Victor Horsley Memorial Lecture
ON
**THE RELATIONS OF SURGERY AND
PHYSIOLOGY.**

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BY

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I FEEL it a peculiar honour to have been asked to give the first Victor Horsley Memorial Lecture. I had the less hesitation in acceding to the request that I should do so because I am not only his oldest surviving scientific friend, but also his first fellow worker. It is nearly half a century ago that he made his appearance as an eager, intelligent student in the old Physiological Laboratory at University College. Sharpey had but recently retired from the teaching of physiology, although his personal influence was still felt. His place had been taken by Burdon-Sanderson, whose dominant idea was to make the work of the subject as experimental as possible; and anyone who has known Victor Horsley will readily understand with what keen interest this idea would inspire him. There can indeed be no doubt it was this training in experimental physiology which determined Horsley's future career, both as a physiologist and as a scientific surgeon. And it is this double career which may appropriately be chosen as an example of the mutually beneficial influence of surgery and physiology.

I had almost been tempted by our long and intimate friendship, which began so auspiciously at University College in 1875 and lasted until the day of his death in Mesopotamia in 1916, to dwell, on this the first opportunity of commemorating his career, upon the personal traits which were so striking a feature of Horsley's character—his enthusiasm, his love of truth and hatred of hypocrisy, his energetic striving for everything he judged to be right and inflexible antagonism to everything he thought wrong. But has not all that been done far better than I or anyone else could hope to do it, in the history which Mr. Stephen Paget has set forth in that inimitable style which characterizes all his writings? It is fortunate that the life of Victor Horsley was entrusted to such a biographer; nor was the biographer less fortunate in having such a subject! How splendidly he has taken advantage of his opportunity we all of us know.

I have chosen "The Relations of Surgery and Physiology" as the text upon which to base the remarks I have to make to-day. It is my object to show that these subjects are mutually dependent; that Physiology must call in the aid of Surgery to solve many of its most intricate problems, and that Surgery cannot make any real advance unless it proceeds hand in hand with Physiology.

It was not Horsley himself who established this principle, but he happened upon the time when it was beginning to be evident. Only a few years before, it might have been admitted that there was a certain amount of interdependence between Medicine and Physiology, but no one would have thought of connecting Surgery with anything but Anatomy. That experiments on animals were necessary in order to elucidate the functions of the body had indeed been conceded. It was recognized from Harvey onwards—yes, and even long before Harvey—that no true advance could be made in physiology without such experiments. The operations involved in them have somewhat unfortunately received the designation of "vivisection," and this title has caused many who are ignorant of their nature to regard them as of an entirely different character from surgical operations in the human subject—although they are conducted in exactly the same manner as in man, with the same precautions to prevent unnecessary pain, and with every effort to avoid unsatisfactory complications which might result from wound-infection and the like. But many of the older surgeons refused to believe that an operation on the lower animals could be utilized to obtain

information which would be useful to them in the performance of similar operations in man, nor should I be surprised to hear that there are some who still hold this view. It is fortunate for the world that Victor Horsley was not one of these.

As I have remarked, he happened upon a time when the importance of animal experimentation as a guide to surgery was beginning to be recognized. There were two directions in which this tendency was particularly apparent. One of these involved the investigation of the functions of the brain: the other those of what we now term endocrine organs—the uses of which were then for the most part completely obscure. And it was just these two subjects which attracted the attention of the physiologically trained but hitherto unknown young surgeon whose work was to throw so much light upon these dark places of the organism; places which hardly anyone had hitherto ventured to approach. It is on this account that I propose to deal first with these particular aspects of the question of the relations of Surgery and Physiology. I will begin with the subject of the functions of the brain and its related subject, cranial surgery.

THE FUNCTIONS OF THE BRAIN AND CRANIAL SURGERY.

Not very long before the entry of Victor Horsley to University College as a medical student, a young Scotch physician named David Ferrier published an elaborate series of researches on the results of electric stimulation of the cerebral cortex in animals. Some of these were confirmatory of experiments performed on the dog and cat by Fritsch and Hitzig, although the method of stimulation employed by Ferrier was a vast improvement on that used by the German observers. But what rendered Ferrier's results really important was the fact that he extended these researches to the brains of monkeys, which are entirely different in the conformation of the cerebral cortex from the brains of the dog and cat, but present a remarkable resemblance to the brain of the highest member of the order Primates, man. It is scarcely necessary to say that the brilliant experiments of Ferrier aroused universal interest. I shall myself never forget the impression made upon me by one such experiment which Ferrier showed to Burdon-Sanderson and the rest of us who were working in his laboratory. The confident way in which he could predict what would be the movement resulting from touching this or that portion of the cortex with the electrodes was calculated to arouse our wonder and admiration; and the demonstration always provokes the same feelings in every audience of students when the experiment is repeated before them. It was these experiments—supplemented as they have since been by those of Horsley and Beever on the brain of the orang, and by the yet more recent and accurate results obtained by Sherrington and Grünbaum upon the chimpanzee and gorilla—which have enabled the surgeon to locate the seat of an injury and tumour in the human brain, and to remove the tumour or to deal with the source of injury with advantage to the patient.

In all researches in experimental physiology, there are two chief methods employed to elucidate the functions of an organ. One is the artificial stimulation of the organ, causing it to pass into a condition of activity, the effect of such activity being duly noted. The other is the production of an injury in the organ, or its complete removal, the effect, if any, which results from such injury or removal being observed. With regard to the functions of the brain, this last aspect of the subject had by no means been neglected by antecedent workers, but discrepant results had been obtained. Indeed, up to the time of which I am speaking—that is, the epoch of Fritsch and Hitzig, and of Ferrier—physiologists were disposed to agree with Flourens that the whole cortex acted as one undivided organ and that the several parts of the body are not individually represented in it; in other words, that there is no such thing as localization of functions in the cerebrum. One acute clinical observer, Hughlings Jackson, had, it is true, pointed out that the phenomena of traumatic epilepsy seem undoubtedly to indicate the existence of some kind of localization in the cortex; since the "march" of the movements which result from the excitation producing the epileptic fit is different according to the seat of injury.

