nerve supply of the heart may be active in producing the condition, and it is a common experience that the removal of dilatation also reduces the heart-rate to more leisurely and regular action. In essential or paroxysmal tachycardia, however, we have an interesting nervous condition, at present unexplained, but usually associated with cardiac dilatation, in which the delirious heart appears to escape from all nerve control, inhibitory and accelerant, depressant and augmentative, and to revel for a time in the fœtal tic-tac of emancipated visceral rhythmicality. This form of runaway heart is usually pulled up sharp by what appears to be an augmented inhibitory action of the vagus, which asserts its authority with surprising abruptness. The sphygmograms illustrate these phenomena (Fig. 30, Tracings 3 and 4).

This sudden restitution to normal visceral motion is not unknown in other organs. The defective biliary secretion of non-catarrhal inhibited hepatic motion may be rapidly followed by normal secretion. The oliguria of an actively podagral state may as quickly be succeeded by copious urination, just as the mental irritability of suppressed gout may suddenly lessen when the disorder finds localisation in a joint. That these rapid changes may be due to neural conditions, there is good reason to believe. It is related of vom Stein, the patriotic and able opponent of the first Napoleon, that when he was dismissed by the King of Prussia at the dictation of the ill-mannered Corsican, he developed a severe attack of gout, which resisted all treatment, balneological

[1] *Op. cit.*

and other, until Queen Louisa, overruling the weak complaisance of her not too heroic Consort, procured vom Stein's recall to office. The gout disappeared forthwith, and the metabolic and excretory cripple of yesterday, restored to mental and bodily vigour, successfully organised the overthrow of the insolent invader of his country. The depressed man, as a whole, including all his viscera, responded to the call for action, and was enabled to do so by drawing upon that latent reserve of energy, the amount of which cannot be gauged until the absolute necessity for its utilisation arises.

Just as visceral disorder may be the stimulus underlying somatic sensory phenomena, so also somatic motor phenomena may be due to visceral disorder. Irritative, septic, and stagnant conditions in the gastro-intestinal canal may apparently be the efficient cause of clonic and tonic disturbances of the somatic muscular system. In the case of the myoclonus multiplex, which affects some neurotic and neurasthenic dyspeptics, it is probable that these painless spasms are due to some general irritant in the blood, frequently aggravated by a certain amount of tabagism. But the question of a reflex of unabsorptive and non-toxic origin in widespread tetany is more difficult to decide. The bilateral tetany of the infant, for example, with carpo-pedal contracture, so frequently observed at our children's hospitals, and usually in association with gastro-intestinal irritation of a pronounced type, or with the recent history of such, might very plausibly be argued to be a reflex due to bilateral stimulation of the bilateral innervation of such a single tube as the alimentary canal. This view is, moreover, still more plausible in those cases in which the higher centres are quite unaffected, and the patient grins complacently at his carpo-pedal condition. It is, however, possible that there are toxic agents which in certain quantities act like strychnine chiefly upon the spinal cord, and the alcoholic extract obtained from the gastric juice by Bouveret and Devic [1] seems to have been capable of producing tetanic convulsions on intravenous injection. The motor disturbances, moreover, need not be limited to the lower segment of the nervous system, but may, according to the authors quoted, become generalised and even attended by epileptoid phenomena and unconsciousness. Under these circumstances, however plausible at first sight a reflex explanation of tetany may appear, it is probable that the toxic view now more generally entertained is the correct one. In minor degrees of the affection, it is just possible that reflex action may also play a part. In

[1] *Rev. de méd.*, Paris, January 1892, p. 48; February, p. 97.

any case, the intimate connection between the visceral disorder and the neuro-muscular phenomena in question is indubitable. Whether some cases of somatic contracture of a so-called "hysterical" nature are of visceral origin cannot be stated positively, notwithstanding the large rôle previously assigned to the sexual system in these disorders. Renal calculus may, however, provoke a lateral contraction of the trunk on the affected side, which must be regarded as a true reflex; and I have observed the same condition in a neurotic patient, the subject of consolidation of the base of the left lung due to aortic valvular disease. The length of time for which "hysterical" contracture may persist removes auto-intoxicant influences from the purview of causes, and the final discovery in some cases of central sclerotic changes indicates the possibility either of original disease there, or of so-called functional changes becoming organic lesions, whether the original stimulus were splanchnic or not. These somatic hysterical contractures bear a very strong resemblance to an interesting group of cases which Mr. Clinton Dent brought before the Medical Society of London in 1897,[1] in which a spastic condition of portions of the alimentary canal may stimulate tumour, cause severe pain on the principles laid down in a previous lecture, and even justify the operation of laparotomy from the urgency of discomfort. This intestinal neurosis or contracture appears, like its somatic equivalent, to be in the first instance reflex, rather than due to a more general poisoning of the centres.

[1] *Trans. Med. Soc. London*, 1897, vol. xx. p. 257.

LECTURE VI.—(*continued*).

BODY AND MIND.

THE brain, regarded as one of the viscera, both from its own interest and importance in the organism, and from the nature of this lectureship, is worthy of separate consideration, although I have endeavoured, in what has already been said, to show its intimate connection with the rest of the body, and thus to divest it of that glamour with which the older physicians and metaphysicians invested it, and which blinded them to the essentially visceral nature of the organ of mind. One can respect both their veneration and their prejudices. These were, however, partly founded on fear—fear lest a rude prying into the secrets of consciousness might rob them of some of that sense of the sanctity and mystery of life, the capacity to entertain which is part of the nature of man. Their fears were groundless. The impatient dogmatism of an occasionally recrudescent materialism fails at each attempt to illuminate. Man will have none of it. The creature that can entertain the idea of the Infinite will be satisfied with nothing less. Did we, however, bear in mind more constantly the material substratum of mind, and the possibility of injuring through the mind, not some diaphanous and impalpable condition which would close over the wound inflicted by an inconsiderate word or deed, as the shadowy form of a ghost might over the rapier thrust of a human antagonist, but remembered that discourtesy and cruelty may, as they do, work havoc upon texture, without which mind, as we now understand it, could not exist, it is, I think probable, that, in the absence of an irredeemable brutality of disposition, such a materialistic conception would promote courtesy, gentleness, and the other amiable virtues of altruistic civilisation. The physiology and pathology of the emotions, however, considered in the spirit and by the methods of modern research, is still, I think, an un-

written volume. The cell, considered from the point of view of the metaphysical psychologist, will, I believe, one day yield quite as important results as psychology viewed from the standpoint of the physicist and histologist. In other words, such a volume must be the work of both schools, and, like many human guesses at truth, be a compromise between contending errors.

