THE COLLECTED PAPERS

OF

JOSEPH, BARON LISTER

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THE COLLECTED PAPERS

OF

JOSEPH, BARON LISTER

MEMBER OF THE ORDER OF MERIT
FELLOW AND SOMETIME PRESIDENT OF THE ROYAL SOCIETY
KNIGHT GRAND CROSS OF THE DANISH ORDER OF THE DANEBROG
KNIGHT OF THE PRUSSIAN ORDRE POUR LE MÉRITE
ASSOCIÉ ÉTRANGER DE L'INSTITUT DE FRANCE
ETC. ETC.

IN TWO VOLUMES

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PREFACE

When, on the 5th of April, 1907, Lord Lister attained his eightieth birthday, he was the recipient of many congratulations, not only from his fellow countrymen, but from representatives of medicine and surgery throughout the world, and a unanimous desire was then expressed that some permanent memorial should be instituted of so happy an occasion, and of a life so rich in benefits to mankind.

No memorial seemed more appropriate than a collected edition of his scientific papers, scattered through many different periodical publications, inasmuch as in them are recorded the steps by which the great revolution in surgery with which his name will be imperishably associated was brought about, and by their perusal succeeding generations may learn at first hand the great principle on which that revolution was based. The proposal, it was ascertained, commended itself to Lord Lister, and the Committee which has prepared these volumes for the press has had the inestimable advantage of his guidance and advice.

The two volumes contain all the papers and addresses which he himself considers to possess permanent interest and importance; the omissions in fact are few in number, and consist almost solely of addresses on certain official occasions dealing with matters of ephemeral or merely local interest. The papers have been classified under four general heads, according as they deal with Physiology, Pathology and Bacteriology, the Antiseptic System, or General Surgery, while various general addresses and lectures are gathered together in a fifth part. In arranging the several papers in each Part chronological order has generally been followed.

The Committee has thought it well to preface the text of the papers and addresses themselves by a brief introduction giving some account of the state of surgery at the date when Lord Lister began his work, indicating the growth of the principle by which he was guided, and tracing the early stages of its application to practical surgery. Without some such preliminary statement, those unacquainted with the position of surgery, and the conditions prevalent in surgical wards in the middle of the nineteenth century, may fail adequately to understand the difficulty and complexity of the problem as it presented itself to him, and the brilliancy of the long chain of reasoning and experiment by which he was led to its triumphant solution.

NOTE

These volumes were prepared for the press by a Committee consisting of:

Sir Hector C. Cameron.
Sir W. Watson Cheyne, Bt., C.B., F.R.S.
Rickman J. Godlee, M.S.
C. J. Martin, M.D., F.R.S.
Dawson Williams, M.D., F.R.C.P.

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Portrait of Lord Lister. From a photograph taken in Edinburgh in 1856 . *Frontispiece*

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PART II

CHRONOLOGICAL NOTE

Born April 5, 1827.

Graduated B.A. 1847, M.B. 1852, University of London.

Edinburgh: House Surgeon, 1854; Extra-Mural Lecturer, 1855, and Assistant Surgeon, Royal Infirmary, 1856.

Glasgow: Professor of Surgery, 1860–9.

Edinburgh: Professor of Clinical Surgery, 1869–77.

London: King's College, Professor of Clinical Surgery, 1877–93.

INTRODUCTION

It is not proposed to enter into any biographical details in the following notes, which are merely intended to indicate the sequence of events in the course of Lord Lister's work, and thus to enable the reader to follow the development of his great discovery. His work was carried out at different periods and under the varying circumstances of different hospitals and clinical schools.

The first of these periods was one of preparation, ending in his graduation in medicine at the University of London in 1852. Among the men whose influence during this period was of the greatest importance in determining his future line of thought and work were his father, Joseph Jackson Lister, William Sharpey, Professor of Physiology, and Thomas Graham, Professor of Chemistry in University College.

Joseph Jackson Lister was a merchant in the City of London who devoted his leisure to scientific pursuits, and especially to the perfecting of the microscope, and his name will always be remembered as the first to solve the problem of the production of achromatic lenses. He was a man of extreme accuracy of thought, a most methodical worker, a good classical scholar, and skilful with brush and pencil. His influence on his son's character and career was very great. This has been acknowledged with gratitude by Lord Lister himself, not only in the obituary of his father, reprinted in the second of these volumes, but also on many other occasions.

During his career at University College, Lister came specially under the influence of Sharpey, and under his guidance early applied himself to the study of various physiological problems. Papers describing the results of three important researches made by him at this period are reproduced in this volume. They relate to the contractile tissue of the iris, to the muscular tissue of the skin, and to the flow of lacteal fluid in the mesentery of the mouse respectively. His keen interest, too, in the study of chemistry under Graham had an abiding effect, for it equipped his mind with a sound knowledge of the principles and methods of chemical science, which greatly aided him in many ways in his future researches, not least in devising various forms of antiseptic dressings, a task which entailed great labour and patience in the conduct of a long series of experiments extending over many years.

The second of the periods referred to was that of his first residence in Edinburgh (1852–60). After completing his course at University College, and his time of residence in University College Hospital as House Physician and House Surgeon with Dr. Walsh and Mr. Erichsen respectively, he went to Edinburgh, taking an introduction from Dr. Sharpey to James Syme, Professor of Clinical Surgery in the University, on what was intended to be only a short visit. As a matter of fact, however, this visit led to Lister's settling in Edinburgh, where he remained until he received a call to occupy the chair of surgery in the University of Glasgow. Lister appears at once to have conceived a great admiration for Syme, then at the zenith of his great powers as a clinical teacher. He respected not only Syme's skill and resource as an operator, but also the strength of his intellect and the soundness of his judgement. Syme formed a just estimate of the powers of his visitor, for on a vacancy unexpectedly occurring he appointed Lister his House Surgeon in the Edinburgh Royal Infirmary. This association resulted in a warm personal friendship, which was cemented by Lister's marriage a few years later with Syme's eldest daughter, a lady who to the end of her life was indeed her husband's helpmeet in all his scientific investigations.

Lister became successively Lecturer in Surgery in the Extra-Mural School, and Assistant Surgeon to the Royal Infirmary, and held these appointments at the time of his translation to Glasgow. The work which Lister did during this period of his life, and the direction of his thoughts, cannot be better indicated than by a glance at the writings he then published. The earliest papers were on the duration of vitality in the tissues, on the structure of involuntary muscular fibre, and on the cutaneous pigmentary system of the frog. Another group of papers dealt with the early stages of inflammation, with gangrene from arteritis, and with the coagulation of the blood both within and without the blood-vessels, while a third group was concerned with the nervous system and included observations on the functions of the visceral nerves, with special reference to the inhibitory system, on the parts of the nervous system regulating the contraction of the arteries, and on the structure of nerve-fibre. It is not difficult to perceive the interrelation of these several lines of study and investigation, and the perusal of the papers in which they are embodied affords an interesting example of acute reasoning applied to the interpretation of the results of accurate observation and experiment.