But such a complete localization as we now know to exist was unsuspected, and it was largely on this account that so much interest was aroused by the excitation experiments of Ferrier.

But if excitation of a particular area of the cerebral cortex provokes certain movements, it does not follow that we are to regard that area as representing a nerve centre for governing or producing those movements unless removal of the area is followed by paralysis of the movements. We may leave out of present consideration whether the so-called centre is automatic—that is, works spontaneously—or whether it only represents the point of arrival of sensory impulses and the point of departure of the corresponding impulses to motor centres in the lower part of the central nervous system—that is, whether it is a reflex centre. For this question, which was warmly debated at one time, may now be considered to be definitely settled in favour of the second hypothesis. In either case the final result of excitation and of ablation will be in the first case production of definite movements, in the second the inability to perform them.

At the period I am speaking of, many of the facts had been established, but the explanation was a matter of controversy. There were, moreover, still certain parts of the hemisphere which Ferrier had not explored, or which in his hands had yielded negative replies. And the results of the extirpations which he had performed in conjunction with his colleague Gerald Yeo, then professor of physiology in King's College, were not altogether satisfactory, nor did they agree in certain particulars with the work of others, especially that of Herman Munk of Berlin, who was working on much the same lines both in the dog and monkey.

This, then, was a problem still needing elucidation, and when in 1883 I succeeded Burdon-Sanderson in the Chair of Physiology at University College it was one of the first investigations at which I resolved to work, especially with the view of determining more exactly the results of removal of definite areas of the cortex. Now Ferrier and Yeo's work—I am referring only to their earlier work, the later was accomplished under different conditions—had been done by pre-Listerian methods, and I felt convinced that this might be the source of some of the discrepancies exhibited, as compared with the results of Munk and others. My own surgical training was unfortunately also pre-Listerian owing to the slow progress which was made in London in the adoption of Lister's methods, and the active opposition with which they were met by many of the leading London surgeons. I therefore recognized the necessity of securing as a collaborator a young and skilful surgeon thoroughly imbued with Listerian ideas and enthusiastically interested in physiology. You may easily understand that I had no difficulty in making my selection, for Victor Horsley fulfilled all these conditions, and we were already on terms of personal intimacy. Gleefully did he accept the proposition that we should carry out this work together, and many were the hours which we devoted to it. In every case the first part of an experiment consisted in exploring by induction currents, after the manner of Ferrier, the particular area we desired to investigate, and the second part in removing the explored area, re-covering the brain and sewing up the wound. In these operations we made use of every Listerian practice, including to our woeful discomfort the recently introduced carbolic spray—a source of endless objurgations!

To these operations Horsley brought a remarkable amount of surgical skill. Our quadrumanous patients were kept under the best possible conditions, and in most cases made speedy recoveries. It is not saying too much if I add that Horsley obtained from these experiments a surgical experience of a unique kind. This experience he was presently—in his capacity of surgeon to the great hospital in Queen Square—to apply to the alleviation of human suffering in a domain which even the boldest surgeons had not ventured seriously to attack.

There is no better illustration of the mutual benefit which results when Surgery and Physiology go hand in hand than the history of our early efforts in this field of investigation. The benefit to Horsley I have pointed out. And for myself, I acknowledge with gratitude the debt I owe to my colleague for the opportunity I was afforded of learning the application of Listerian surgery to animal experimentation, a

lesson the benefit of which I am more than ever conscious of after nearly forty years' experience, much as things have changed both in Physiology and in Surgery since that far-off, but never-to-be-forgotten time.

Our partnership was a fruitful one. We were able to extend Ferrier's observations in the monkey's brain to parts which he had not explored, although in this particular he had not left much for future investigation. But the young worker may take it from me who have grown old and experienced in scientific investigation, that if he wishes to discover new things he will do well to repeat with the aid of modern contrivances any experiment which has been long accepted as affording the last and most incontrovertible word on the subject. Almost certainly he will find some point which has been overlooked by the original investigator, and needless to say by those who have merely aimed at getting the same results. And almost certainly the exception will prove—that is, will test—the rule, and he may easily find that which has been looked upon from time immemorial as scientific gospel is badly in need of re-editing. In my experience nothing is so fertile in discovery as going carefully with one's eyes open, and with the aid of new methods, along a well worn track. I say with one's eyes open, for if one shuts them to everything that is not exactly what one expects to see many a discovery will be overlooked.

It is not my purpose to give an account of our work on the brain—work which, begun together, was eventually by force of circumstances carried on independently or in conjunction with other workers. One word, however, I would say about a trait in my colleague which, although in no way unfavourable to his character, rendered the actual conduct of our joint investigation somewhat laborious. He was too energetic. He would think nothing of performing several operations at a sitting, and acquired so much skill at them that they occupied a relatively small amount of time. But the operation was one thing, the study of the symptoms quite another. Now it takes a long time to make a thorough investigation of symptoms in the human subject—although in this case the subject himself can give much assistance. But when it comes to making the same kind of investigation in animals, and especially in monkeys, which are often wild, and the attention of which it is always difficult to fix, an unconscionable amount of time has to be devoted every day to each case. It so happened that just about this time Horsley was leading an extremely busy life. He was surgical registrar at University College Hospital—a position involving a huge amount of clerical work—and later assistant surgeon there; professor superintendent of the Brown Animal Sanatory Institution; assistant professor of pathology in University College; had a considerable if not very remunerative private practice; and, last but not least, was engaged to be married. The result of all this was that most of the observations on the operated animals had to be made by his colleague, and when there were several to be examined the amount of time that these occupied every day rendered the duty severe. All the clinical notes thus taken day by day had to be collated, and eventually boiled down—a process which involved many prolonged conjoint sessions. Upon the results of this collaboration I need not dwell. Are they not written in the chronicles of the Royal Society? And are they not decently buried in the *Philosophical Transactions*? May they rest there in peace!