We have seen that the condition of one viscus may influence the state of another, either through the agency of the nervous system directly, or through the medium of the blood. The nervous system being segmented and with localising reflexes, the influence of a stimulating organ upon an organ stimulated by it may be partial and of a particular kind. Influence exerted through the blood, an omniambient fluid, is general, and may therefore affect many organs. Thus the dislocated kidney may cause tachycardia, and the atrophied thyroid gland myxœdema, with its general depression of vitality and general blunting of motion throughout the body. In order to impress upon ourselves the influence of the body upon the mind, and conversely, the influence of the mind upon the body, it will be convenient to emphasise the visceral nature of the brain, and to examine briefly the anatomical differences between its constituent organules, by which diminutive I mean the different portions of the brain with distinct though associable functions. In its organular constitution the brain is not singular. The liver exercises more functions than one.

The functions of the brain are receptive, retentive or connective and executive. Just as the functions of the stomach are the reception, digestion, and transmission of food, so the higher brain receives and inwardly digests impressions and transmutes them into action, voluntary, emotional, regulative, and trophic.

If we regard the brain, as physiology teaches us to do, as the seat of sensation, and local sensations in other viscera as those referred thither by the dominating centre, we must also acknowledge the partially independent activities of peripheral organs, and see in these the elements of a reversed process, namely, the stimulation of the centre by the periphery, or, more correctly, the stimulation of the viscus, which is the seat of predominant sensation and motion, by the molecular activities of the other viscera. The empty stomach normally constitutes the hungry man. Fill his stomach and his hunger disappears. The brain appreciates the existence or non-existence of a condition which is in a measure local, namely, appetite. What is true, moreover, of

one appetite is true of all. What is true of the semi-independent activity of one organ is true of all organs. The receptive organules of the brain perceive the other-visceral stimulation, the retentive organules prolong the reception, that is, retain impressions, and the executive organules carry out the behests of those functional and persistent products of such impressions, the will and the emotions.

A good deal of not very entertaining merriment has been the result of Descartes' suggestion, that the pineal gland might be the seat of the soul, a suggestion for which he gives very philosophical but not quite satisfactory reasons. More serious writers have attacked him with an earnestness which shows that his views, although indefensible in some particulars, contained a germ of permanent force—of truth. As that Scots worthy, Duncan Forbes of Culloden, remarked, "*Quidquid clare et distincte percipio est verum,*" was the foundation upon which Descartes built, and Forbes acknowledged it was a good one.[1] Like many positive assertions, however, this also requires important qualification. Descartes distinctly perceived the truth that impressions received from various sources by the receptive organules are unifiable into simple conceptions by some portion of the brain. The mistake he made was in being too positive about the seat of such simplification, in his well-known proposition concerning the pineal gland.[2] Taking warning, therefore, by Descartes' example, but pursuing our theme in the spirit of his researches, it will be interesting to inquire whether there is any recognisable anatomical distinction between the systems of organules to which I have referred, and to endeavour to ascertain how that multi-unity mind results from their operation, how it is influenced by other organs, and how it influences them. If we but partially succeed, the effort is worth making. The anatomical question, no more than the physiological, is not by any means novel, being as old as the comparative histology of the different portions of the brain, but the collective examination of such histology with a view to associating it with cerebral function is of comparatively recent date. When details of the anatomy and physiology of the brain are better known, it may be confidently anticipated that what is true of the large will also be found to be true of the minute, and that the histological character

[1] "Reflexions on the Sources of Incredulity with regard to Religion," Edinburgh, 1752, p. 43.

[2] "Œuvres," Paris, 1844, p. 224.

of a part having a special function will be recognised as being as distinctive as that function itself. According to Kölliker,[1] Meynert was the first, in 1867, to note a histological difference in the occipital lobe from other portions of the brain. In this country, Bevan Lewis's work in this direction is well known, his results having first been published in papers,[2] and more recently in his Treatise.[3] Lewis recognised sensory and motor types in the histological character of the cortex cerebri, as well as some subsidiary types which he named from the localities in which they occur. The point, however, which his researches appear to have settled most satisfactorily is the occurrence of the giant pyramids, or, as he prefers to call them, "ganglion cells," most characteristically in small groups in the motor areas of Fritsch and Hitzig and Ferrier. Golgi and others have also investigated this point, and to Hammerberg, a young Swedish physician too soon deceased, Kölliker allots a distinguished place in this sphere of work.[4] To his conclusions I shall refer again.

The circumstance which first awakened my own interest in the matter was the histological examination of a portion of the temporo-sphenoidal cortex, in which the central portion of the section differed very strikingly in histological character from either extremity, as these also did from one another. It will be observed, by reference to the figures, that in the central portion (Fig. 31) the cellular elements are more loosely arranged than in the posterior portion, while there also occur what Kölliker calls double pyramids, that is, cells which at either pole have substantial prolongations, which, at about the same distance from the cells, each develop a brush of dendrites. Kölliker states[5] that it is only in the pyriform lobule that he has met with these peculiar cells, and it is only in this region that I also have observed them.

In the posterior portion (Fig. 32) the cells are more closely approximated, and present the characteristic appearance of serried ranks, in which pyramidal cells of the usual type are generally arranged; in this region, however, those of small size preponderate.

The anterior portion (Fig. 33), finally, is characterised by polymorphous cells sending their neuraxons in all directions, and being themselves as various in position. These resemble in a measure the cells of the subcortical centres, but may be distinguished by a

[1] *Op. cit.*, p. 672.
[2] *Proc. Roy. Soc. London*, 1878, 1880.
[3] "Mental Diseases," 1889.
[4] *Op. cit.*, p. 674.
[5] *Op. cit.*, p. 274.