The third distinct period of Lord Lister's life was that during which he occupied the chair of Systematic Surgery in the University of Glasgow (1860 to 1869). He there found himself in charge of a large number of beds in the old Royal Infirmary, to which, serving as it did the requirements of a great manufacturing city, accidental wounds of all sorts and degrees were daily admitted. From its wards, as he has related in the papers on the effects of the antiseptic system upon the salubrity of a general hospital here republished,[1] septic diseases were seldom absent, and the mortality from wounds and after all surgical operations was enormous. At the beginning of his career in Glasgow we find him continuing his work on the coagulation of the blood, the subject to which he devoted the Croonian Lecture delivered before the Royal Society in 1863; but he published also several important contributions to practical surgery, including the introduction of a new method of excising the wrist-joint, and the preparation of articles on anaesthetics and on amputation for *Holmes's System of Surgery*.[2]

But the gravity and constant prevalence of septic diseases in his wards, and the distressing mortality which occurred in consequence thereof, often in the most promising cases, so disappointed, pained, and distressed him, that his thoughts became more and more turned to the question of the cause and prevention of these disasters. Very many methods were tried in the hope of improving the treatment of wounds and the salubrity of his wards, for he was not satisfied to accept the fatalistic view then prevalent that septic diseases of wounds were unavoidable incidents, as much acts of God as a hail in harvest, and matters, therefore, in regard to which the surgeon had no personal responsibility. It was out of this divine discontent with things as they then were that there grew up the great work of his life, the introduction of the antiseptic method of wound treatment. During the remainder of this period of his life the majority of the papers he published were concerned with this subject, and others, such as those on the methods of ligaturing blood-vessels and stitching wounds, had a direct and essential bearing upon it. While his main aim was from the first and always the prevention of sepsis in wounds, he at the same time recognised, equally from the beginning, the importance of diminishing and as far as possible neutralizing the irritation of the wound and the general toxic effects which might be produced by the chemical substances employed as antiseptics.

The fourth period in his life was that during which he occupied the chair of Clinical Surgery in the University of Edinburgh. To this he was appointed by the Crown on the resignation of Mr. Syme. He assumed its duties at the beginning of the winter session of 1869. Already in Glasgow the soundness of the principles on which he was proceeding had been thoroughly established, but the methods by which those principles were carried into practice were still cumbrous and far from perfect; during his incumbency of the Edinburgh Chair he was largely occupied in devising and testing improvements in the methods of carrying out the antiseptic principle, with the object of rendering its use in

[1] Vol. ii, pp. 123 and 156.

[2] These articles, revised at a later date, are reprinted by permission of Messrs. Longmans at p. 135 of this volume, and p. 378 of volume ii.

everyday practice simpler. The writings published during this period are, as will be seen by reference to the second volume, chiefly devoted to such matters. At the same time he carried out investigations and published papers on other allied subjects, as, for example, on the germ theory of putrefaction, and on lactic fermentation.

The last period of Lister's active life dated from 1877, when he went to London in response to an invitation from the authorities of King's College, to fill the chair of Clinical Surgery in succession to Sir William Fergusson. This period, which extends until his retirement from active surgical work in 1892, may be characterized as one in which the final details of antiseptic surgery were more or less perfected. Various fresh antiseptics were tested, especially with the view of obtaining some antiseptic dressing which, while as reliable as the carbolic gauze, might yet prove less directly irritating, and being non-volatile might be trusted for longer periods, thus avoiding the necessity for frequent change of dressings and disturbance of the wounds. During this period, his method of treatment approximated more and more to his ideal of converting open wounds, as regards their subsequent course, to the condition of subcutaneous injuries.

These preliminary remarks cannot be more appropriately brought to a close than by a reference to the unwearied help that Lady Lister afforded to her husband in the pursuit of his investigations throughout her life. Those who were admitted to the inner circle can never forget the vivid interest which she took in the details of his work, and the many closely written volumes of dictated notes in her handwriting containing full records of the experiments on which the conclusions expressed in the essays reproduced in these volumes were largely founded.

PHYSIOLOGICAL AND PATHOLOGICAL WORK

In his Huxley lecture,[1] delivered in 1900, Lord Lister has given an account of some of his early physiological researches. In it he dwelt particularly on those researches which were more intimately connected with the development of his ideas upon the nature and causation of inflammation and suppuration.

From this account it can be seen how Lister's ideas of these processes gradually matured. It wanted only the conception of infection to complete them, and this was supplied in Pasteur's discovery of the causation of putrefaction, the full significance of which Lister was thus able at once to realize.

This chapter of scientific discovery could hardly have been more pleasingly

[1] Vol. ii, p. 515.

told than by the author himself, so that it is here only necessary briefly to review Lister's principal investigations in physiology and pathology as contributions to these sciences.

It is not surprising that Lister's first investigations should have been histological. His father, Joseph Jackson Lister, who had by his optical experiments very greatly improved the compound microscope, was an accomplished microscopist and made important discoveries concerning the structure of zoophytes and acidians. At this period the theory of the microscope was being rapidly developed, and each consequent improvement in this instrument of research opened up further fields to the investigator. Kölliker had recently discovered the cellular structure of plain muscular tissue and the first investigations of Lister were concerned with the contractile tissue of the iris[1] and skin[2], and with the structure of involuntary muscular fibre generally.[3] The observations and conclusions of Kölliker were at this time by no means universally accepted, but Lister's work not only vindicated their accuracy, but cleared away many apparent discrepancies between the observations of different observers. He also made a number of new observations upon the structure and distribution of smooth muscle fibres. These three papers were illustrated by excellent camera-lucida drawings made by Lister himself, which are reproduced in the present volume.

At the time when the last of these papers was written Lister had already commenced an inquiry into the process of inflammation,[4] a subject to which he seems to have been irresistibly attracted from the first ; around it, henceforth, almost all his researches centred, although he often made wide excursions to investigate physiological problems encountered in efforts to interpret some one or other of the processes concerned in inflammation.

The investigation of the nature of the process of inflammation was, for the most part, made by direct observation upon the frog's web, a method which permitted the study of the phenomena from the beginning. Therein lay its great fertility. His observations were, however, carefully controlled by observations made upon the higher animals and man. The phenomena of stasis, and the vascular reaction, immediate and subsequent, following the application of irritants of all classes were for the first time accurately described. The former was shown to be due to the direct action of the irritant upon the blood-cells and blood-vessels, and the latter to be occasioned reflexly through the nervous system. These observations upon the early stages of inflammation were communicated to the Royal Society in 1857. They have formed the basis of all subsequent discoveries, and the conclusions drawn are as valid to-day as then.

[1] Vol. i, p. 1. [2] Vol. i, p. 9. [3] Vol. i, p. 15. [4] Vol. i, p. 209.

The vascular reaction to irritation was found by Lister, as has been said, to be indirectly produced through the medium of the central nervous system. That the calibre of the arteries was controlled by the nervous system had recently been established by Claude Bernard's discovery that section of the cervical sympathetic was followed by dilatation of the blood-vessels in the head and neck, and Waller's observation that stimulation of this nerve caused constriction in the same area. Waller and Budge also had just shown that the fibres of the cervical sympathetic, stimulation of which occasioned constriction of the vessels, emanated from the upper dorsal region of the spinal cord. On the other hand, Wharton Jones had stated that whilst division of the sciatic nerve was followed by extreme dilatation of the vessels in the frog's web, section of the roots of the sciatic within the spinal canal failed to produce this effect, whence he inferred that the constrictor fibres in the sciatic trunk came not from the cord but from the 'Sympathetic system'.

Lister, who was no doubt interested in the control of the calibre of the blood-vessels primarily on account of his observations upon the vascular reaction in inflammation, proceeded to make an investigation to ascertain which parts of the nervous system regulated the contraction of the arteries,[1] with the view of clearing up the apparent discrepancy suggested by the observations of Waller and Budge and Wharton Jones respectively.