The experience which Horsley had gained in these experiments—commenced in the laboratory at University College and continued at the Brown Institution—was invaluable to him in dealing with cranial surgery in man, and when the position of surgeon to the Hospital for Nervous Diseases in Queen Square fell vacant Horsley received the appointment. He lost no time in applying the knowledge he had acquired in the laboratory to the operating theatre in the hospital. Paget gives an interesting and humorous account of the first operation he performed there for a cranial tumour (p. 120). It was upon a Scotchman, was in every way successful, and was witnessed by a distinguished company, which included Hughlings Jackson and Ferrier. It was, of course, followed by many others, and these were often attended by eminent foreign surgeons, for Horsley's reputation as a cranial surgeon soon became widespread.

The facility with which he used either hand contributed not a little to the dexterity of his operations, and he never, in any circumstances, lost the sang-froid which is essential to the surgeon.

THE FUNCTIONS OF THE THYROID GLAND.

Although by the work which Horsley had done upon the brains of monkeys and apes he had become one of the most skilful and scientific operators upon that part of human anatomy, he was much too all-round a man to confine himself to a single object, and we must next follow his career in another subject—that, namely, dealing with the functions of the thyroid gland, to which he brought equally keen enthusiasm for physiological investigation and skill in surgical procedure. Like that upon the functions of the brain, this also has an interesting preliminary history.

The year before Victor Horsley was born, Moritz Schiff of Geneva, one of the most active physiologists of the middle of the last century, had published the results of observations he had made upon animals, the thyroids of which he had extirpated. But at that time neither physiologists nor medical men were prepared to take much interest in the thyroid, nor indeed in any of the so-called ductless glands, which now under another name occupy so prominent position both in physiology and in clinical medicine. Schiff's work, therefore, which was not without interest and importance, passed unnoticed, and the matter was allowed to rest for many years. But just about the time that Horsley was starting his surgical career, the subject of the thyroid and its functions had come into prominence on account of the fact that it was becoming the practice amongst surgeons in Switzerland—in which country tumours of the thyroid are common—to remove such tumours entirely when they were inconveniently large. In such cases of complete removal very serious symptoms resulted—symptoms which closely resembled those which had been described some ten years previously by Sir William Gull as a cretinoid condition of adult life, and were later shown by Ord to be associated with absence or atrophy of the thyroid: Ord applied the term "myxoedema" to the syndrome. The symptoms resulting from thyroid removal were recognized by the Swiss surgeons J. and A. Reverdin as resembling those of myxoedema, and they gave to them the name *operative myxoedema*. Th. Kocher, who described them at about the same time, spoke of the syndrome as *cachexia strumipriva* or *thyreopriva*, the name by which it is now generally known, although the term "operative myxoedema" best describes its cause and symptoms. These observations of the Swiss surgeons were published in 1883, and led immediately to a great revival of interest in the thyroid both amongst physicians and clinicians. Schiff himself repeated and extended his old experiments, and many other physiologists took up the subject, interest in which is indeed by no means exhausted even at the present day.

How Victor Horsley came to start experiments upon the thyroid is narrated by Paget:

"On November 23rd, 1883, at a meeting of the Clinical Society of London, there was a discussion over a case of myxoedema shown by Dr. Drewitt; and Felix Semon called attention to Kocher's observations and said positively that cretinism, myxoedema, and cachexia strumipriva were closely allied conditions, having in common either absence or more probably complete degeneration of the thyroid gland: and that they could hardly be attributed to any other cause. On December 14th the Clinical Society appointed a Committee to investigate the whole subject. Ord was Chairman, Hadden was Honorary Secretary, and Horsley was a member of the Committee.

"It was of necessity that the investigation should include an experimental study of the healthy gland in healthy animals . . . and recognizing 'the hitherto undreamt of importance of the thyroid gland,' they asked Horsley to study it by the experimental method. They needed a physiologist and a surgeon, and they had them in him."

Horsley started this investigation in my laboratory at University College, working at first with Rickman Godlee, who was also a member of the Committee. They made several experiments together upon monkeys: we had a room specially prepared and warmed for keeping those animals. But very soon the work was transferred to the Wandsworth Road, Horsley being now professor superintendent of the Brown Institution there, and he found it

inconvenient to carry on work in both places. So he continued the investigation alone, and dealt with the results in the lectures which he was expected to give annually at the University of London, the first of these being published in the *British Medical Journal* in January, 1885, and the next in the *Lancet* in 1886. It is somewhat singular that, with the exception of two short notes communicated to the Royal Society, he never took the trouble to send the results of these experiments upon the thyroid to any scientific periodical, although they were mentioned in his annual reports to the Committee of the Brown Institution, and ultimately appeared in the report of the Committee on Myxoedema, published in 1888.