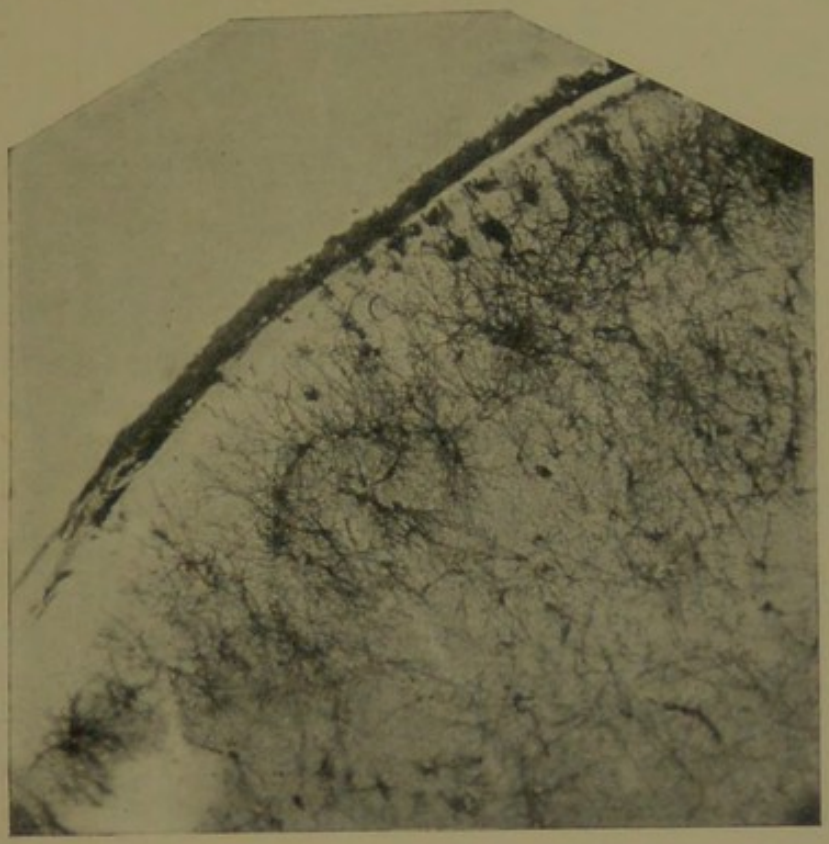

FIG. 31.—Central (receptive) portion of pyriform lobule in a cat's fœtus at term, under low power. Golgi preparation.

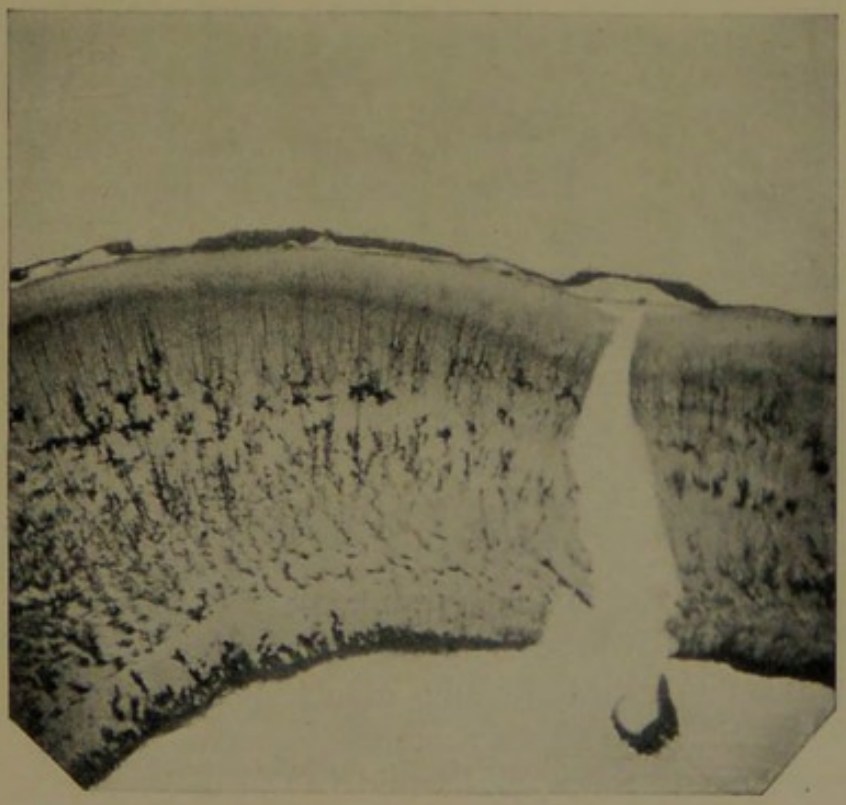

FIG. 32.—Posterior (projective) portion of pyriform lobule from a cat's fœtus at term, seen under low power. Golgi preparation.

nearer approach to the pyramidal type. Well-stained specimens from the corpus striatum (Fig. 34) are shown for purposes of comparison.

The section of the temporo-sphenoidal lobe of which I have spoken was taken from the brain of a fœtal cat at term, and stained by the quick Golgi method. In a section which I made of the same part from the brain of an adult cat, which I received from my colleague, Mr. Peyton Beale, and which was stained by him by a modification of the Cox-Golgi method of his own devising, I found the same essential features present. Preparations from different portions of the brain also show roughly a specific character in regional histology, but I shall not now examine the matter in greater detail, than by stating Hammerberg's conclusions on this point, which are given by Kölliker[1] as follows:—"(1) It appears that in all convolutions of the usual kind, a layer of small pyramids with some irregular cells, the fourth layer of Hammerberg, is invariably pushed between the medium sized and larger pyramidal cells. (2) The layer of polymorphous cells (Hammerberg's spindle-cell layer) is larger than we have hitherto known. (3) These cells, in so far as they are spindle shaped, lie horizontally in the convolutions. (4) The large pyramidal cells are most developed in the frontal convolutions. (5) The giant pyramids only occur in small areas around the central convolutions. (6) Occipital convolutions are distinguished by a large number of small cells. (7) The frontal lobe and the island are distinguished by an unusual number of medium-sized cells, corresponding in all respects with the larger pyramidal cells, while these are themselves altogether absent."

Kölliker does not altogether endorse all these conclusions, but they are sufficiently correct to demonstrate the point under discussion, namely, the histological peculiarities of different portions of the cortex. Kölliker, with the caution and sagacity born of an unrivalled experience, deems it prudent in the meantime to assume that all brain cells act alike, notwithstanding differences in configuration; but, as Bevan Lewis very justly remarks, the association of function with organisation is an accepted doctrine in natural science, and a tentative use of hypothesis is permissible even if the future should cast into the limbo of oblivion as much ingenious speculation as time has already done.

It struck me that we might find in the differences shown by the temporo-sphenoidal lobe to which I have referred, a clue to the

[1] *Op. cit.*, S. 676.