The experiments were made upon the frog, and the size of the vessels of the web directly observed and measured by an eyepiece-micrometer. Both webs were simultaneously under observation, so that when the nervous connexions of the one side were interfered with, the other served as a control. With this simple technique he conducted a series of experiments, which even at the present time could not fail to excite admiration on account of the simple directness of their conception and the ingenuity with which they were carried out. He showed how Wharton Jones was led to a false conclusion, and established the fact that the fibres controlling the calibre of the vessels in the web of the frog issue from the spinal cord, as do those through which sensation and motion are effected in the hind limbs. He further demonstrated that the greatest focus whence those fibres emerged was at the posterior end of the cord, so that if this portion of the spinal axis were removed, intense dilatation ensued. Unless, however, the amount of cord removed was extensive, after an interval of some days the vessels recovered to some extent their former calibre, showing that the supply is not absolutely confined to any limited region. Experiments on frogs in which the whole nervous system had been destroyed, and upon amputated limbs also, led him to conclude that there must in addition be

[1] Vol. i, p. 27.

a local co-ordinating mechanism, but that this local mechanism was dominated by the central nervous system.

In the course of these investigations Lister had under frequent observation the stellate pigment-cells of the frog's skin, the concentration and diffusion of the chromatophorous particles within which produce the temporary variations in colour of the animal. The diffusion of the particles throughout the stellate cells causes the tint to darken, whereas their concentration in the body of the cell produces the opposite effect. Lister noticed that when the animal struggled, the particles moved suddenly and energetically in the direction of the body of the cell, as if acted upon by some stimulus. Convinced that he was observing a vital phenomenon of great physiological importance, he determined to investigate it.[1]

Von Wittich had found that the process was under the influence of the nervous system and that the sciatic nerve contained fibres which controlled the condition of the pigment-cells of the hind limbs. Lister confirmed these observations and further succeeded in demonstrating the mechanism of control, and showed that the adaptation of the colour of the frog to its surroundings was brought about reflexly by light entering the eye.

Lister also made observations of the first importance upon the nervous mechanism of the musculature of the gut.[2] These experiments were primarily undertaken to test Pflüger's conclusion that the splanchnic nerves contained special inhibitory fibres distributed to the muscular coats of the intestine. Lister verified Pflüger's results, but did not accept his interpretation. He came to the conclusion that both the observations of Pflüger and his own experimental results were not inconsistent with the view that the same fibres produce increased and diminished muscular activity, according to the strength of the stimulus impressed upon them. Although later work has justified the interpretation of Pflüger, the experiments devised by Lister to test this hypothesis led him to important conclusions regarding the mechanism of intestinal movements, namely, that there was an intrinsic nervous apparatus which co-ordinated the movements of successive muscular fibres in peristalsis, and that the latter could be stimulated or checked by impulses coming from other parts of the nervous system.

Another department of physiology to which Lister made considerable contributions was the causation of the coagulation of blood.[3] His attention seems to have been drawn to this subject by the coagulation of blood in an inflamed artery, and the question presented to him was, why does blood clot in contact with an inflamed vascular wall, whereas it remains fluid when surrounded by healthy endothelium ?

[1] Vol. i, p. 48. [2] Vol. i, p. 87. [3] Vol. i, pp. 99, 105, 109, and 182.

At this time knowledge of physiological chemistry was but little advanced. It is only now, fifty years after Lister's work, that we are beginning to arrive at an adequate interpretation of the complicated phenomena of coagulation, and that an answer to the question with which Lister was confronted is forthcoming. At that date all that could be vouchsafed to the most patient and gifted experimenter was to remove false conceptions and accumulate a number of accurate observations to serve as guide-posts for future workers. This Lister accomplished. He showed the untenability of the then prevalent theory of Richardson that coagulation was due to the escape of ammonia when blood was shed. Both in so doing and afterwards in seeking for an explanation why blood should comport itself so differently when in healthy living vessels, and when in contact with ordinary solids, he discovered a large number of cardinal facts concerning coagulation which have been, and will in the future still be, of service to investigators in their efforts towards complete understanding of the phenomena of the clotting of blood.

SURGICAL WORK

A just conception of the value of Lister's surgical work can only be formed if the state of surgery and the conditions of surgical practice towards the middle of the last century are borne in mind. The results of surgical operations are now so generally good that it is hard to realize what they were before Lister began his reform. At that time, though they naturally varied a good deal in different hands and under different sanitary conditions, the broad facts with regard to the very unsatisfactory results of the surgical treatment of wounds and the dangers of operations were much the same in every country and in every hospital. Putrefaction of the discharges present in and escaping from the wounds occurred in almost every case, and was accompanied by more or less local inflammation. Wounds were, during their early stages, swollen and painful, and this local inflammation was constantly attended by more or less fever, which usually lasted for several days. Union by first intention was of very rare occurrence ; it was indeed impossible in large wounds, owing to the fact that the ligatures with which the vessels were tied had subsequently to be extruded by a process of granulation and suppuration ; the suppuration which necessarily occurred along the track of the ligatures usually spread to the rest of the wound. Associated with this process of separation of the ligatures was another danger, from the dread of which the surgeon's mind was never free : this was the fear that the process by which this separation was brought about might open up the lumen of the vessel, and lead to so-called secondary haemorrhage.

Still more serious than these local troubles was the frequent occurrence of general septic diseases, such as septicaemia, pyaemia, erysipelas, tetanus, or hospital gangrene. In a large proportion of the cases in which a wound of any considerable size was produced, whether by an accident or by the surgeon's knife, the patient suffered more or less severely from one or other of these surgical diseases. After major amputations, for example, the mortality was very high; the average in the practice of various surgeons at that time varied from 30 to 50 per cent. Lister collected his statistics of amputation for two years (1864 and 1866), just before he introduced the antiseptic method of treatment, and found the mortality to be 45 per cent.[1] The causes of death are not definitely stated, but almost all the deaths were due to infective diseases; for example, of six deaths following amputation of the upper extremity four were due to pyaemia and one to hospital gangrene. In his paper on excision of the wrist-joint, published in 1865, he refers to fifteen cases in which he had performed this operation, and incidentally remarks that six were attacked by hospital gangrene, while one died of pyaemia.[2]

Volkmann, in one of his earliest papers [3] on antiseptic treatment, stated that for the four years preceding the adoption of Lister's method, that is down to 1872, he had left his wounds entirely open. During the first year in which this method was carried out, the results were very favourable, and he was thoroughly convinced of its superiority over the plans which he had formerly adopted. As time went on, however, and as overcrowding of the wards became unavoidable, infective diseases of wounds increased progressively, and at last, in the summer and autumn of 1871, the deaths from pyaemia and septicaemia were so numerous that he made up his mind to close the hospital altogether for a time. Before resorting to this desperate remedy, however, he determined to try the Listerian method for a few weeks, and the result of this trial was entirely to alter the aspect of affairs.

Similar facts were published by Nussbaum of Munich, who commenced the treatment two years later than Volkmann. The hospital at Munich, a building by no means satisfactory as regards sanitary arrangements, became a hot-bed of septic infections to so great an extent that almost every case of open wound was attacked by one or other of these diseases. Pyaemia was rife, affecting nearly all cases of compound fracture, wounds of bones, and amputations. Erysipelas was constantly present. During 1872 hospital gangrene also appeared, and steadily spread in spite of all the precautions which experience dictated or ingenuity could devise; in that year 26 per cent. of all the wounds were attacked by this dreaded disease; during 1873 the proportion increased to

[1] See vol. ii, p. 129. [2] See vol. ii, p. 440 [3] *Beiträge zur Chirurgie.*

50 per cent., and it ultimately reached 80 per cent. Erysipelas, too, which in 1872 was of a comparatively mild type, became much more virulent as well as more frequent. All this occurred in spite of the use of antiseptic lotions, of the open method, and other devices. In 1878, after he had put Lister's method to the test of practice, Nussbaum published an essay entitled *Sonst und Jetzt*, in which he drew the following striking contrast between the previous state of affairs and that which followed the introduction of Listerism :

Formerly.	*Now.*
Injuries of the head, compound fractures, amputations and excisions, in fact almost all patients in whom bones were injured, were attacked by pyaemia. For example, of 17 cases of amputation 11 died from this cause. Even patients with severe whitlow died from it.	No pyaemia.
Hospital gangrene had got the upper hand to such an extent, that in spite of the open method, in spite of continuous water-baths, in spite of the use of chlorine water, or the actual cautery, finally 80 per cent. of all wounds and ulcers were attacked, large arteries being opened into.	No hospital gangrene.
Almost every wound was attacked with erysipelas.	No erysipelas.