The reason for this silence on the part of an investigator like Horsley, who never in any other subject had the least hesitation in giving his results to the world whenever they were sufficiently definite, was, I imagine, a certain indefiniteness and variability in the effects obtained from the removal of the gland. For some animals were simply rendered apathetic, with slow movements, a low body temperature, and a general deficiency in vitality; others showed acute nervous symptoms, with muscular tremors, which might pass into fits of greater or less violence, and terminate in death. Horsley himself seems to have thought that these were stages of the same condition. But we now know that the two kinds of symptoms were due to entirely different causes, as in the one case the thyroid alone had been removed, and in the other the removal had included the parathyroids. Unfortunately, at the date of these experiments, the parathyroids, although they had been seen and described some years earlier, had not been recognized as organs having an entirely different function from the thyroid. It was only some years later (1891) that Ernest Gley, the eminent professor of physiology in the Collège de France, discovered this function, and showed that the symptoms of nerve excitation are entirely due to the removal of the parathyroids, and are not seen when these, or some of them, are left intact in removing the thyroid. On the other hand, removal of the thyroid alone without the parathyroids produces all the symptoms of cretinism and cachexia strumipriva.

The fact that when dealing with young animals the parathyroids (unless looked for, and they were at that time unknown) are more likely to be removed along with the thyroid (as age advances, some of them move further away from the thyroid) accounts for the circumstance that Horsley found most of his young animals died in a few days with violent nervous symptoms. In consequence of this he missed the very important point that the thyroid exerts a remarkable influence on growth and nutrition, including the nutrition of nerve cells; which is indeed now established as one of its principal functions. But we cannot blame him for missing this point, since our knowledge of the thyro-parathyroid apparatus was not sufficiently advanced at the time.

THE PITUITARY BODY.

There is another important endocrine organ to which Horsley devoted a good deal of attention—namely, the pituitary body. He was, I believe, the first to endeavour to determine the effect of removal of this organ, for about 1886 he made one or two attempts to reach and destroy it through the pharynx and base of the skull. The conclusion he arrived at was that it is an organ which is not essential to life. Many years later he repeated these experiments and apparently saw no reason to alter his opinion, although in the meantime a number of other investigators who adopted other means of reaching the gland had come to an opposite conclusion. There is now no doubt that in most adult animals at least the loss of the pituitary body or even of its anterior lobe alone is incompatible with life, and had Horsley proceeded to attack the gland by the same (lateral) route as has been employed by most other investigators, a route in which every step of the operation is visible, and perfect asepsis can be ensured, he would, I am sure, have obtained the same results. His original method offers many difficulties from the liability to haemorrhage and sepsis, and from the impossibility of seeing what one is removing when working at the bottom of a deep and narrow hole.

Horsley was inclined to regard the results obtained by

those who operated by the lateral method as due to interference with the brain, but this could not be so, for exactly the same operation can be performed for exposure of the pituitary, but if it is left untouched no adverse symptoms follow. Moreover, one of my assistants, Mr. Norman Dott, himself a skilful surgeon, has recently devised a method of destroying the gland completely in the cat, by a process of electrolysis, without any exposure or any injury to the brain. The sella turcica is reached by passing a fine trochar conveying a carefully guarded needle along the outer margin of the orbit, and through the sphenoidal fissure. This needle conveys the necessary current and the whole operation occupies only a minute or two. By careful adjustment of the position of the electrolysis needle it is possible to destroy either the anterior or posterior portion of the pituitary. If the anterior part is destroyed, the animal will inevitably die within two or three days, a result precisely similar to that obtained by Paulesco, Harvey Cushing, and others, when operating on adult dogs by the lateral method.*

Although Horsley had occasion to perform on the human subject a certain number of operations for removal of tumours of the pituitary, his physiological experience in connexion with this organ had not the same influence in determining the corresponding surgical proceedings in man as had the experiments upon the brain. This was partly owing to the fact that tumours of the pituitary are rare, and that the methods for getting at the pituitary in the human subject are different from those employed for animals. Moreover, such tumours are often very slow-growing, and are not attended with immediate risk of life; whereas complete removal of the gland is dangerous if not fatal. And with regard to tumours of the thyroid, they can often be successfully treated without operation, and only occasionally pass from the hands of the physician into those of the surgeon. But I have, I hope, said enough about the physiological and surgical work of Horsley to illustrate the subject of this address, the close relationship that should exist between Physiology and Surgery. Horsley himself laid particular stress upon this. Mr. Paget tells us that when in January, 1911, the first Lannelongue prize—which was to be awarded once in five years to the surgeon who in the previous ten years shall have done most for the advancement of surgery—was presented to him:

"He spoke a few words of thanks . . . and said that his own country, which had long been under the influence of John Hunter, had later come under the influence of Claude Bernard, who had joined together physiology and surgery. That is what I have striven to realize. Unfortunately if surgical science advances with fair rapidity, its practice progresses slowly. That is because we are held in bondage by tradition from which we have difficulty in freeing ourselves."

Clearly he meant by this the supposed dependence of surgery on anatomy, when he himself so clearly saw that it is physiology which it must in future depend upon, or only so far on anatomy as mechanical considerations may render necessary.

WILLIAM SHARPEY.

I am now going to give you an illustration of the advantage of the association of Physiology and Surgery from the career of the most eminent surgeon of our generation, Joseph Lister. Lister was essentially and fundamentally a physiologist. He was easily the most distinguished pupil of William Sharpey, and William Sharpey was unrivalled as a teacher of physiology. This is the more strange, since Sharpey himself did little or no original work in the subject. Nevertheless, no one gave more encouragement to his pupils to conduct physiological inquiries or more sympathy in their researches than he. The failure on his own part to carry out physiological investigations was due to his training. This was wholly anatomical. When he went to study in Germany it was Rudolphi's dissecting room he frequented, not Johannes Müller's lecture room and laboratory. Had he attached himself to the last named, he would have consorted with all the great German physiological workers of the middle of the last century—Helmholtz, du Bois-Reymond, Ludwig, Brücke: or had he gone to Magendie in Paris instead of to the anatomical and