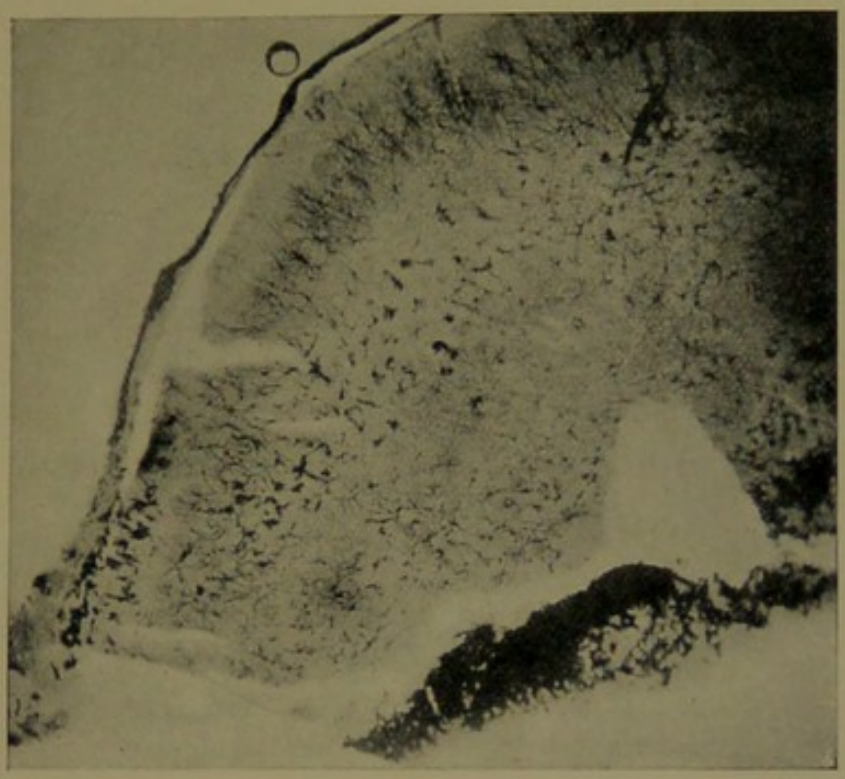

FIG. 33.—Anterior (retentive) portion of pyriform lobule from a cat's fœtus at term, seen under low power. Golgi preparation.

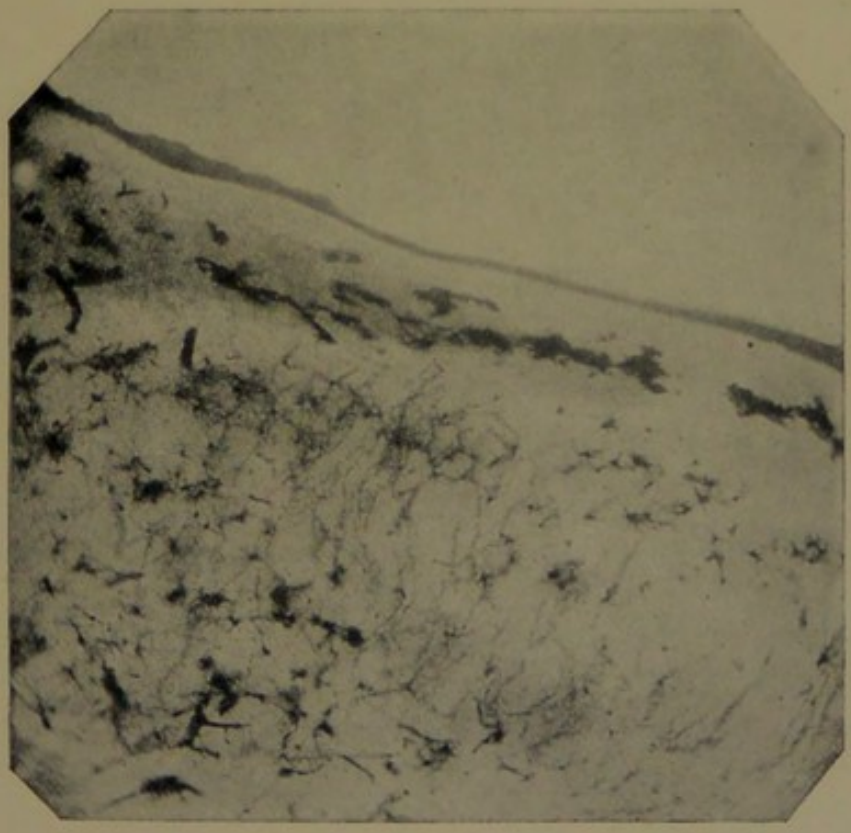

FIG. 34.—Cells and fibres of the corpus striatum of a cat's fœtus at term, seen under low power. Golgi preparation.

characters of the receptive, retentive or connective and projective organules of the brain respectively, and to gain more light upon the subject I examined the cerebral structures concerned in the sense of smell, taken as a type of special sensation.

Physiological experiment and the clinical observation of disease in the neighbourhood of the uncinate and hippocampal gyri point to these being intimately associated with the sense of smell. In selecting this sense rather than that of sight for the purposes of argument bearing upon the cortical structures concerned in the evolution of thought from impressions received, I have been guided by the circumstance that these impressions converge upon the chief site, so far as physiologists are at present agreed, of general tactile sensibility. The few remarks I shall make as regards the deeper anatomy of smell must be regarded as suggestive rather than demonstrational; more would not be germane to our present task. Foster and Sherrington suggest[1] that the uncinate gyrus may not be the site of "full olfactory sensations," and that these may find completion in the cornu ammonis. It is not necessary to follow in detail all the different tracts, even so far as they are known, which lead to the supposed centres of smell. It is enough to know, as the authors just quoted state,[2] that a portion of these reaches the front end of the hippocampal gyrus, often called the "uncinate gyrus." There are, however, certain features in the histology of the cornu ammonis which suggest that it may bear somewhat the same relation to the uncinate gyrus as a portion of the temporo-sphenoidal lobe, that the cerebellum does to the cerebrum.

Sir William Turner[3] mentions the fact that Mr. A. B. Stirling recognised a granular layer in the hippocampus which so resembled the similar structure in the cerebellum, that it might appropriately be called the "rust-coloured layer of the hippocampus." In some sections of the cornu I have also met with cells which bear a considerable likeness to the Purkinjean bodies of the cerebellum, though they are smaller than these. If a longitudinal section be made of the cornu ammonis, so as to get the full twist of the spiral to the end of the grey matter, cells may be seen, especially at the very extremity, which exhibit the resemblance I speak of. I show specimens which contain these. The sections also demonstrate very well the fact of the invariably vertical position, relatively to the surface from which they spring, of the pyramidal cells of the

[1] *Op. cit.*, p. 1181. [2] *Op. cit.*, p. 1180.
[3] "Introduction to Human Anatomy," 1882, part i. p. 291.

cornu, and of the smaller and deeper pyramidoid cells of this structure. The true significance of this comparative histology of the cornu is as little known as that of the cerebellum, but if we are justified in regarding the cerebellum as subordinate to the cerebrum, it appears feasible on histological grounds to suggest that the cornu may also be subordinate to the more superficial areas in the temporo-sphenoidal lobe, some of the characters of which have been briefly sketched. What, then, may be assumed to be the histological character of the sensory area on which the afferent tracts of the sense of smell converge? As we have seen, there are two portions of the lower temporo-sphenoidal section referred to which differ considerably in histological features from a third part. This third part has all the characters of marshalled pyramids of the ordinary type, which are found in portions of the cortex which we know have distinctly motor properties. It would seem, therefore, rational to assume that the sensory function of the temporo-sphenoidal lobe is exercised by those parts which have not the features of the motor cortex; that, in short, the essentially receptive cortex, the cortex for special sensibility, is not that distinguished by pyramids of the ordinary type.