It would be easy to produce a great cloud of witnesses to the appalling state of matters in various hospitals before the introduction of the Listerian method, but their testimony would merely be a repetition of the above statements. It is true that these untoward results were witnessed most often and in their direst form under hospital conditions of a particularly insanitary kind, and that their frequency and severity varied considerably, according to the methods of wound treatment adopted. Nevertheless these infective diseases were present everywhere, and it will readily be understood that the dread of them, never absent from the surgeon's mind, was a serious bar to progress.

Further, the operations undertaken in those days were very different from those now commonly performed. Surgical intervention was then limited more or less entirely to operations absolutely necessary for the saving of life. Operations of expediency, designed to add to the patient's comfort or to make his life more useful, were not deemed justifiable owing to the probability of the onset of some form of infection, and the consequent risk of the development of one of the severe general infections which so frequently ended in death. The major operations then performed were for the most part amputations for injury and disease, excision of joints, amputation of the breast, removal of tumours, operations on the jaw and tongue, trephining, operations for strangulated hernia, operations on the urinary organs, and certain plastic operations. Abdominal surgery, as we now understand it, did not exist, the extensive operations for malignant growths and tuberculous disease now generally practised were not performed, and the numerous exploratory operations undertaken at the present day were not even contemplated. In fact, modern surgery dates from the introduction of the Listerian methods.

The treatment of wounds as practised at different periods varied greatly, according to the views taken by different surgeons as to the causes of the septic troubles which were so prone to arise. But until Lister framed and began to test the antiseptic hypothesis, the whole subject of the diseases of wounds was in a state of chaos.

It may be interesting to mention some of the chief methods of wound treatment in vogue during the early part of the nineteenth century. At that time the air was looked on as the cause, in some way or other, of the troubles resulting from wounds, and many surgeons attempted to exclude it by putting on great masses of dressings and ointments. A reaction against this method of treatment set in, leading to the development of what was called the open method of treating wounds. In that plan the wound was left freely open, no more being done than to provide means for allowing the discharges to flow freely away, and to prevent contact of clothing. This gave results in many ways superior to those obtained from methods previously in vogue.

Another plan which also furnished good results and is still employed in suitable cases, was constant irrigation of wounds with water, or the immersion of the wounded part in a water bath. The bath gave excellent results in the hands of Vallette and others, especially when combined with the use of various substances which we now know to possess antiseptic properties, such as tincture of benzoin, creosote, and iron salts.

About this time also subcutaneous surgery was introduced, but unfortunately it was a method applicable only in a very limited number of cases. John Hunter had at an earlier date pointed out the advantage of healing by scabbing, and to obtain this became a frequent object in the treatment of small wounds. Nevertheless the most common method of treating wounds was, perhaps, by a water dressing, a piece of lint dipped in water being applied over the surface of the wound, and covered by oiled silk. This method led to putrefaction and suppuration in the wound in the great majority of cases.

Shortly before Lister began his work some surgeons had begun to employ various substances, with the avowed intention of diminishing the putrefaction of the discharges in wounds. Among the materials thus employed were alcohol, glycerine, chlorine compounds, iodine, chloride of iron, coal-tar preparations, and even carbolic acid. But the methods followed in the employment of these substances were imperfect, and, not being founded on any precise knowledge of the causes of putrefaction, they failed to ensure the desired result.

The method which Lister himself employed before he took up antiseptic work is thus described by Sir Hector Cameron, who was his dresser and house surgeon at the time he began his antiseptic work :—

He was in the habit at this time of treating all recent wounds by the simple plan which had been for many years taught and practised by Mr. Syme in the Edinburgh Hospital. After the principal arteries had been secured by ligaturing them with well-waxed silk strings, and smaller bleeding-points were arrested by torsion as originally suggested by Amussat, two folded pads of lint were placed on each side of the lips of the wound so as to exercise pressure, while a larger piece of the same absorbent material was placed over these, and secured by a fairly firm bandage. Drainage was effected by bringing the ends of the long silk ligatures out at one or both ends of the wound, and the sutures used were of silver wire. This dressing was left undisturbed for several days, unless a complaint of pain or a quickened pulse demanded earlier interference. Occasionally, union by first intention occurred except in the tracks of the ligatures, but so long as these remained there was no security against the supervention of one or other of the many hospital diseases which were always present in the wards. More often the wound—whatever its original nature—inflamed and suppurated freely ; it was then treated either with water dressing covered by gutta-percha tissue, or poulticed with linseed-meal poultices. In either case, the coverings of the wound were frequently changed, and at each renewal the pus was squeezed out as thoroughly as possible (counter openings being made if necessary), and the wound well washed with a mixture of warm water and Condy's Fluid, usually poured out of a kettle. Lister soon began to enjoin on all persons in his clinique the practice of scrupulous cleanliness, which was at that time by no means always a characteristic of surgical practice. The washing of hands was insisted on after dressing each individual case, and large piles of clean towels stood on the tables of his wards for the use of his dressers and nurses.

In consequence of the reported results of some experiments on dogs by Polli of Milan, he tried at this time the free exhibition of sulphite of soda or potash in solution as a cure and also as a prophylactic of pyaemia and other septic diseases. Every patient operated on or admitted to his wards with a wound had this remedy administered to him in suitable doses from the very first, and it was also used largely in washing and dressing wounds. All these, and many other attempts to improve the salubrity of his wards, unfortunately availed little or nothing.

Cameron ends his description of the treatment of wounds at that time as follows :—

When I first became a dresser, the carrying out of such details was my daily occupation. Every wound discharged pus freely, and putrefactive changes occurred in the discharges of all, producing in the atmosphere of every surgical ward, no matter how well ventilated, a fetid sickening odour, which tried the student on his first introduction to surgical work just as much as the unaccustomed sights of the operating theatre. It is hardly necessary to add that fatal wound diseases and complications were never absent at any time from the hospitals of that day.

Such then was the state of surgical practice about the time when Lister began his work. From his student days, the subjects which had most attracted his attention were inflammation and the general septic diseases which so constantly followed the infliction of wounds, and when he commenced surgical teaching in Edinburgh the nature of inflammation occupied a very prominent place in his lectures as in his thoughts. Being dissatisfied with the views held at that time, he proceeded to investigate the subject for himself, and produced his classical papers on the early stages of inflammation, on the pigment cells of the frog, and on the nervous regulation of the arteries ; subsequently, as has been mentioned above, his attention was turned to the subject of coagulation of the blood, and to the behaviour of blood in healthy and diseased blood-vessels. But although these investigations furnished most important results and were of inestimable value in his subsequent work, yet they did not directly lead him to the antiseptic principle in surgery.