surgical schools there, he would have consorted with Claude Bernard, would have become the outstanding physiological investigator in Great Britain, and would have occupied the place in London which Bernard occupied in Paris. But the tendency of the Edinburgh School in his day was wholly in the direction of anatomy, doubtless owing to the fact that the anatomical chair in Edinburgh has always been occupied by a succession of pure anatomists; whereas, although there existed a chair of physiology even prior to that of anatomy (rightly known as the "Institutes of Medicine"), it was never held by a physiologist until the appointment of Rutherford in 1884, of whom I am myself the unworthy successor. Fortunately we have illustrious examples to the contrary now, but the anatomy of those days exercised an influence upon its devotees which was not favourable to active research and least of all to experimental work. It must further be remembered that Sharpey was actually a lecturer on pure anatomy in Edinburgh when he was invited to occupy the chair of general anatomy and physiology at University College. Up to that time he had not taught physiology, nor had he received any training in it, although he had interested himself in certain physiological problems, especially those connected with the growth of bone and the action of cilia. It was too late for him to undergo a fresh course of training, and he was busy with his new duties. He had, therefore, to get up his physiology as best he could. The Council of University College would have done well if it had given him a free year to study physiology in France or Germany, but in those days there seemed to be no idea that anything of the kind was necessary: the governing bodies of universities rarely do the right thing in these matters! So Sharpey had to be content to teach a subject in which he was only self-trained. The more credit to him that he became so successful. For it is certainly due to his teaching, both directly and through his pupils, that the physiology of the latter part of the nineteenth century became preponderatingly an English science. I trust we still remain in the forefront, but we must admit that other nationalities have during the last five and twenty years made notable advances and are able to challenge any predominance we may have had.

LISTER: PHYSIOLOGIST AND SURGEON.

If I have been led away by the reverence I have for his memory to speak at greater length of Sharpey than I had intended, I have justification for doing so because of his intimate connexion with Lister.

Lister, long before he was a surgeon, was an experimental physiologist, and he continued to be one throughout his whole career. He had had no opportunity of being trained in experimental work, but he was a born experimentalist and trained himself. Whether he would have done better to have worked with Claude Bernard in Paris or with Carl Ludwig in Leipzig must be a matter of opinion, but his self-training had at any rate the advantage of developing his originality. His first scientific investigations were made with the aid of the microscope—an instrument with which he had, through his father, the discoverer of the achromatic lens, been familiar from his earliest days. He was amongst the first to demonstrate the existence of a dilatator pupillae in the iris and to show that, like the sphincter pupillae, which was already known, the dilatator is composed of plain muscle cells. Many later observers, less skilful or less accurate than Lister, have denied the existence of this muscle, but his work has been vindicated and confirmed by the most modern methods of physiology and histology. He also published observations on the arrectores pilorum which confirmed those of Koelliker, and are especially remarkable because he used a new and now universally employed method—that of microscopic sections—for the investigation. Doubtless the student of the present day, familiar with paraffin-soaked tissues and mechanical microtomes, would despise the rough mode of preparation used by Lister, and thus described by him:

"A portion of shaved scalp being placed between two thin slips of deal, a piece of string is tied round them so as to exercise a slight degree of compression; the preparation is now laid aside for about twenty-four hours, when it is found to have dried to an almost horny condition. It then adheres firmly by

* The details of this method will be published in the next number of the *Quarterly Journal of Experimental Physiology*.

its lower surface to one of the slips, and thus it can be held securely, while extremely thin and equable sections are cut with great facility in any plane that may be desired. These sections when moistened with a drop of water and treated with acetic acid are as well suited for the investigation of the muscular tissue as if they had not been dried.*

The existence of such cells in plain muscle had been denied by Ellis in a paper published in the *Philosophical Transactions*, although Koelliker had produced abundant evidence to the contrary. And every student can now easily demonstrate them. But in those days it was not so easy, and the fact that Lister undertook a difficult investigation and succeeded so admirably in obtaining a definite result placed him at once in the first rank of physiological histologists.†

Although these observations were not in themselves purely physiological their importance is entirely so, and had this not been the case it is doubtful if Lister would have spent so much time and trouble over them. It is interesting to remark that both investigations were inspired by the work of Koelliker, who was the predominant histologist of his time, but whose training and early work were physiological. Koelliker was an intimate friend of Sharpey, and it was through Sharpey that Lister made his acquaintance. Incidentally I may, perhaps, be allowed to mention that it was through Sharpey that I myself made the acquaintance and experienced the constant and kindly encouragement of both Koelliker and Lister.

The distinctively physiological bias of Lister's mind was soon to be evidenced—(1) by his work on absorption from the intestine and on the flow of chyle in the lacteals, and (2) by his researches on the vascular changes accompanying inflammation. The first of these researches were made in 1853 while he was still in London, and shortly after he had graduated. Their chief object was to ascertain whether solid particles mixed with the food can be absorbed by the lacteals. He observed these vessels in the mesentery of the mouse, and the conclusion he came to was that no such absorption occurs—a conclusion which has never been modified since. The experiments on inflammation were made, or at any rate completed, after he had been definitely established as a young surgeon in Edinburgh; a place he visited on Sharpey's recommendation in 1853, with the intention of spending a month there; but he became Syme's assistant and later his son-in-law, and the month extended to seven years!