It comes, therefore, to be a choice between two portions. Of these, one, as we saw, has a structure which is apparently peculiar to this portion of the temporo-sphenoidal lobe; the other part has the polymorphous character of those irregular cells which lie chiefly below, but also to some extent among, the pyramids. It would therefore seem rational to assume, and I am aware that I am assuming much, that the part peculiar to this portion of the temporo-sphenoidal lobe is more likely to be associated with its special sensory function, than that portion which has more general characteristics.

I have selected this lobule, as I have already stated, and one of the senses running up to it, rather than the centre of vision, because the structure of it and the mechanism of smell seem so peculiar, and because it is situated in what is avowedly considered the most sensory region of the brain. But peculiarities are also to be found, as has been stated, in the occipital lobe, and we must remember that mind is not the product of one, but of all the senses—of a *correlation of the senses* by means of which unity, coherency, is evolved from many sources of impression, although not, as Descartes supposed, in the pineal gland. I feel, therefore, disposed to regard the characteristics I have referred to as a chief type of the receptive organule, but not the only type, and desire

tentatively to express this opinion with all the diffidence which an acknowledged uncertainty should and, I trust, does inspire.

The retentive or connective organule.—It may be remembered that I ventured to define mind last year as "a mode of vital motion manifested by some cells of the cerebral cortex, and as the more or less permanent product or effect of such motion which we call memory." Memory or retentiveness, we know, is not an exclusively cerebral property. The behaviour of the decapitated frog is sufficient evidence to the contrary; but physiologists have also shown that the tendency of progress in development is to increase cerebral at the expense of spinal retentiveness. In man, spinal memory is probably reduced to simple reflex action, which is a receptive-motor rather than a retentive-motor phenomenon. For our present purpose, therefore, it is not necessary to widen the subject by inquiring whether there be or not a histological basis to spinal memory. As a study in comparative mnemonic histology, however, the inquiry might not be without interest.

Cerebral memory may be impressional and conclusional; that is, the automatic record of impressions received through the senses, or the record of the results of that inward digestion of such impressions by the recepto-retento-motor process we call thought or reasoning, in the exercise of which more cerebral organules than one take part. The histological characters of the storehouse of memory or the retentive organule need not, however, vary with the method of filling it. If, therefore, there be reason in regarding the histological type of the receptive organule to be such as has been described, and the histological type of the motor organule, on which I shall say a few words presently, to be of the pyramidal type, it seems feasible to argue, or assume or imagine, as you will, that the polymorphous cell, with its universality of axonic direction and equal universality of dendritic receptivity, is the type of that retentive and connective organule, the repletion and utilisation of which is the mainstay of mental life, as the greater or less storage of supplies—potential energy—is the necessary condition for the exercise of any power whatever, or kinetic energy.

The retentive organule in its histological features has some likeness to the cells of the subcortical centres. These may be regarded as an extension of the spinal cord into the brain, and the lower nuclei, we have reason to believe, may be the seat of simple reflex actions like the cord. These are, however, no more independent of the cortex than the spinal cord is, and perhaps no less. The vegetative centres, although beyond the power of

will, are not, as we have seen, beyond the power of emotion, and emotion is a cortical, not subcortical, phenomenon, although the motion inseparable from it is, so to speak, involuntary, that is, the executive energy of emotion is projected peripherally before it reaches the seat of will. Between this, however, and simple reflex action there is the important distinction, that the consciousness is fully aware of the efferent event in the case of emotion, which it need not be in the case of simple reflex action.

The projective organule.—I have used the term projective here

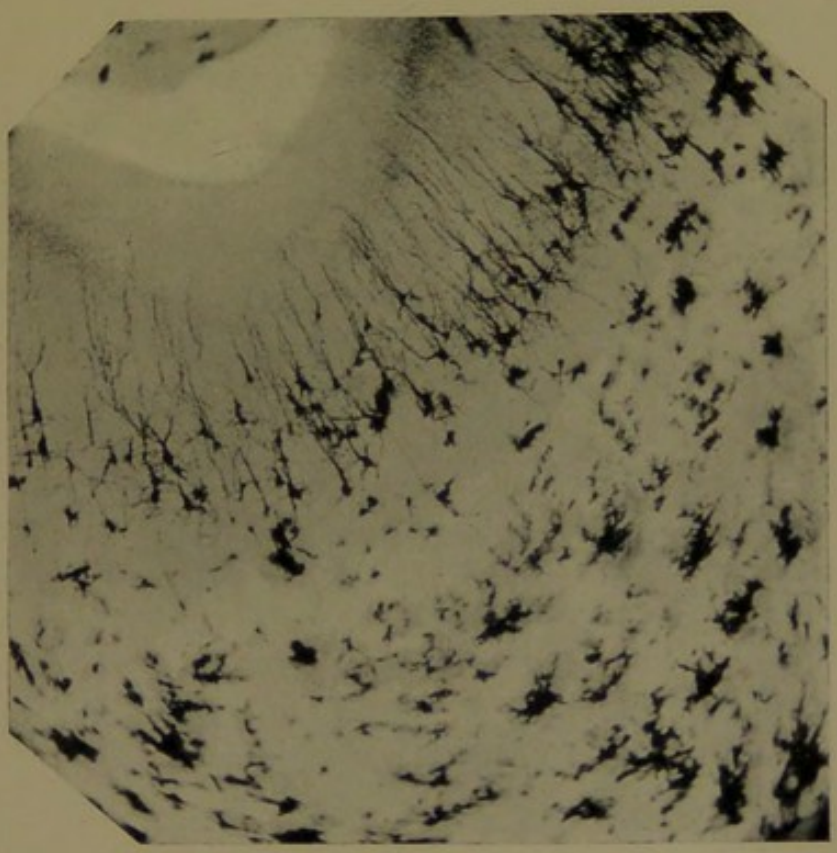

Fig. 35.—Pyramidal cells from the fronto-parietal region of a cat's fœtus at term. (⅓ obj., no eye-piece.)

instead of motor, because I have employed a term intermediate between sensory and motor to distinguish the mnemonic sensori-motor source whence mental motion probably derives a considerable portion of its impulse. I have already mentioned Bevan Lewis's belief that the largest cells of the projective or motor type—the giant pyramids—are to be met with in the parieto-frontal region of greatest provocable movement (Fig. 35), as also the practically unvarying direction of the primary axons of pyramidal cells generally. A nerve cell, be it receptive, retentive or connective, or projective, is of necessity a mixed cell. It receives, transmutes, or

transmits impressions. It has an individual resistance which has to be overcome, and in the overcoming of which fresh energy is evolved. There are, moreover, preponderant centres for the evolution of energy, otherwise direction could not be given to motion, and the universe itself would have been a chaotic pyrotechnic display of short duration, if it had existed at all, which, having flared imposingly into being like the rocket, would, like the residual stick, have fallen into the abyss of oblivion in a similarly ridiculous manner.