In spite of the light thrown on inflammatory processes by his researches, there still remained the fact that inflammation and suppuration constantly occurred after the infliction of open wounds, and that the various septic diseases frequently attacked the simplest wounds and rendered the most skilful operations unavailing. Most surgeons had become resigned to the occurrence of inflammation and suppuration in wounds, and looked on them as natural and inevitable consequences. Many indeed regarded the occurrence of 'healthy' suppuration as a thing to be desired, because it was observed that once suppuration was established the patient's condition improved. It was therefore assumed that the sooner suppuration occurred the better. Hence the aim of many was to hasten the formation of this 'laudable' pus, and at the same time to control 'the excessive action' in the wound which was supposed to lead to the various septic diseases.

This was not Lister's view. His ideal of what should happen in a wound was what occurred in a subcutaneous injury such as a simple fracture, in which repair took place without any inflammation, suppuration, constitutional disease, or general sepsis. In his opinion the occurrence of inflammation and suppuration in a wound was by no means a desirable thing, but was, in fact, contrary to the natural processes, as exemplified by subcutaneous injuries, and was therefore to be avoided rather than aimed at.

At an early period Lister had come to recognise that the essential cause of the troubles after operations and injuries was in some way or other connected with the putrefaction of the blood and discharges in wounds. Putrefaction did not occur in subcutaneous injuries, or in wounds which healed by first intention, and in these there were no septic troubles, while conversely, as soon as putrefaction appeared, inflammation and other septic diseases followed. He concluded, therefore, that these complications were due to the formation of irritating materials in the discharges of the wounds as the result of putrefactive fermentation, and that the aim of treatment should be to get rid of the putrefactive process.

In his Huxley Lecture[1] he refers to the treatment of hospital gangrene while he was house surgeon to Mr. Erichsen, and it is clear that even then he looked on the various diseases of wounds as essentially the result of putrefaction of the discharges. At that time the general teaching was that these putrefactive changes were the result of the action of the air, and more especially of the oxygen, on the organic fluids present in the wounds. He was never satisfied with this explanation ; like John Hunter, he was at an early period puzzled by a case of general surgical emphysema after fracture of the ribs with puncture of the lungs, for although air was present in the tissues and in contact with a large amount of blood, putrefaction and septic troubles nevertheless did not occur. This puzzle was constantly present in his mind until the solution was revealed by the researches of Pasteur.

It is interesting to note in passing that even after the introduction of antiseptic surgery, some surgeons, unwilling to give up the oxygen theory, spoke of the antiseptic dressings as 'occlusive', their assumption being that the dressings excluded oxygen. Lister himself always recognised the hopelessness of any attempt to exclude oxygen, and never made any efforts in that direction. He had already, as has been pointed out, tried to mitigate the putrefactive process by scrupulous cleanliness, insisting on the washing of the hands between the dressings, a plentiful supply of towels in the wards, and the use of various substances which we now know to possess antiseptic properties. No appreciable improvement resulted, and it was perhaps fortunate for the development of antiseptic surgery that Lister's wards were so insanitary that these attempts at cleanliness were of little avail. It is important to remember this fact, for the considerable improvement which in numerous instances followed on the recognition of the great importance of scrupulous cleanliness, led many surgeons to attribute the good results of antiseptic surgery entirely to simple cleanliness and not to the destruction of bacteria.

At this time (the early 'sixties' of the last century) Lister, then Professor

[1] Vol. ii, p. 515.

of Surgery in the University of Glasgow, was constantly speculating on these matters, especially on the cause of the putrefaction of the discharges in wounds, and during one of his discussions with friends the suggestion was made that the perusal of Pasteur's papers on fermentation and spontaneous generation, which had then recently appeared, might be of assistance to him. This suggestion was fertile, and it may well be imagined how great a revelation to Lister were these researches of Pasteur. The oxygen theory of putrefaction, which had seemed to oppose all advance, was at once swept away, and the problem was now seen to be not to exclude intangible gases, but to deal with living organic particles which could be destroyed and the characteristics of which could be carefully studied.

It is interesting to note that previous to the appearance of Pasteur's work three papers had been published which really laid the foundation of the germ theory and of modern bacteriology; these were by Schultze in 1836, Schwann in 1837, and Cagniard-Latour in 1838. The two latter authors brought forward a large amount of evidence which satisfied them that the alcoholic fermentation of grape-juice was due not to oxygen but to the growth in the fluid of the *Torula cerevisiae*. Schwann also studied the putrefactive decomposition of meat-juice and other organic substances, and came to the conclusion that it was not the gases of the air which caused these changes, but organic particles which floated in the air, and could be destroyed by heat. He went further and ascribed all fermentative processes to the growth of the organisms found in fermenting liquids. In 1854 additional evidence was brought forward by Schröder and Dusch, who showed that it was not necessary, following the example of previous observers, to calcine the air which had access to the flasks, but that putrefaction did not occur in organic fluids contained in flasks if the air entering the flasks were filtered through cotton-wool. Pasteur finally (1864) completed the proof by showing that it was not necessary either to heat the air or to filter it before admitting it to properly prepared organic fluids, but that if it were conducted along a tortuous tube in which the dust could settle before it reached the fluid, no change took place in the organic matter. He showed also that if flasks containing putrefactive material were left open in a place where the air had been undisturbed sufficiently long to allow the dust to settle, as, for example, in a cellar, no decomposition took place, nor did any micro-organisms appear in the fluids.

Apart from these researches on the causes of fermentation, much heated discussion had gone on for many years as to the significance of the minute 'animalculae' which appeared in decomposing fluids, and the question whether these organisms originated *de novo* from the organic fluids in which they were found, or whether they always came from pre-existing organisms which had somehow or other gained admission to the fluids, had been warmly debated. Pasteur's work, however, really struck the final blow at the doctrine of spontaneous generation, although many further convincing proofs were brought forward later by other experimenters, notably by Tyndall and by Lister himself.

The information, then, which Lister obtained from studying Pasteur's work was (1) that organic fluids which had been boiled but were still prone to the development of organisms and to fermentative changes, could be preserved without any change if the air admitted to the material after boiling had been calcined, or filtered, or had been kept at rest so long, or reached the fluids so slowly, that all the dust had had time to settle; (2) that the organisms found in the decomposing fluids were not produced spontaneously by changes in albuminoid materials, for they might appear and grow in artificial fluids containing mineral substances only; (3) that these organisms were present in the dust of the atmosphere, and in that deposited on surrounding objects; and (4) that the decomposition of the organic fluids coincided with the development of these organisms. If they were absent, no decomposition occurred; as soon as they were admitted and began to grow, fermentative changes appeared.

This was the work to which Lister's attention was called, and it is easy to imagine the flood of light thrown on the whole subject of decomposition in wounds by its perusal. Lister at once applied himself to the task of finding some means of preventing the development of these living organisms in wounds. He formulated the hypothesis that the inflammation and septic diseases which occurred after wounds were due to the putrefaction of the discharges of the wounds; while this putrefaction was in its turn due to the entrance of living micro-organisms from the air, and from the dust on surrounding objects. He made the deduction that if the access of living organisms could be prevented, and their growth in wounds arrested without at the same time damaging the wounds seriously by the means employed for this purpose, an open wound would follow the same course as a subcutaneous injury. No doubt this first conception was incomplete, but it was thoroughly sound, and while subsequent work has enormously extended the facts, the basal idea that it is the entrance of organisms into the wound from without which produces the inflammatory and septic troubles, and that therefore the aim of treatment must be to exclude or destroy them or inhibit their growth, still remains the fundamental principle of the treatment of wounds. The great variety of bacteria which may enter wounds, their very different behaviour, their various pathogenic properties, their origin, and the reaction of the tissues to their growth, are all subsequent developments which have had their influence on the details of the method, but which have in no way affected the original Listerian principle.