Having become conscious of the ignorance of surgeons regarding the earlier stages of inflammation, he set to work to investigate these on physiological lines. For this purpose he made use chiefly of the frog's web, but employed also for confirmatory evidence the vessels in the bat's wing—an object he had learned the study of under one of his most distinguished teachers in University College, also a physiologically-minded surgeon, Wharton Jones, the discoverer of the amoeboid movement of leucocytes. As his biographer truly remarks, Lister's work on inflammation "impresses the reader by the beauty and simplicity of the experiments described, the originality of the thoughts and the soundness of the reasoning. . . . The paper was well received at home and on the Continent, and its conclusions have with scarcely an exception stood the test of time."‡

In the same year Lister published, also in the *Philosophical Transactions*, results of experiments of a purely physiological nature—namely, "An inquiry regarding the parts of the nervous system which regulate the contraction of the arteries," and on the "Cutaneous pigmentary system of the frog." Both of these contained new and important observations. It is, however, not unnatural that his predominant work, which has revolutionized Surgery, should have overshadowed his earlier physiological observations, a fact which Lister himself recognized and regretted. I am not sure in my own mind that he was not prouder of his physiological researches than of his contributions to surgery.

His most important contribution to Physiology was when he was very fully occupied with surgical work and teaching.

* Quoted from *Lord Lister*, by Sir Rickman Godlee. 1917.

† The earlier papers on this subject were published in the *Quarterly Journal of Microscopical Science* for 1853: the fuller investigation in the *Transactions of the Royal Society of Edinburgh* for 1857.

‡ The actual mode of causation of the vascular changes which Lister was the first to describe was not explained until many years later, the explanation being furnished by the experiments of Dr. Ninian Bruce. (*Quart. Journ. Exper. Physiol.*, vol. vi, p. 339, 1913.)

It was upon a subject which must always possess a peculiar interest for the surgeon—the cause of blood coagulation. I know of no better or more precise piece of work than this. All kinds of theories were extant on this subject: there are a good many still. Dr. Benjamin Richardson, having found that the addition of ammonia to blood would prevent its coagulation, thought that this furnished sufficient evidence to support the idea that the reason why blood coagulates when drawn is that exposure to air allows the escape of ammonia. And although the researches of Alexander Schmidt had shown, what modern investigations have confirmed, that coagulation is the result of a chemical reaction between substances dissolved in the blood, the reason why this reaction does not occur in the living vessels was completely obscure; the theory which was most favoured being that of Brücke, which explained the phenomenon by supposing that the living wall of the vessel exercises a restraining influence upon the blood in contact with it—which is evidently not an explanation at all. Lister devised a simple experiment which at once upset both theories, and indicated the real cause of blood coagulation—namely, the contact of blood with foreign matter or with injured or dead tissues. He showed that blood can be kept fluid in a segment of a large vessel exposed freely to the air, and could even be poured from one such segment to another so as to allow free escape of any ammonia which might be (but isn't!) present; moreover, while passing through the air the blood would, of course, be removed from contact with the wall of the living blood-vessel. Nevertheless, such blood remained fluid unless the inner coat of the vessel were injured or unless the blood were allowed to come in contact even within the vessel with a foreign body. Lister showed that it is the presence of the injured tissue or foreign body that determines the chemical reactions which produce the coagulum, and not the presence of the living tissues which prevents such reaction. This fundamental fact was settled for all time by the simple experiment of the so-called "living test tubes" devised by him. The account of this and many other experiments on the subject is to be found in the *Proceedings of the Royal Society* for 1863. It formed the subject of the Croonian Lecture for that year.

LISTER ON THE NEED OF EXPERIMENT FOR THE ADVANCEMENT OF MEDICINE AND SURGERY.

By this time Lister was in the full swing of surgical practice in Edinburgh, and was giving lectures on the Principles and Practice of Surgery in the extramural school. The principles he taught were physiological, both normal and as applied to disease. And he recognized that Surgery if it is to be considered a science at all must be founded upon and can only make progress by the aid of experiments.

His great discovery was so founded. His experiments were made with test tubes, with animals, with patients. But he would never venture to perform a serious experiment upon man without having ascertained by animal experimentation that it was likely to prove successful and was therefore justifiable. On the subject of vivisection his trumpet gives no uncertain sound. When requested by no less a personage than Queen Victoria to make some public declaration against vivisection he replies as follows to her private secretary:

"I should deeply regret that I cannot see my way to complying with this request, were I not persuaded that my doing so would not promote the real good of the community, which I know to be Her Majesty's only object in the matter. And I feel bound to endeavour to express shortly the reasons for my opinion.

"With this object I can hardly do better than begin by saying that I have myself often performed experiments upon the lower animals, and that, if I have been privileged in my professional career to do anything for the good of my fellow men, more is to be attributed to these experiments than to any other work in which I have engaged. When they were performed without chloroform, as has not unfrequently been the case, they have been done at a very great sacrifice of my own feelings; but the greatness of the object in view has appeared to me to over-ride such considerations. . . . It is sometimes said that, although such experiments may be needful and right for the purposes of discovery, they are not justifiable for the demonstration of truths already ascertained. It would, I believe, be very wrong to draw any such line of distinction. To take a single instance: to debar the student of medicine from having his eyes opened to the truth of the circulation by seeing the blood coursing through the vessels

of the living web of the frog's foot, would be undoubtedly a mistake: for no amount of verbal teaching could do for him what a glance through the microscope at that sight at once effects."

And after explaining at considerable length the relatively painless nature of physiological experiments as compared with the cruelties which are inflicted every day for the sake of improving the quality or appearance of food, or even in sports such as fishing, shooting, and fox-hunting, he points out that the sportsman is not commonly regarded as cruel because the inflicting of suffering on the hunted animal is not his main object (which is indeed merely the gratification of himself and his friends), and continues:

"But surely those who regard this amusement as justifiable are strangely inconsistent if they brand with the epithet cruel the man who performs an experiment upon an animal at great sacrifice to his own feelings and with every care to render the pain as slight as is compatible with the high object in view."