The preponderance of energy in nerve-cells is in the sphere of sensibility or receptivity, because this is the aspect of animal life which is turned, as it were, towards the sources of general energy —food of all kinds—in the universe which surrounds it, and the impressions received from whence through the senses are converted into various forms of energy, from the simplest reflex act to the highest effort of conscious thought. Kinesis, movement, projection is, however, the preponderant function in common which the executive section of the brain, the projective organule, possesses, and in this specialisation of function lies the argument for specific organisation. The special organ of cerebral kinesis appears to be the pyramidal cell, differing in size and in distribution, as it probably does, in the range of its projective power and in the character of the movement evoked, be it a gross muscular contraction, an imperceptible secretion, or a subtle movement of thought. A thought is a product or outcome of executive energy—*an act*—which has its roots in the imperishable around us, and in impressions within us, and is rendered intelligible to others by symbols which are in a measure a reflex of our feelings, and represent more or less distinctly such impressions. Thought is not consciousness, although to think we must be conscious. "Consciousness" is life manifest in brain, as "motion" in its conventional sense is life manifest in muscle. Both are based upon "irritability," which is the primary expression of life in all living matter. Thought is regulated consciousness, as co-ordinated movement is regulated motion in muscle. Movement in the somatic system is regulated by consciousness and will, and in the splanchnic by consciousness and emotion in its various phases of calm and excitement, and in a subordinate degree by a so-called automatic power. Life, therefore, is expressed in irritability and its various manifestations in different organs, but is itself an unexplained *fact*. "Im Anfang war die That." Beyond and before "irritability" were the constituents of life. Why not then life itself? And if life,

why not consciousness among other manifestations of life? Such Primal Consciousness is, according to Herbert Spencer and his followers, necessarily existent but Unknowable; according to others not less worthy of respect than they, made known. At this point the process men call Science comes face to face with the process men call Revelation, and it is not our duty at present to pursue this line of thought further. The subject has been ably but too iconoclastically treated by Maudsley.[1]

I offer no apology for this digression, if digression it be, for that physician must have a very limited experience who has not observed both the baneful and beneficial consequences of the influence of these questions on the life and health of his patients. Who has not felt the hopelessness of dealing with the profound melancholy of the religious maniac, or observed the invigorating influence upon the body of a happier conception of the relation of the individual to the forces in and around him of which he is one expression. I had at one time as a patient an elderly lady, who, many years before my acquaintance with her, had for a time been insane. For some years I knew her as a kindly and shrewd woman of sound common sense. One morning I was hurriedly summoned to visit her, and found her recovering from an attack apparently of a syncopal nature. When she had revived, she told me she had, while in the condition stated, had a terrible experience. She had seen hell opened, and filled with all the accompaniments of torture with which students of fantastic eschatology are familiar, and had been apprised of the fact that her irrevocable destiny was to be in flames. The delusion became fixed, and though she lived for several years, the black cloud of her melancholy never lifted for a moment. An interesting visceral concomitant of this state was that a broncho-pneumonic condition, from which she regularly suffered every winter previously while I had known her, and which was accompanied by unmistakable local signs, never recurred. External influences in the presence of her profound sorrow and approaching doom had no influence upon her. As Thekla, about to seek the grave of Max Piccolomini, remarked, "Frei geht das Unglück durch die ganze Erde"—Misfortune travels safe throughout the world.

To convey to others the operations of our consciousness—our thoughts—we have to refer them more or less symbolically to things which their senses may perceive outside themselves, and which we can perceive in common with them. We have each our

[1] "Natural Causes and Supernatural Seemings," 3rd ed., London, 1897.

own Ego, but we may have non-Egos in common with others. In these non-Egos lie the sources of our language, and to their unchangeability and perpetual perceptibility we refer as a standard to determine whether thoughts conveyed to us by another are in agreement with the truth of things or rational, or in disagreement with such or irrational. In the essentially threefold sources of mind one or more factors may be disordered. Language, for example, may be affected in its sensory, its executive, or its retento-motor or connective phase; and in the latter, the disorder may be impressional or conclusional, to use the terms already employed. There may be defect in memory without confusion of ideas, and confusion of ideas with a considerable retention of impressional memory. In all these spheres disorder may be based upon organic or upon so-called functional disease. That functional change may become organic or permanent is a fact which is becoming more appreciated in the present day, from the investigations into the life history of the nerve cell to which I referred in the fourth lecture. These likewise make it clear to us how peripheral impressions from all parts and organs of the body may act upon the centres, and how also such central effects may react upon the splanchnic and somatic periphery. It is not difficult, moreover, to conceive how the short-circuit motions in the mental organules may lead to excessive action and exhaustion having general consequences, and how a compound of peripheral and central excitations may wear out both body and mind by the unregulated play of the emotions, due to a want of control, which may have its roots in inherited or acquired disease, and of which even moral turpitude may be but a symptom.

In bringing to a close this course of lectures, of the many defects in which no one can be more conscious than I am, I have again to express my thanks to the Fellows of the College for the indulgent courtesy which induced them to appoint me to the office, and to pray that the leniency they have already shown may suggest excuses for the inadequate manner in which I have executed my task. I am aware that I have touched but the fringe of a great subject of entrancing interest and supreme moment, the better knowledge of which is calculated to have an important influence upon much that is of interest to us as men and as physicians. If, however, in their opinion I have added anything in the course of these lectures to such knowledge—if, buried in the worthless quartz

of much nebulous hypothesis, they should deem it possible to detect some grains of golden truth—I shall feel happy in believing that my labour has not been altogether in vain, and that I have shown myself sensible of the honour they conferred upon me in appointing me to the Lectureship.

APPENDIX[1]

ON THE INNERVATION OF THE INTRACRANIAL VESSELS.