With the light thus shed on the problems on which he had been pondering for years, Lister at once threw all his energies into the application to the treatment of wounds of the principle established by these researches *in vitro.* It was evident that filtration of the air which reached wounds was not a practical plan, nor could heat be used to destroy the organisms in all places from which they might contaminate the wounds, for these organisms were not merely floating in the air, but were deposited on all surrounding objects, and to operate in an atmosphere of filtered air, or of air previously subjected to heat, could not meet the requirements of the case. Hence he turned to the search for chemical substances which possessed the power of destroying these living particles. About that time experiments had been made at Carlisle on the disinfection of sewage by German creosote, the active agent in which was crude carbolic acid; the interesting results so obtained suggested to Lister that this substance might serve his purpose, and he accordingly procured a supply. He determined to test the new principle first in the treatment of compound fractures, the results in these injuries being especially bad at that time in his wards. He had to wait some months before he could put his ideas into practice, but at length the opportunity came, and on the 12th of August, 1865, he was able to put the matter to the test, with results which amply justified his hypothesis. It is very curious that the material thus more or less accidentally selected in the first instance as an antiseptic has turned out to be the most suitable of any yet known and tested for various purposes in connexion with the asepsis of wounds, especially for the disinfection of the skin.

Now followed a period of the most remarkable activity, involving an amount of mental exertion and patient toil which probably no other man would have had the genius or indeed the physique to carry through. Lister came to this work equipped in an entirely exceptional manner. Endowed with extraordinary mental insight, and provided with much physiological and chemical knowledge, he had spent years in considering and investigating the subject of wounds, and he was thus able to grasp the significance of the numerous new phenomena which he observed while carrying out his methods of treatment. During this early period every case contributed fresh information, and led to constant improvement in his attempts to imitate nature's processes, and this constant modification of his methods in accordance with fresh observations is remarkable evidence of his clearness of vision, and a striking proof of the elasticity of his mind and of the absence of bias. To the very end of his active work as a surgeon he was never entirely satisfied, but was always straining for something better, having ever in mind his one great ideal of making the conditions existing in an open identical with those in a subcutaneous wound.

This activity took three great directions: (1) bacteriological work, especially in connexion with the germ theory of putrefaction; (2) constant striving after improvements in the methods employed in carrying out the principle which he had laid down as essential in the treatment of wounds; and (3) improvements in the treatment of various diseases and injuries, rendered possible by the fact that operations had lost their greatest dangers.

BACTERIOLOGICAL WORK

In the early days Lister did a great deal of bacteriological work, partly in order to satisfy himself as to the accuracy of the theory on which he had based his system of treatment, and partly to test suggested alterations in his methods. Very little of this work has been published, indeed most of it was never intended for publication, but what he has written shows the impress of his genius. He repeated Pasteur's experiments, especially that of the flask with the contorted neck, and he showed that the same results might be obtained by another method, namely by the use of glasses provided with loosely fitting glass covers.[1] He also pointed out the importance of properly sterilizing by heat all vessels employed in these experiments, and he introduced the methods of dry sterilization which are still employed for this purpose.[2] He devised a flask for the storage of organic fluids and also methods of filling tubes and vessels from these flasks, which are most valuable when working with fluid media.[3]

Perhaps his most important work in pure bacteriology was that on lactic fermentation. In that he obtained for the first time a pure cultivation of a single species of bacterium (*Bacillus lactis*), and he demonstrated that the lactic fermentation was due to the growth of this organism in milk. In this connexion he devised a plan of separating different kinds of bacteria from one another by repeated dilution which, though very laborious, remained practically the only satisfactory means of obtaining pure cultures till the introduction of Koch's method of cultivation on solid media.

Experiments were also made on the sterility of the natural fluids of the body, such as milk and urine, before they came into contact with the external air. A great deal of work was done in the way of testing new antiseptics and the value of different dressings, in fact almost every one of the later stages in his methods was tested in this way. Very interesting also is his work on the value of

[1] Vol. i. p. 279. [2] Vol. i, p. 278. [3] Vol. ii, p. 55.

the inhibitory action of antiseptics on the growth of bacteria, as distinguished from their destructive action.[1]

Apart from these experiments *in vitro*, it must be realized that the introduction of the antiseptic system was one vast experiment on the living body. Up to that time, with perhaps the exception of observations by Davaine upon anthrax, no work had been done which demonstrated any pathogenic action of bacteria. Indeed during the early development of antiseptic surgery the question of pathogenic bacteria, as we now know it, did not arise. In the first instance it was 'putrefaction' in the discharges of a wound which was attacked, and though this was looked on as due to the bacteria present in these discharges, no classification of these bacteria into species was thought of, and no differentiation into pathogenic and non-pathogenic organisms was made. It was simply a case of preventing the entrance of bacteria as a class into wounds and their development there. Very soon, however, we find Lister pointing out that there must be different species of bacteria, and that putrefaction was not the only injurious fermentation which might occur in wounds, for he noted that in some cases, although there was no odour in the discharges, suppuration nevertheless occurred; thus, in a footnote to a paper published in 1870[2] he says: 'This group (cases of putrefactive suppuration) ought to include the products of other ferments besides those of putrefaction, for I am satisfied that inodorous ferments sometimes occur in the animal fluids and produce salts which stimulate to suppuration; also viruses inducing suppuration are very probably of the same essential nature (ferments), though some at least are odourless, as in the case of erysipelas.' It is true that he attributed the odourless suppuration in some of these cases to reflex disturbance of the nervous system, produced, for example, by tension in the wound, yet at the same time he recognised that, in some instances at any rate, it was due to bacterial infection. Indeed it was more especially with the view of demonstrating that there are different kinds of bacteria, each with its own fermentative action, that he undertook his work on lactic fermentation. Very soon also we find him beginning to realize the possibility of the penetration of bacteria into the body from the wound, and thus the distinction between pathogenic and non-pathogenic bacteria.

Under the system he evolved not only did inflammation and suppuration disappear, but also pyaemia, hospital gangrene, erysipelas, and tetanus. In his demonstrations at the hospital he was fond of pointing out how erysipelas spread like fairy rings, as if the organisms which produce it were advancing in the tissues before the redness and dying out behind it, a view strikingly confirmed subsequently by Koch and others. He also remarked, with some diffidence it is true,

[1] Vol. i, p. 278. [2] Vol. ii, p. 140.

on the disappearance of tetanus from his wards, as if that also were a disease due to bacteria.

Another subject on which he soon began to speculate was the protective arrangements of the body. He succeeded in preserving urine and milk from alteration without subjecting them to any preliminary treatment by boiling or otherwise, thus showing that bacteria did not penetrate along healthy canals, such as milk-ducts. This he attributed to the destructive action of the healthy living organism on the bacteria, and he pointed out that in wounds also it was capable, to a certain extent, of disposing of micro-organisms. Although Lister did not do any experimental bacteriological work on animals, there is no doubt that the remarkable results obtained by his methods of wound treatment, and the energy and insight with which he laid stress on bacteria as the cause of the grave troubles following wounds, had a most important influence on others, leading them to the study of the pathogenic effects of bacteria, and thus served to stimulate the rapid development of the science of bacteriology.

THE DEVELOPMENT OF THE ANTISEPTIC SYSTEM[1]

We have already traced matters up to Lister's first application of his views to a case of compound fracture. That compound fractures should have been the form of injury selected by Lister as likely to afford the most suitable test of his hypothesis is not difficult to understand when it is remembered how great was the contrast in those days between the course followed respectively by simple and compound fractures. The latter were indeed the most fatal of all surgical injuries, and accounted for a large proportion of the cases of pyaemia which were of such frequent occurrence in all hospitals.

