The Oliver-Sharpey Lectures

ON

NEW FACTS IN RELATION TO THE
PROCESSES OF

NERVOUS DEGENERATION AND REGENERATION.

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS,
LONDON, APRIL 29TH AND 30TH,By W. D. HALLIBURTON, M.D., LL.D., F.R.S.,
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LECTURE I.

NERVOUS DEGENERATION.

MR. PRESIDENT AND FELLOWS,—I have first to thank the College for the honour conferred upon me, in selecting me as the Oliver-Sharpey lecturer for the present year. The College has always recognized from the days of Harvey onwards, that scientific medicine must be grounded on physiological knowledge. The founder of this lectureship has exemplified this precept in his own lifework, and Sharpey, the great master whom the lectureship commemorates, always recognized the importance of physiology as the Institutes of Medicine.

Many years ago, when I was a first year's student at University College, I remember Sharpey's commanding figure; for, though he had then relinquished his professorship, he continued to haunt the laboratory which had been the scene of his teaching and of his investigations. I well recollect the sad day on which his remains started from the precincts of University College to their last resting place. His name still lives not only in the memory of those whom he inspired, but will be remembered in relation to his discoveries, and is commemorated at his College by the foundation of the Sharpey Scholarship.

Being myself one of the early Sharpey scholars, the invitation to deliver these lectures was one which was especially acceptable, and I can only trust that what I have to say will be considered worthy both of the great memory to which I have alluded, as well as of the high traditions of this College.

In the days of Harvey the subject of physiological chemistry, chemical physiology or bio-chemistry, as some prefer to term it, did not exist. The late Sir Michael Foster in his *History of Physiology*, when speaking of Vesalius, said: "The great anatomist would no doubt have made use of his bitterest sarcasms had some one assured him that the fantastic school which was busy with occult secrets, and had hopes of turning dross into gold, would one day join hands in the investigation of the problems of life with the exact and clear anatomy so dear to him." Almost the same words might be used in reference to Harvey's attitude. The scientific men of his time paid no heed to chemical learning; they ignored or even despised the beginnings of that branch of knowledge which in later years was to become one of the foundations of physiology, and the mainstay of the art of medicine.

It was the work of Lavoisier in France, of Mulder in Holland, and of Liebig in Germany, that first placed bio-chemistry on a sure basis, but even in Sharpey's time the disciples of this branch of science might have been counted on the fingers of one hand. Sharpey himself retained to the end the anatomical conception of physiological advance. How different things are to-day; how great have been the strides made in chemical physiology and in its sister science, chemical pathology, can be realized by even a superficial survey of modern medical literature.

A few years ago, when I had the honour of delivering before this College the Croonian lectures, I selected as my subject the chemical side of nervous activity, in which I hope I was successful in showing how chemistry has invaded even the difficult country we call the nervous system. I then indicated that although some progress had been made, even in the practical applications of that knowledge, much still remained to be done. The same is

true to-day, but in the few years that have elapsed since I uttered these words a little progress has been made, and it is to some of this new work that I propose to devote the present lectures. One great charm of physiology to the investigator is that fresh facts are always being discovered, and new light is thus shed on the problems of living matter. In so far as I myself have had any small share in such work, my energies have been mainly directed into a bio-chemical groove, and it is one of these questions—nerve degeneration—to which I shall devote the first of the two lectures. But bio-chemistry is not a narrow specialism, and research on such lines usually branches out in many directions; this will be illustrated by the circumstance that for the subject of my second lecture I shall take that of nerve regeneration, in which at present there is but little to be said from the chemical point of view.

In relation to both of these subjects, it would have been impossible to have spoken at all if it were not for the assistance of certain of my colleagues. Among these I would particularly mention Dr. Mott, to whose loyal co-operation and helpful advice I owe so much. Mr. Arthur Edmunds, Dr. Rosenheim, and Miss Tebb are others to whom both Mott and myself are indebted for great assistance in several portions of our conjoint work.