It has long been known that nerve fibres follow the course of vessels both in the dura mater and in the pia mater. Kölliker[2] refers to the researches of Arnold, Purkinje, Pappenheim, Rüdinger, and Bochdalek in this respect. He also states[3] that he has himself followed such nerves in the pia mater to arteries of 9 μ diameter and less, into the substance of the brain, but that these have never been traced to their termination, and that it is certain that in the vascular plexus no nerves are to be found.

Writers on the circulation in the brain may be divided into those who assume that the cerebral vessels are innervated, and those who likewise assume the contrary. A painstaking examination of the matter by Lovell Gulland[4] resulted in his stating that neither by the silver, mercury, nor methylene blue methods could he succeed in demonstrating any nerve fibres in the walls of the pial vessels nor of the intracerebral vessels. Dr. Gulland, however, succeeded, I understand, in July of this year (1898), by Cox's method, in staining nerves in the vessels of the pia mater. Obersteiner described the appearance of nerves on the pial vessels in a gold preparation in 1897.[5] In connection with a course of lectures, on the relation of the nervous system to disease and disorder in the viscera, it became my duty to investigate the matter; and the result of my examination of the innervation of the pia mater and of the vessels coursing through it I now propose shortly to set forth. I also wish to state that my research would in all probability not have been undertaken had not Sir John Batty Tuke impressed upon me the fruitless search of others,

[1] Reprinted from the *Edin. Med. Journ.* for November 1898.

[2] "Gewebelehre," sixth edition, S. 835. [3] *Loc. cit.*

[4] *Journ. Physiol.*, Cambridge and London, 1895, p. 361.

[5] *Neurol. Centralbl.*, Leipzig, 1897, Bd. xvi. S. 356.

for I was under the impression that the facts mentioned by Kölliker had settled the point. On the fifth of May in this year I obtained the fœtus from a cat well advanced in pregnancy. The cat was killed by chloroform and drowning. The brains of the fœtus (or fœtuses if this plural be permissible) were divided into moderately small pieces, and treated by Sihler's hæmatoxylin method, which I recently related,[1] and some portions were further stained by being placed in the hæmatoxylin solution for twenty-four hours after their first immersion. Towards the end of May 1898, I succeeded in staining the nerves coursing with the vessels of the pia mater, twisting in some instances round them, and terminating in a plexiform manner on them, the mode of termination being most visible on the larger vessels.

The further particulars I shall mention in this place will have reference (1) to the character of the structure from which the nerves in question arise; (2) to the size of the vessels in association with which the nerves have been found; (3) to the character of the nerve fibres; (4) to a description of the mode of termination of the nerves on the vessels and in the pia mater; and (5) to the presence of ganglion cells on the stems of the innervating trunks, and to the character of these cells.

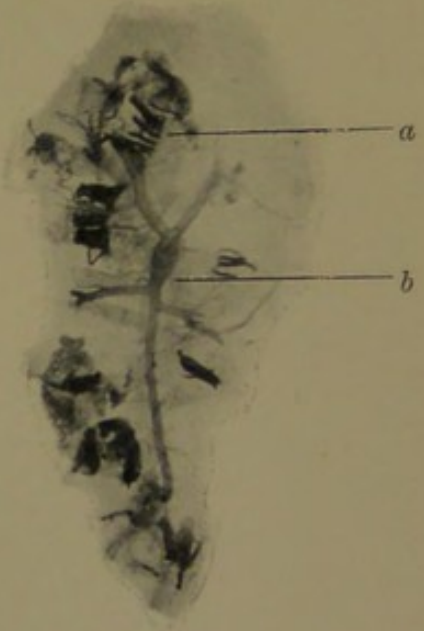

FIG. 36.—*a*, tassel-shaped nerve bundles; *b*, vascular circle.

1. *The character of the structures from which the nerves arise.*—In one of my preparations (Fig. 36) a series of bundles of nerve fibres is to be seen, which, taken in the aggregate, presents somewhat the appearance of a tassel. The individual bundles or strands of the tassel measure on an average 7 μ in diameter. The bundles consist of many smaller bundles of about 1 μ and less, and these of still finer fibres. They lie on each side of an artery which divides into a stout circle, and then proceeds as a single tube. The vessel before dividing measures 18 μ across, each side of the circle 10 μ, and the vessel beyond the circle 15 μ. I was inclined on first sight to think that the vessel was from the base of the brain, and that the tassel-like bodies were the commencement of cranial nerves. But on examination the latter was found

[1] *Edin. Med. Journ.*, January 1898.

to be centripetal to the vessel, and the circle was much too stout for, and otherwise differed from any possible representative of the circle of Willis. I have not yet, by injected preparations, been able to determine the precise origin of these tassel-shaped bundles. The latter have no general sheath, but the individual bundles definitely cohere.

2. *The size of vessels in association with nerves.*—The largest of these in my possession measures 20 μ across, and the smallest about 10 μ. The nerves naturally bear a relation in size to the vessels. Those on the largest vessels measure 2 μ across, and on the smallest are mere threads.

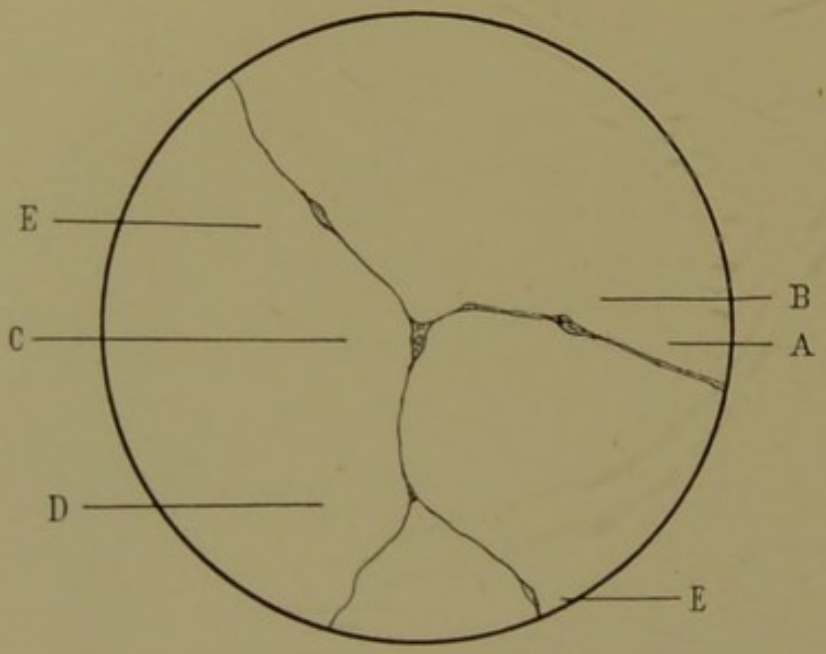

FIG. 37.—A, nerve in pia mater about to form plexus; B. preplexal nucleus; C, triradiate nuclear origin of plexus; D, subsidiary nuclear point of dispersion; E E, nuclear bodies on fibres of plexus.