And in his evidence before the Royal Commission (on November 1st, 1875) he begins by stating that his first experiments upon animals had been made when he was altogether unknown as a person of any sort of reputation whatever: and "When I first took in hand to teach others I felt that there were some points on which I desired more information than I could get satisfactorily from any book, and my first experiments were performed with the object of preparing myself for teaching, while I was not a person of recognized scientific attainments."

With regard to his early experiments upon blood he remarked that they "had the effect of giving me a kind of pathological information, without which I believe I could not by any possibility have made my way in the subject of antiseptics; and that subject, I believe, is becoming recognized as one of considerable practical importance. I have often felt that without the basis which I derived from experiments on the lower animals, I should never have been able to thread my way through the very perplexing and apparently contradictory facts which I met with in the first instance." Also that throughout his whole career after that time he had found experimentation on living animals necessary, and that through the medium of that experimentation originally commenced with other aims he was gradually led "to the development of that method of treatment which is now known as the antiseptic system." Further, with regard to his work on catgut ligatures he definitely states that if he had not made experiments in the first instance on animals he would have had to perform them on man; there was no other alternative.

LISTER AND PASTEUR.

Great as was his work in surgery, Lister never ceased to be a physiologist; to the end of his days he was deeply interested in all forms of experimental work. He was scientific to the core. As we have seen, he insisted that experimental work was the basis of all his researches in antiseptics. His experiments in this as in other directions are characterized by meticulous accuracy, a character which is essential for all scientific investigations. First the facts were ascertained by observation and experiment; then marshalled and collated with observations made by others; the deductions checked by yet other experiments; nothing was left to mere supposition. In this way he arrived at his great generalization which at once transformed surgery from a mere art which might be practised by any ignorant person into a real science which could only be properly advanced by those who adopt the experimental method. Given an adequate knowledge of anatomy—a science which is essential to the physician as well as to the surgeon—the basis of training in both the branches of what is popularly known as the "healing art" must be physiology. Lister would never have arrived at the position he occupies in the history of surgery if he had not been first a physiologist. Doubtless he was fortunate in his opportunity. He came at the right time, just when Pasteur was engaged in the brilliant researches which indicated the essentially parasitic nature of disease. How eagerly Lister seized hold of that opportunity we read in his biography, and his own tribute to the aid he obtained from the researches of Pasteur is unstinted; nevertheless, he had begun his experiments be-

fore he had heard of Pasteur's. I do not know any surgical contemporary of his who could have taken advantage of the opportunity thus offered; at any rate it is certain none of them did so. They all had anatomy at their fingers' ends, but this was the only science which it was then expected they should know, and it did not lead their surgery far along the path of progress.

PHYSIOLOGY THE BASIS OF SURGERY.

It is an old tradition that Anatomy is the exclusive basis of Surgery, but I am happy to think it is every day becoming more of a tradition and less of a practice. Many modern surgeons both in this and in other countries are physiologists as well as surgeons: Physiology has given scientific support to their Surgery, and has been in turn materially assisted by it. It would be invidious for me to mention the names of living individuals, and in an assembly like this it is not necessary: they are known to most of you. Their researches are becoming every day more numerous. They admit that Surgery is based upon experiment, in other words, upon Physiology, and that there is no possibility of its advancing in any other way. Like every other science, surgery without experiment must stand still, and no surgeon has any right to experiment upon the human subject if the lower animals are available for the purpose. That those who are learning operative surgery are debarred by Act of Parliament from practising on animals, although permitted to make any experiments they think fit upon human patients, is an incredible piece of folly, and ours is the only country in the world in which so heinous a measure could have been passed into law; the only nation where misplaced sentiment is allowed to displace reasoning, and where the necessities of humanity are subordinated to those of the brute creation. I wonder, does the public fully understand that by the present law no student is permitted to perform any operation upon an animal with the object of enabling him to do the same operation upon man, and to acquire the necessary skill to do it without danger to his patients. Which of you, I may ask, would like to be a first patient to be operated on, even for so simple an operation as the extraction of the crystalline lens? Yet the skill of the operator *must* be acquired by experience, and therefore men, women, and children must take the place of dogs, cats, and rabbits! Truly we are a nation of Pecksniffs! As Sir Rickman Godlee pertinently remarks, the strangest anomaly, as it must appear to our less sanctimonious brethren in the rest of the civilized world, is that our law, while it forbids the granting of a special licence to a distinguished doctor to experiment on a chloroformed frog in his own study in pursuit of science, allows anyone who can afford it to hunt a stag to death, or set two greyhounds to course a hare, and wager money on the result.

While it is the case that the progress of surgery must depend upon physiology, it is equally true that the progress of physiology depends upon surgery. Without an adequate knowledge of surgery many experiments which are necessary for the advancement of physiology could not be attempted. I have already given you instances of this. But I will call to mind the experiments on depancreatized animals which are at present in progress—experiments which are filling not only the pages of the medical and physiological journals but even the columns of the daily press. It is not everybody who is endowed, as Lord Lister and Sir Victor Horsley were, with the requisite knowledge and skill in both subjects to work single-handed. At the present time team work, suitably directed, is all the vogue; and this is largely why our knowledge regarding insulin has made such rapid advances within so short a time. Surely such a combination of physicians, surgeons, physiologists, biochemists, pathologists has never before been assembled to conduct any investigation as those who have been working in Toronto. In every physiological investigation on animals one of the team at any rate should be a surgeon, and I can conceive of no more advantageous training for a young surgeon than that which he will obtain by taking part in such an investigation.

Examples of the mutual value of co-operation between

the surgeon and the physiologist could easily be multiplied, but I hope that those I have put before you may suffice, and have some influence in promoting that close intercourse between surgery and physiology which is essential for the progress of both branches of science.

LISTERIAN METHODS IN SURGERY.