One more word of introduction, and only one, before I pass to the subject proper of my first lecture. It is impossible in our present state of knowledge to avoid controversial questions. I have to-day to deal with one and to-morrow with another. Polemics are always distasteful to me, and I trust I may deal with both without a single note of personal feeling. The proverbial disagreement among doctors is especially true of physiologists; and this is really as it ought to be. Whilst knowledge is in the making there must be divergencies of opinion, and it is only by a full and free discussion of these, and by the renewed research of which criticism is the stimulus that any certainty in the way of truth can be arrived at.

NERVE DEGENERATION.

It is more than fifty years ago that the elder Waller described the degeneration that occurs in nerve fibres which are cut off from the cells of which they are outgrowths. So complete and exact was his description of this phenomenon, now known as Wallerian degeneration, that in the intervening years but little has been added from the anatomical and histological standpoint to what he taught. But in order to understand completely the chemical transformations which lead to these anatomical appearances, it is first necessary to know the chemical composition of the healthy nervous structures involved. It is just at this fundamental point that we meet with a great hiatus in knowledge. We know something of (because we can easily estimate it) the proportions between water and solids in the various districts of the nervous system; we know, further, that among the solids protein matter, and especially nucleo-protein, largely predominates, particularly in grey matter; but it is in relation to the phosphorized fatty constituents, the presence of which forms such a striking characteristic of all nervous material, that our ignorance is greatest. Thudichum did yeoman service in his attempts to unravel this problem, and the value of his investigations is only just beginning to be appreciated. His work is marred, it is true, by too hasty generalizations, and by such faults as are always seen in a new endeavour—faults which subsequent observers should be grateful for, as they profit by them and avoid them. No one who has not attempted to work at the chemistry of the brain can imagine the difficulties that meet one at every turn. In America Waldemar Koch, and Gies may be mentioned among those who have had the courage to enter this thorny field, and in my own laboratory Dr. Rosenheim and Miss Tebb are prosecuting similar researches. The phosphorized fats are not the only complex substances which are present. The crystalline monatomic alcohol called cholesterol is present in a free condition in considerable amount; this cannot be devoid of physiological moment, and yet absolutely nothing is known either of its mode of origin, its destination, or its function. Then there are complex nitrogenous glucosides, called the cerebrins or cerebroside; here, again, although some of them have been separated in a fairly pure condition, analysed, and labelled

with fantastic names, we have no certain knowledge either of their constitution or of their use. One notes with some regret the final disappearance of the substance originally termed "protagon" by Liebreich. This is one of the few materials that can be obtained in a crystalline form from nervous structures by cooling a warm alcoholic extract of brain, for instance. It has passed through many vicissitudes, being alternately regarded as a mixture and as a chemical individual. The work of Gies in New York, and of the workers in my laboratory have, however, finally demonstrated that it has no independent existence.

It will, however, be beside my purpose to dwell too long on the lack of the knowledge we hope to obtain some day, or to go any more fully into incomplete researches now in progress. When the day arrives of perfect knowledge in such matters there may be a very different story to tell. We must, however, take things as they are, and at any rate I think we are pretty safe in taking lecithin as a type of the phosphorized fats, and we are acquainted both with its composition and with the products of its decomposition. It is present in considerable amounts in nervous tissues, and it is owing to its presence that the black staining with osmic acid of the fatty sheath of nerve fibres is mainly due. The use of osmic acid as a reagent for the detection of fat depends on the presence in the fat of oleic acid and its compounds. Oleic acid is the only representative of the acrylic series of fatty acids found in the body, and all the acids of this unsaturated series possess the power of taking oxygen from osmic acid—osmium tetroxide—and so reducing it to the condition of a lower oxide which has a black colour. Fats which are compounds of acids of the acetic series—such as palmitin and stearin—do not give the reaction.

When Wallerian degeneration occurs the degenerated fatty sheath is stained much more readily with osmic acid than the healthy medullary sheath. It will strike the black colour with osmic acid even in the presence of chromic salts, and it is this circumstance that has led to the adoption of a mixture of the two acids, known as Marchi's reagent, for the detection of degenerated fibres. The intense black staining which the degenerated myelin gives is due either to an increase of the oleic acid radical or more probably to a loosening of its combination with other atomic groups, so that it is able to exert its reducing action more forcibly.