3. *The character of the nerve fibres.*—The dimensions of the trunks are as stated above. The individual bundles of the nerves measure about ·5 μ across, and are interrupted at intervals by a nuclear body. These nuclear bodies are more numerous on the finer fibres, and are an adumbration of the nuclear dispersing and connecting points of the penultimate and ultimate plexuses. The nerves have a sheath which shows connective tissue corpuscles in the larger branches, and a hyaline sheath which exists on the smaller is lost when the fibre becomes single at a point of departure from the parent trunk. The nerves which innervate the pia mater are similar in character to those which follow, twist

round, and end upon the vessels, and may occasionally be actually seen to take their departure from the nerve on the

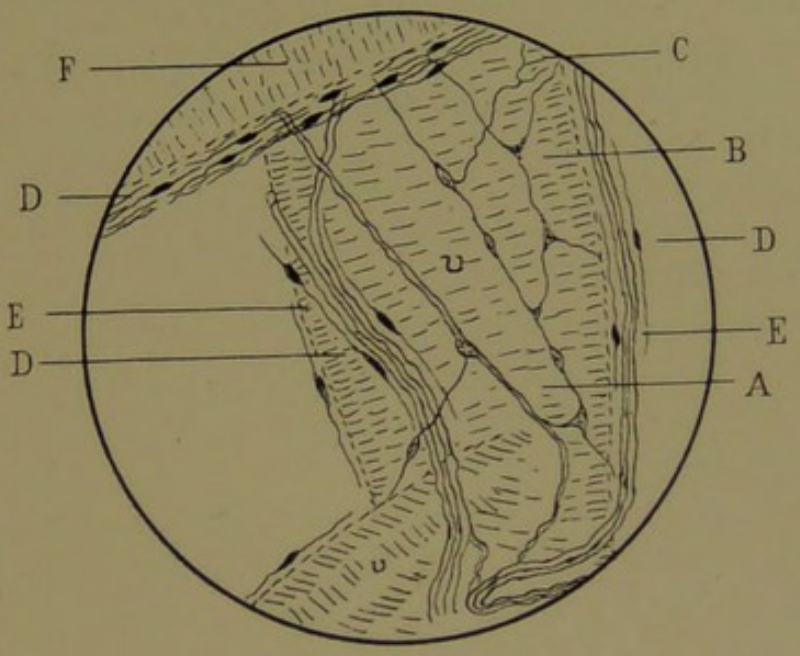

FIG. 38.—A, source of vascular plexus; B, triradiate nuclei in plexus; C, finer ramification; D D D, nuclei and fibres of vascular and neural sheaths; E E, large nerves; *v*, pial vessel; F, crossing vessel.

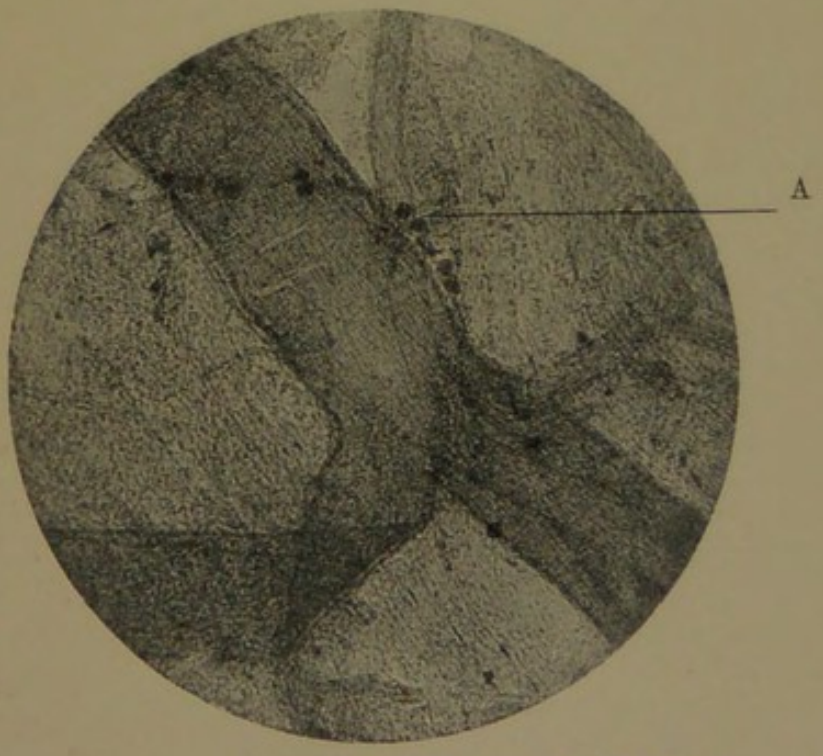

FIG. 39.—A, ganglion cells on vessel of pia mater.

vessel. In other cases no vessel is at hand to settle this point.

4. *The mode of termination of the nerves.*—The nerves terminate both in the pia mater and on the vessels by a plexus, which in its ultimate distribution is so fine as to give the appearance of an excessively fine dichotomous ramification (Figs. 37 and 38). The nuclear points of dispersion vary in size, according as they are penultimate or ultimate, from bodies 1·5 to 2 μ across to fine points which cannot be accurately measured, but which are certainly not more than ·5 μ, while the finest ramifications end by a series of small refracting points. These are presumably what some term nerve endings, but whether they are portions of a very fine and endless plexus I cannot positively affirm. The plexus on the vessels is best seen, for sufficient reasons, on the larger branches.

5. *Ganglion cells.*—Nerve trunks, both at what I have termed the tassel-shaped sources, and some passing through the pia mater apparently on their way to vessels, as well those on the vessels, in some instances show ganglion cells (Fig. 39). These are all *unipolar*, measure from 2·5 to 1 μ across, and have a well-marked nucleus and nucleolus. A specimen (Fig. 39) shows ganglion cells on a nerve trunk, which twists as a spiral round the artery entwining the latter like a garland of roses. The well-defined and completely developed character of these cells, with their well-marked axone, preclude the possibility, in my opinion, of their being embryonic and transient structures.

Although, therefore, I have not detected an innervation of the small arteries of the vascular plexus, I believe it is legitimate to conclude that further research will still more extend the anatomical distribution of the cerebral vascular nerves, and think we already have sufficient evidence of such innervation to modify current conceptions of the physiology of the intracranial viscus.

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