The object aimed at being the prevention of the putrefaction in the wound brought about by organisms introduced either at the time of the accident or subsequently during the course of the treatment, means were taken to obviate both dangers. The first indication was fulfilled by introducing into the wound a pledget of calico or lint held in a pair of forceps and saturated with undiluted crude carbolic acid; with this all the interstices of the wound were thoroughly swabbed out. The second indication was met by placing over the wound, and overlapping it in all directions, for about half an inch, a double layer of lint saturated in the same material. This lint was covered by a piece of thin block-tin or sheet-

[1] In this section the history of the evolution of wound treatment which Sir Hector Cameron has given in his James Watson Lectures before the Faculty of Physicians and Surgeons of Glasgow has been largely drawn upon, and to that volume readers who desire a fuller guide to Part III of these collected papers are referred (*Lord Lister and the Evolution of Wound Treatment during the last Forty Years.* Glasgow. J. MacLehose & Sons. 1907. Post 8vo, pp. 96). See also vol ii. pp. 349, 365.

lead, moulded in a concave form so as to fit over the mass of lint. It was fixed in position by strips of adhesive plaster, the limb being placed in suitable splints. The carbolic acid and blood mingling in the small piece of lint formed a thick paste, and converted the whole into a sort of crust or scab, which adhered to the wound with great tenacity. Once a day the tin cap was removed, and the crust of lint and blood was painted over lightly on its outer surface with carbolic acid. What was aimed at was to keep this crust from becoming septic, while its under surface in contact with the wound, becoming gradually free from the carbolic acid which it at first contained, should cease to be irritating in itself, and therefore no longer interfere with the process of healing. The dressing was of the nature of an artificial scab, but with this difference, that the substance of the scab was charged with an antiseptic introduced with the object of destroying any germs of putrefaction which might find their way to the scab from the skin, or from the splints padded with soft absorbent material to receive such bloody discharges as oozed from the wound during the first day or two. It was, however, recognised that the vapour of the carbolic acid retained under the cap of tin interfered with the process of cicatrization, and therefore, after it seemed likely that the wound was so far repaired as no longer to communicate with the seat of fracture, the antiseptic crust was detached, and the final closure of the surface wound allowed to take place under some simple form of dressing.

The results of the application of the principle to the treatment of compound fractures could not have been more striking, for the patients suffered neither from putrefaction and inflammation in the wound nor from general septic diseases. The necessity for primary amputation in the majority of cases disappeared, many limbs and lives were saved, and the treatment of these injuries underwent a radical change.

There is no instance in the history of surgery, and indeed few in the history of science, in which a deduction has been so completely verified when put to the test.

Its success in this particular class of cases naturally suggested and even urged the extension of the principle to others, and it was not long before an opportunity occurred of employing it in a case of psoas abscess, an affection from which at that period few adults recovered, while it was only slightly less fatal in children. The patient was a middle-aged woman, and the abscess, which was pointing in one loin, was about to burst. It was incised, and some of its thick contents mixed with the crude carbolic acid; two pieces of lint soaked in this mixture were laid over and around the wound and covered with a cap of block-tin. When the dressing was removed next day, there was no escape of pus as was usual under the treatment then customary, and pressure caused only a drop or two of serous fluid to exude. This result, though highly satisfactory, produced a momentary embarrassment, for there was no pus or blood with which to mix the carbolic acid for the new dressing. This difficulty was overcome by thickening a solution of carbolic acid in boiled linseed oil (1 in 4) with whitening (carbonate of lime). This putty-like material was spread upon a piece of block-tin and laid over the incision, care being taken that this dressing overlapped it widely in all directions; it was fixed in position by strips of adhesive plaster, and an absorbent compress was bandaged over all. The dressing was renewed daily. The result was entirely satisfactory; the abscess cavity remained free from any septic change, and eventually healed, having yielded no pus from first to last, but only a steadily diminishing quantity of clear serous fluid.

This case taught many important lessons; it not only afforded a fresh proof, under slightly different conditions, of the truth of the theory, but was the first demonstration of facts since grown familiar, but which could not then certainly have been foretold. These were that after the original contents of an abscess, whether acute or chronic, were evacuated, if changes in its interior resulting from contact with outside morbid agents be avoided, instead of pus only a thin serous fluid would be discharged and would rapidly diminish in quantity; that in consequence it was neither essential to open the abscess at a dependent part, nor necessary to make counter-openings; that under such circumstances no constitutional disturbance need be feared; and lastly, that such abscesses, if a careful course of antiseptic treatment were persevered in, might be expected to close permanently.

A purer specimen of carbolic acid was obtained before long and found to be soluble in water in the ratio of one part in twenty (five per cent.). After the introduction of this carbolic lotion the method followed in the treatment of compound fracture was first to wash out the interior of the wound thoroughly with a five per cent. solution of the acid, and then to cover its surface with a piece of lint saturated with carbolic oil (1 to 4) large enough to overlap it in every direction; over this was put a large dressing of the putty, smoothly spread on calico to the thickness of about a quarter of an inch. At first, a further covering of block-tin was employed, but its use was afterwards dispensed with as unnecessary. The dressing of putty was changed daily, but the piece of oiled lint, soon saturated with blood, was left next the wound, harbouring under it a crust of blood of greater or less thickness. It became usually fairly dry, and when the time arrived for removing the crust and discontinuing the splints, either a firm cicatrix or a superficial granulating sore was exposed to view. In opening an abscess a large piece of lint soaked in a solution of carbolic acid (1 to 4) was placed over the portion of the skin to be incised and left for a little to act upon it. The lower edge of it was then raised, the incision made, and the curtain of lint let fall, the abscess being evacuated by gentle pressure under its protection. The antiseptic was not injected into the cavity of the abscess, experience having shown that while such injection was quite superfluous, it could only do mischief by causing irritation. A narrow strip of lint dipped in the same oily solution was introduced through the incision to prevent primary union and at the same time to act as a drain. On removal of the oily antiseptic curtain a dressing of the putty, spread on a piece of block-tin, was immediately fixed over the incision by adhesive plaster and bandaged to the part. The thin discharge flowed out beneath the edges of the putty, which was renewed once a day.

The use of block-tin was not long continued: the putty was spread upon calico, and in this form the dressing was extended to the treatment of incised wounds made by the surgeon. Although the results obtained with this antiseptic putty dressing were strikingly satisfactory, its employment was attended by certain practical inconveniences, and Lister devoted a great deal of patient research to devising a substitute which should be not less effective to achieve the main object in view, but more convenient in use. After many experiments, he found a suitable material in shellac prepared in the following manner. When mixed with carbolic acid (1 to 4) shellac forms a flexible mass from which, as from a reservoir, the acid is constantly and not too rapidly given off. The practical objection to its use in this form was that it adhered too firmly to the skin, but this was overcome by spreading the mixture on calico and then painting a solution of india-rubber in benzene over the surface. The thin layer of india-rubber left on the surface of the shellac when the benzene evaporated prevented the plaster sticking to the skin, while the carbolic acid as it was liberated from the shellac passed freely through it. This new dressing presented many practical advantages. It was not disintegrated by friction like putty, and being much lighter was not only far less cumbrous, but could be more easily maintained in position; while, further, it was always ready for use, whereas the putty had to be specially prepared by the surgeon on each occasion. It was adopted alike for the treatment of injuries, abscesses, and incised wounds. In the last the method of treatment was as follows: During the performance of an operation the wound was from time to time irrigated with carbolic lotion, and more especially was filled with this lotion while it was being stitched up. The lotion was then expressed from the wound, the lac-plaster immediately applied, overlapping the surface to a considerable area around the wound, cloths being placed about the margin in order to absorb the discharge that passed out from under the lac-plaster. Attention was also paid to the drainage of wounds, and for this purpose a strip of lint soaked in a solution of carbolic acid and oil (1 to 4) was inserted at one angle of the wound and retained for at least forty-eight hours.