Lecithin is a fat which yields on hydrolytic decomposition four groups of materials. They may be represented in the following simple way;

An ordinary fat yields only two—namely, fatty acid and glycerin. The phosphoric acid obtained contains all the phosphorus of the original lecithin, and unites with glycerin to form glycero-phosphoric acid. The fourth decomposition product—choline—is an ammonium-like base, and contains all the nitrogen of the lecithin. I dealt with these points more fully in my Croonian lectures, but it may be necessary to remind my hearers of these main facts in order to pave the way to what we are coming. I would further remind you that Mott and

I showed that in degenerative diseases of the nervous system, as well as in the degeneration artificially produced in animals by the cutting of nerves, the products of degeneration pass into the circulating fluids, and can be detected there. We further showed that in a certain stage of the degenerative process in a nerve all traces of phosphorized fat disappear, and the fat or fatty acid which is absorbed more slowly remains in the nerve sheath for a considerable time, and while it is present it continues to give the Marchi reaction.

THE DETECTION OF CHOLINE.

In our work we laid special stress on the importance of the discovery of choline in the blood and cerebro-spinal fluid. If this is found, there is available a definite proof of the breakdown of nervous tissues. We further indicated that the detection of choline in such situations might be of practical service in diagnosing organic nervous diseases, for functional disturbances are often difficult to distinguish from these by the observance of mere symptoms. This discovery has been confirmed by numerous subsequent observers, and the expectation that the test would be diagnostically useful has also been fulfilled. On the other hand, our methods for the detection of choline have been subjected to criticism, and it has been this criticism which has stimulated us to further work on the subject,

and has led us to modify the tests we previously published, and also to rectify some of our conclusions.

As the invention of the choline test has been hitherto the main practical outcome of our work from the clinical point of view, I take this opportunity, when I am addressing physicians, of amplifying this part of my subject by mentioning the main objections that have been raised to our work, the further examination to which we have in consequence subjected our methods, and the present conclusions at which we have arrived. I think you will find that we have succeeded in confirming all our main previous statements, and what is more important, rendering the means of detecting choline absolutely trustworthy.

The tests for choline which Mott and I chiefly dealt with were two in number.

The cerebro-spinal fluid or the blood was first extracted with absolute alcohol; the alcoholic extract was evaporated to dryness, and the residue again taken up with alcohol, and this operation was repeated several times in order to avoid any contamination with potassium salts. We imagined at the time that potassium salts were quite insoluble in absolute alcohol. The final residue was dissolved in alcohol again, and an alcoholic solution of platinum chloride added; the yellow precipitate so produced was washed with alcohol by decantation, and finally dissolved in 15 per cent. alcohol; on evaporation of this at a fairly low temperature, yellow crystals, prisms, and octahedra separated out, and these consist of the double chloride of choline and platinum. The same test with slight modifications was also adopted by Donath in Germany, who was one of numerous others to confirm our results.*

The second test was a physiological one. It consisted in taking the final residue after alcoholic extraction, and dissolving it in salt solution. When this solution is injected into the blood stream of anaesthetized animals it produces a temporary fall of arterial blood pressure; if,

* Donath's statement that choline is similarly also found in the fluids of epileptics requires confirmation. If the diagnosis of epilepsy in these cases was correct, and the existence of choline is confirmed, it appears necessary to remove epilepsy from the list of functional diseases.

Fig. 1.—Crystals of platino-chlorides of choline and platino-chloride of potassium, on the same slide. (From a photograph by Otto Rosenheim.)

however, the animal has been previously poisoned with atropine, the fall is either absent or replaced by a rise. This action is characteristic of choline, and is quite different from the effect produced by the substances most likely to be confused with choline, which are the chlorides of ammonium and of potassium. It is, however, a test which is not available for ordinary clinical use, and so special interest attaches to the chemical test which can be obtained with smaller quantities either of the cerebro-spinal fluid or of the blood.