I have often wondered what difference it would have made to my own life if Joseph Lister had been elected to the chair of surgery in University College in 1866, instead of John Marshall. It is easily the worst mistake that the Council of the College ever made. The echo of the election was remaining when I joined the College in the winter of 1866 as a very young student. I came to know Marshall very well. He was a good friend to me and I had a great respect and liking for him. But he was the most uninspiring teacher that I ever sat under. His systematic lectures were desperately dull, and being given late in the afternoon with a monotonous, musical utterance, most of his audience were soon fast asleep: I was one of the sleepers! Nor was his clinical teaching any better. His operating was slow and the reverse of brilliant. Whether he ever fully embraced Listerian methods—at the time I joined they were unknown outside Glasgow—I do not certainly know, but I much doubt if he did. He was not a physiologist although he published a textbook of physiology, largely founded on his notes of Sharpey's lectures: I do not think it went through more than one edition. Lister's biographer speaks of Marshall as scientific and a good teacher, but these are terms which I cannot endorse. He had a charming personality, and as he was already on the staff of the hospital he obtained the chair in preference to Lister, who had been many years away from the institution and was unknown both personally and through his work to most of the staff. John Marshall became a Fellow of the Royal Society and President of the Royal College of Surgeons. There is an admirable bust of him at Lincoln's Inn Fields. But Lister's name will be famous when Marshall's is forgotten.

It has always been a source of regret to me—as it must be to all alumni of University College—that Lister's work was not carried out at his old school. But the fates ordained otherwise, and to Glasgow and Edinburgh must be conceded the credit of nursing the new surgery into vigorous existence. I believe it would have made a great difference in the rapidity of the spread of the new doctrines if they had emanated from London, and Lister, no doubt, thought so himself, as his subsequent migration to London showed. The atmosphere of University College—if not of the hospital—was distinctly scientific, and at any rate amongst his scientific colleagues he would have received full encouragement. It was in 1866 that he applied for the appointment—less than a year after he had started his experiments on antiseptics in Glasgow. According to Horsley it was sixteen years (1882) before it was in general use in hospital surgical practice in London. The change occurred when Horsley was a student and long after my own time. And if I have wondered what a difference it would have meant to me, a mere physiologist, to have had a surgical training under Lister, how much greater would have been the difference to Victor Horsley if he had come under the direct influence of this great scientific surgeon. He would have been Lister's house-surgeon instead of Marshall's, and how enormously he would have benefited by the close relationship with Lister, and how keenly he would have followed and assisted in his experiments, those who best know both men can appreciate!

It is easy to speculate on the "might have beens." Sufficient to know that as soon as he came into his own Horsley was foremost in his adoption of Listerian methods, and it was in consequence of this that that particular combination of surgery with physiology which I chose as my first illustration of the mutual benefits they confer on one another was effected. If Lister had come to University College in 1866 I should have learned his methods from the master himself, but I should have missed the opportunity of being associated with so delightful a colleague as he whose memory we are assembled to-day to commemorate, and whose loss not only to physiology and surgery, but to the whole world, will be felt for many a year.

An Address

ON

CHRONIC INTESTINAL STASIS AND CANCER.*

BY

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At present surgery and medicine appear to be one horrible mêlée of attempts to understand and treat end-results, little or no endeavour being made to obviate the development of these conditions. In surgery operations increasing in severity replace less extensive procedures; whereas in such a condition as ulcer of the stomach, while no attempt is made to remove the factors which produce it together with many necessarily associated results, the possibility of the recurrence of the ulcer is only eliminated by the removal of the entire organ. The safety with which such operations can be performed, and the ease with which a surgeon can acquire sufficient skill to effect them at comparatively little risk, tend to increase the number and severity of these operations. Everyone worships the god "technique," to the complete elimination of the importance of dealing with the causation, and therefore the prevention, of disease which should be our real object in life.

The profession is only just beginning to realize the enormous part played by the defective functioning of the gastro-intestinal tract, the consequent fouling of the food supply, and the poisoning and deterioration of the tissues by septic material absorbed from the intestine.

DIET OF CIVILIZED AND UNCIVILIZED.

That we pay dearly for the luxury we enjoy in our food and habits of life is shown clearly by the fact that civilization brings in its train a very large number of diseased conditions which do not exist in those leading the simple life of the native. That these conditions are all due to acquired defects in the functioning of the gastro-intestinal tract is, in my opinion, undoubted, since they occur at once in the native when he is placed in a civilized community; and it can be shown that these diseases bear a direct proportion to the degree of civilization enjoyed.

Roughly the difference between the civilized and the uncivilized is a matter of diet. While the latter eat much food that is uncooked or only imperfectly cooked and which contains a large proportion of indigestible matter, the former eliminate from their meals all but the digestible. By this means the bulk of the food and its stimulating action on the intestinal wall are diminished as much as possible and the material stagnates and becomes poisonous. As evidence of these statements I will quote an extract from a lecture by a great observer, Colonel McCarrison. He spent nine years in the Himalayas, during which time he had a large practice, performing more than 400 capital operations each year. During that time he never saw one case of asthenic dyspepsia, of gastric or duodenal ulcer, of appendicitis, of mucous colitis, or of cancer. I would call your attention to this sequence, all evidence of chronic intestinal stasis, since I am certain that cancer is the last stage in the sequence, and that it never attacks a healthy organ. The diet of these people is very simple. They live chiefly on corn ground between stones. This is made into a cake which is imperfectly roasted over a charcoal fire. They very rarely eat meat. Mr. F. L. Hoffman the eminent American statistician writes me as follows: "Your views regarding dietary or nutritional causation (of cancer) coincide with my own based upon extensive research among native races. I recently returned from a trip to South America, where I lived for seven

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