It is the chemical test which has been mainly the cause of the criticisms to which I have alluded. Some of our critics seem to have thought that we had been content to diagnose the crystals of the choline platinum compound by mere inspection, which is usually a fallacious method of identifying any crystalline substance. If our original papers are consulted, it will be seen that this is not the case; in some cases where we were successful in obtaining a large supply of material, we examined other properties of these crystals (their solubilities, the amount of platinum in them, etc.), and, moreover, found that in heating they gave out the odour of trimethylamine; and we further supported our statement that choline was present by performing other tests in addition.

Some critics—for instance, Vincent and Cramer—regarded our contentions as “*a priori* improbable” and “scarcely conceivable,” but they did not examine either pathological blood or cerebro-spinal fluid in order to determine whether the facts as we had stated them were correct or not.

The first serious piece of criticism came from Guy's Hospital. Allen and French pointed out that the treatment with absolute alcohol did not get rid of potassium salts entirely; and as the platino-chloride of potassium is exactly similar in form to that of choline platino-chloride inspection of crystals obtained by our method was insufficient to distinguish them. Inspection of crystals is usually the only test which a clinical observer has time for; and if the amount of material is small it is probably the only available test. On account of this uncertainty, Allen and French abandoned the platinum test entirely, and adopted instead a modification of the iodine test for choline in which there is no risk of such confusion. By the help of this reaction, Allen subsequently confirmed our statements concerning the presence of choline in the blood of patients suffering from acute degeneration of nervous structures.

The accompanying drawing from a photograph (Fig. 1) will illustrate the impossibility of identifying the two platino-chlorides in question by their crystalline form. At this lapse of time I cannot remember which of the crystals are those composed of the choline and which of the potassium

compound. They are quite indistinguishable by mere inspection; but they can be distinguished, as I shall presently show, and were actually distinguished in the specimen from which the photograph was made.

Shortly after Allen and French published their observations, a paper by Mansfeld appeared in one of the German journals criticising Donath's results on much the same lines. I thought, therefore, it was high time for us to take up the matter once more, and I therefore placed it in the hands of Dr. Otto Rosenheim, whose knowledge of chemistry and chemical technique is much superior to my own, and he carried out the research in my laboratory. In the course of his work he came to the conclusion that the solubilities of potassium and ammonium salts in absolute alcohol and of their platino-chlorides in 15 per cent. alcohol, though small, were nevertheless such as to make a contamination of the final choline platino-chloride, with platino-chlorides of potassium or ammonium, a possible source of error. It was therefore necessary to search for other tests for choline which are not given by these inorganic salts.

As an outcome of his work he discovered three such tests, but I shall be content here with describing one only, since it is simple and easily applied, and, moreover, is absolutely decisive. Like Allen's, it is a modification of the iodine test, and it is performed in the following way: A strong solution of iodine in potassium iodide is added to a preparation of the choline platinum chloride

crystals; these then alter in a characteristic way, and the change may be watched with the microscope. In the course of a minute or so the yellow crystals as shown in Fig. 1 disappear, and their place is taken by dark-brown plates and prisms in large quantities. They show marked dichroism, they are doubly refracting, and have a superficial resemblance to the well-known haemin crystals. Their appearance is depicted in Fig. 2. They are composed of a periodide of choline ($C_5H_{14}NOI_2$), but are extremely unstable, and if the slide is allowed to stand, so that the liquid gradually evaporates, the crystals begin to disappear, and their place is taken by brown oily droplets, or sometimes clear spaces showing the skeletons of the crystals are seen. This indicates the formation of a lower iodide, and the

appearance is depicted in the next figure (Fig. 3). If now a fresh drop of the iodine solution is added, the crystals gradually form once more, and their formation and disappearance can be watched repeatedly.

If platino-chlorides of potassium or ammonium are present on the same slide, they remain unchanged under the action of the iodine solution.

It was possible by this simple test to detect choline in 20 c.cm. of blood when choline had been added in the pro-

Fig. 2.—Photomicrograph of the crystals of choline periodide. (O. Rosenheim.)

Fig. 3.—This shows the disintegration and the formation of oily droplets which occurs when the choline periodide is exposed to the air. (From a photograph by O. Rosenheim.)

portion 1 to 20,000. When 5 c.cm. of blood containing choline in the proportion 1 to 2,000 were used, the whole field was covered with crystals, which could be seen with the naked eye.

In the same number of the *Journal of Physiology* in which Rosenheim published these interesting and striking results, Donath answered his critics by publishing another distinctive character of the crystals of the platino-chloride of choline. They are doubly refracting, and so appear bright in the dark field of the polarizing microscope, and show changes in illumination when they are rotated in the field. In this way every microscopic fragment of the choline platino-chloride is rendered visible which by ordinary microscopic methods might escape detection owing to their transparency. The platino-chlorides of potassium and ammonium do not exhibit this phenomenon. Donath puts his case very well when he says:

"The occurrence of inorganic chlorides which have hitherto interfered with the testing for choline by the platinum reaction on account of their slight solubility in absolute alcohol, is a circumstance which has lost its terrors, so much so that an actual addition of potassium-chloride has become part of my method, and causes no difficulty when the polarization test is applied."

He then proceeds to give a list of cases where he has examined the cerebro-spinal fluid removed by lumbar puncture from patients suffering from various nervous diseases, and illustrates his results by a series of photomicrographs showing the crystals under various positions in the field of the polarizing microscope.

Dr. Rosenheim has confirmed these statements, and the next figure illustrates the appearances observed.

In Fig. 4 (A) the crystals of the platino-chloride of choline are seen as separated from an actual case of pathological cerebro-spinal fluid. In this case they were crystallized from an aqueous solution, and have taken the needle-like form they usually exhibit when crystallized in this way. Mixed with them are seen a number of small octahedra of the platino-chloride of potassium. Fig. 4 (B) shows the same preparation under polarized light; the crystals of the choline salt show up as bright needles, but the crystals of the potassium salt have disappeared from view. The crystals of the choline salt in this case further gave Rosenheim's new iodine reaction.

In some cases Rosenheim made out another fact which is not devoid of significance. If he obtains from cerebro-spinal fluid which contains choline a slide of the crystals of the mixed platino-chlorides, and places it under the field of the polarizing microscope, the inorganic

platino-chlorides exhibit no double refraction, but a large proportion of the crystals present show the phenomenon. If he then subjects the same slide to his iodine test many of the doubly refracting crystals are transformed into the brown crystals of the periodide of choline, but some remain unaltered, and others yield crystals of different form from the choline periodide.

In other words, some of the doubly refracting crystals are not choline compounds, but probably crystals of other organic platino-chlorides. This is only what one would expect. Mott and I were always from the first careful to point out that choline is not the only product of nervous breakdown; the complex chemical structure of nervous material to which I have alluded in some of the earlier passages of this lecture would lead one to suppose that the cleavage products which are liberated during the degenerative process would be exceedingly numerous. We called attention, among other points, to the great increase of the nucleoprotein which passes into the cerebro-spinal fluid in such circumstances. The importance of the detection of choline arises because it is at present the only one of these numerous substances which has been identified with certainty, and which can be detected with comparative ease. Its presence indicates the breakdown of one of the best known of the constituents of nervous matter (lecithin), but suggests that it must be accompanied by the presence of numerous other similar and even dissimilar compounds.

During the last year Dr. Mott has sent from Claybury Asylum a great number of specimens of cerebro-spinal fluid to Dr. Rosenheim, and the latter has subjected them to his new tests. The number of specimens of blood similarly sent has been small, and hitherto choline has only been detected in one of these; they were in the main from cases where choline would hardly be expected to occur, for, as Mott pointed out, active degeneration must be recent for the test to be a decisive one.

But the examination of the cerebro-spinal fluids have been fully satisfactory, and a sufficient number of positive results have been obtained to corroborate the views of Mott and myself. I do not propose to anticipate any further Dr. Rosenheim's full paper on the subject, except to say that it has ultimately been found better to shorten

the procedure of testing by applying the iodine reaction direct to the alcoholic extract of the fluid. There is no necessity to prepare the platino-chloride first and apply the iodine test to those crystals. It was found that some of the other bases already referred to, the identity of which is still uncertain, often by their presence interfere with the iodine reaction when it is applied to the mixture

Fig. 4 (A).—Preparation of crystals of the platino-chlorides of choline (needles) and of potassium (octahedra) obtained from a specimen of cerebro-spinal fluid from a case of general paralysis of the insane. (O. Rosenheim.)

Fig. 4 (B).—The same preparation in the dark field of the polarizing microscope; the crystals of the choline salt are bright, but the crystals of the potassium salt have become invisible. (O. Rosenheim.)

of the crystalline platino-chlorides. This is an additional reason for using the test in the direct manner.

I had, happily, kept a considerable number of the preparations of crystals which Mott and I had made years ago, and from which we drew our previous conclusions. On examining these afresh by the new means of identification we now possess, I have found that without doubt they do not consist wholly of the choline compound, but contain a considerable admixture of inorganic platino-chlorides, especially the platino-chloride of potassium.

We, however, still hold that the obtaining of a large crop of crystals, whether they be those of the choline salt or a mixture of the potassium and choline salts, is diagnostic of extensive breakdown in nervous tissues. The contrast between such cases and the insignificant yield from normal blood is most striking. This is quite intelligible when we take into account the very high percentage of potassium that nervous tissues contain. This has been amply demonstrated by the microchemical work of Macallum and of Macdonald. The rôle which Macdonald assigns to the potassium salts in nervous phenomena it is unnecessary to discuss here, interesting and important as his views are.

This has suggested to us a new piece of work which has only just been started—namely, the actual estimation of the potassium in the cerebro-spinal fluid and blood in cases of acute degenerative diseases of the nervous system in comparison with the normal. I am sorry I cannot at present give any final figures, but, so far as the preliminary work goes, it indicates a considerable increase of the potassium in those cases where disintegration has occurred, and where choline is also discoverable.

THE PHYSIOLOGICAL TEST FOR CHOLINE.

I have devoted so much time to the chemical test for choline because that is the one so obviously suitable for clinical work. The physiological effect on the blood pressure that choline exercises is, however, not devoid of interest, and a brief mention of some recent work in this direction will conclude what I have to say. Swale Vincent, in his earlier work on the physiological action of extracts of nervous tissues, found that the intravascular injection of such extracts caused in anaesthetized animals a considerable fall of blood pressure. I had simultaneously published similar results, and attributed the fall to the presence of choline. Vincent, however, denied that choline was present. He subsequently, with Cramer, amended this statement, but was of opinion that the choline present was in the form of dicholine anhydride. The existence of this compound is very problematical, and the analytical evidence presented is not very convincing; still the suggestion that compounds or modifications of choline may exist is not devoid of interest. Vincent and Cramer also found what I had missed—namely, that there are other substances present in such extracts which are readily soluble in ether, and which produce a much more powerful depressor effect on the blood pressure than choline, and that in the case of such substances the depressor effect is not abolished by atropinization. The identification of these other materials was not attempted. It is quite possible that these substances are absolutely distinct from choline; and, on the other hand, the view is permissible that they are choline derivatives. This second view gains point from a study of some experiments which Reid Hunt and Taveau brought forward at the meeting of the British Medical Association in Toronto last year.

Dr. Hunt is one of numerous American pathologists who have repeated and confirmed the original statements of Mott and myself, and has thrown himself into the choline controversy with characteristic transatlantic enthusiasm. He has prepared and studied the physiological action of as many as 19 compounds of choline, and suggests the possibility that some of these may be formed in the body. Some of them are more and others less active than choline itself; the most powerful is acetylcholine; this is one hundred times more active in producing a fall of blood pressure than adrenaline is in producing a rise; the injection of a few cubic centimetres of a solution containing it, diluted with one hundred million times its volume of water, produces a distinct effect in a rabbit. The action of acetylcholine is not annulled by atropine, and it is capable of overcoming the effect of adrenaline. On the other hand, some of the choline

derivatives examined were less powerful than choline itself; the introduction of a phenyl group, for instance, diminishes its depressor effect.

As an outcome of his work, Dr. Reid Hunt recommends two new tests for choline; one is the formation of the acetyl compound to render the physiological test more sensitive: the other is the formation of the benzoyl compound; this gives a distinctive crystalline platinum salt which cannot be confused with the platino-chlorides of ammonium or potassium. I have not actually tested these methods myself, but I think I have said sufficient to show that in the future those engaged in research will have no lack of methods to render the testing for choline a matter of no difficulty.

REFERENCES.

The bibliography of this subject up to 1905 will be found very completely given in my article on *Die Biochemie der Nerven*, in the *Ergebnisse der Physiologie*, vol. iv, p. 23, 1905. The principal papers which have appeared since are the following: J. Donath, *Journal of Physiology*, vol. xxxiii, p. 211; Rosenheim, *ibid.*, p. 220; Reid Hunt and Taveau, *BRITISH MEDICAL JOURNAL*, 1906, ii, p. 1788. Several observers have surmised that the breakdown of lecithin is due to the activity of a ferment; the ferment has, however, not been isolated. Marinesco (*La Presse Médicale*, February 16th, 1907) suggests that the ferment is formed by the neurilemmal cells, which actively multiply during Wallerian degeneration.

REMARKS ON A CASE OF SEVERE COMPOUND FRACTURE OF THE SKULL: RECOVERY.

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THE result of a severe injury of the head on the higher faculties is very uncertain and variable, and therefore it is always wise not to venture upon a hasty prognosis. After a severe concussion of the brain the patient may be often roused from a state of partial insensibility, and may even respond to simple questions, yet from the facial expression and the slowness of the articulation it is evident that a thick cloud is hanging over the intelligence, and this may soon end in fatal coma. Sometimes a moderate amount of shock and mental confusion is followed by the acute excitement of cerebro-meningitis, which terminates in damage to the sensory functions and permanent impairment of the faculties. On the other hand, cases of dangerous injury attended with deep insensibility and other grave symptoms do occur, and yet the patient ultimately recovers without any permanent disorder of the mental powers, as in the following case:

REPORT OF CASE BY DR. M'ELDOWNEY.

The patient was a young man, 18 years of age, who was just convalescent from an attack of typhoid fever. On March 21st, 1904, he retired to rest in fair health, but about 7 o'clock next morning he was found in bed in an insensible condition, with extensive head injuries inflicted with a heavy poker found in the room covered with blood and hair, and much bent by the force used in inflicting the blows. His head and face were enveloped with dried blood, the bed and carpet were saturated, and the ceiling and walls were spattered in every direction.

On my arrival at the house the patient was sufficiently conscious to say, "Hullo, doctor!" but he did not reply to questions, and shortly afterwards vomited and became unconscious. The pulse was then extremely rapid and feeble; the pupils were equal, half dilated, and insensible to light.

About 9.30 a.m. Mr. Ward Cousins met me in consultation. The patient was wrapped in blankets and placed on a table in another room; his head was then shaved and the scalp thoroughly sterilized. By this time the patient had rallied somewhat; his pulse had improved, and he showed some signs of restlessness and pain. An anaesthetic was administered, and we proceeded at once to examine the injuries and to carry out surgical treatment. The fracture extended over the posterior and inferior part of the right parietal bone, and involved also the upper edges of the squamous portion of the temporal and occipital bones. The diagram (Fig. 1) exhibits the outline of the broken and lacerated area where the fragments were driven in and firmly jammed together. The injury, however, extended over a larger portion of the cranium, for the edges of the opening were fissured and depressed in all directions. The dura mater and scalp were both extensively torn, and cerebral matter had escaped in two places into the wound through lacerations caused by portions of the bone, which had been driven into the brain (Fig. 2).

With the aid of the trephine and forceps all the fractured pieces were removed, and the depressed edges were elevated into position. The torn dura mater was, as far as possible, closed with catgut, the injured and bruised scalp placed in position and united by silkworm-gut sutures. Gauze drains having been introduced, the dressings were then applied.

Very little vomiting followed the operation. The patient