It will be observed that these early antiseptic dressings were not absorbent, and were therefore impervious to the discharges from the wound. Though the carbolic acid they contained could not be washed out of them, however great the flow of blood or serum in the early stage, it was constantly given off, thus preventing the entry of infective organisms. The fluids of the wound were, alike by the putty and the lac-plaster, shed from it in an antiseptic atmosphere maintained between the dressing and the skin by the carbolic acid slowly and constantly liberated from the putty or lac. Under the lac-plaster the wound healed without a scab.

The favourable reports of some surgeons on the use as an antiseptic dressing of oakum carefully selected and teased into a fine soft uniform mass next induced Lister to consider the advantages of a dressing which would absorb the fluids of a wound instead of distributing them. His previous objection to the use of porous dressings was founded on the observation[1] that the discharge, if at all free, washed out the antiseptic from the fibres of the material used and, by leaving over the wound a dressing devoid of any antiseptic, opened up the way for the penetration of putrefaction. In oakum, however, each fibre was imbued with the antiseptic (creosote) in an insoluble vehicle, so that the discharge could not wash the antiseptic out of the fibres any more than in flowing beneath the lac-plaster, to a narrow strip of which each individual oakum fibre might fairly be compared.

While impressed with the advantages of an absorbent material thus thoroughly imbued with an antiseptic which would not be washed out of its fibres by the discharges, Lister preferred to devise a dressing in which the proportion of the antiseptic could be accurately adjusted, and free from certain minor practical drawbacks which attended the use of oakum. This led to the introduction of the gauze dressing, which in one form or another has since been and still is used all the world over, either charged with some antiseptic substance or sterilized by heat. A cheap muslin of open texture, known in the trade as 'book-muslin', was charged with resin, paraffin, and carbolic acid. Resin, which is one of the principal constituents of ordinary oakum, holds carbolic acid with great tenacity, so that a mixture of one part to five does not, if applied to the tongue, produce any undue sense of pungency. The paraffin was added to obviate the objection that this mixture was very sticky, as well as apt to be irritating to many skins. The melted ingredients were mixed in the proportion of one part of the acid to four respectively of resin and paraffin, and the mixture was diffused through

[1] Vol. ii, p. 168.

the fibres of the cloth. This antiseptic gauze had carbolic acid thus fixed in every fibre, while the fine spaces between, which give its porous character to the cloth, were still open for the discharge to pass through. It was folded in such a way as to make a thickness of eight plies and placed over the wound, overlapping it widely in all directions. But in order to prevent fluids from going straight through the eight plies of gauze and possibly exhausting its antiseptic ingredients at that part, a piece of very thin macintosh or jaconet, previously washed in the antiseptic lotion, was incorporated with the mass of gauze by being slipped under its top layer, thus leaving seven layers of the gauze next the wound, and compelling the discharges to make their way to the margins of the dressing, instead of coming straight through.

As has already been said, the whole aim of Lister's work was to bring about and maintain in an open wound conditions similar to those which exist in a subcutaneous injury, and from the first he fully recognised that while fermentative changes were the most important they were not the only sources of irritation—that in fact the chemical substance employed to prevent fermentation was also more or less irritating, and interfered with the attainment of his ideal. He therefore now directed his attention to devising means of diminishing or altogether avoiding irritation of the wound by the carbolic acid contained in the dressings. The irritation produced by the antiseptic which came into contact with the wound during the operation was only temporary. The carbolic acid when mixed with the blood lost much of its irritating character, and was moreover absorbed, and disappeared from the wound in a comparatively short time. When once the wound had been closed at the operation, Lister considered it unnecessary to irritate the line of incision or the interior of the wound by subsequent applications of the antiseptic. He therefore never syringed out a wound at a subsequent dressing, as some surgeons were fond of doing; the utmost he did was to have some carbolic lotion flowing over the line of incision and the adjacent skin while the dressings were being changed. This lotion did not penetrate into the interior of the wound, and acted on the surface only for the brief period during which it was exposed. Nevertheless he recognised that the carbolic-acid vapour coming off from the gauze or the lac-plaster was irritating to the line of incision, and therefore he made numerous experiments with the view of finding some material more or less impenetrable to the vapour of carbolic acid, which might be placed directly over the wound below the carbolic gauze, but widely overlapped by the absorbent antiseptic gauze dressing. Though the vapour of carbolic acid passed easily through gutta-percha tissue and thin sheets of india-rubber, the common oil-silk used for covering water dressings was found to be much less penetrable by it. Taking this as a basis, he covered it with gum copal, which was found to offer even stronger opposition to the passage of carbolic acid than oiled silk itself, and lastly, painted over both a solution of dextrine, which permitted the surface to be uniformly wetted. Before being applied to the wound this 'protective plaster' was dipped in a solution of carbolic acid. The acid was soon dissipated, and the plaster became an unstimulating covering to the wound, defending and protecting it from the direct action of the superimposed and widely overlapping antiseptic dressing, but in no way interfering with the outflow of the blood and serum.

While these improvements in the material of the dressings and their manner of application were in progress, another question had been engaging Lister's attention, and had been the subject of much thought and experimental inquiry. From an early stage he had seen that if the full advantages of the antiseptic system and all that it implied were to be realized in general surgical treatment, the method of arresting haemorrhage, and especially the kind of ligature used, must be reconsidered. He had very early obtained evidence that blood-clot could, in the absence of fermentative changes, undergo organization. In 1867[1] he placed on record the following observation: 'I was detaching a portion of the adherent crust from the surface of the vascular structure into which the extravasated blood beneath had been converted by the process of organization, when I exposed a little spherical cavity about as big as a pea, containing brown serum, forming a sort of pocket in the living tissues, which, when scraped with the edge of a knife, bled even at the very margin of the cavity. This appearance showed that the deeper portions of the crust itself had been converted into living tissue. For cavities formed during the process of aggregation, like those with clear liquid contents in a Gruyère cheese, occur in the grumous mass which results from the action of carbolic acid upon blood; and that which I had exposed had evidently been one of these, though its walls were now alive and vascular. Thus the blood which had been acted upon by carbolic acid, though greatly altered in physical characters, and doubtless chemically also, had not been rendered unsuitable for serving as pabulum for the growing elements of new tissue in its vicinity.' He also made an observation which was quite novel at the time, that a piece of dead bone which lay exposed in the wound of a compound fracture, instead of being exfoliated as would have occurred in a septic wound, became absorbed.[2]

These and other similar observations raised the question whether ligatures might not be cut short and left in the wound, for it seemed reasonable to hope that, just as dead bits of tissue had been disposed of by absorption, so more or

[1] Vol. ii, p. 8. [2] Vol. ii, p. 16.

less slender threads of organic material, prepared so as to be free from septic organisms, might be similarly removed.

Lister's experiments and observations on this subject are fully recorded in papers printed in volume ii. He first, on the 12th of December, 1867, tied the left carotid artery of a horse with purse-silk which had been steeped in a strong watery solution of carbolic acid;[1] the ends were cut short, and the wound, which was dressed antiseptically, healed immediately. Six weeks later the horse died, and on laying open the vessel there was found at the cardiac side of the ligature a firm adherent clot, an inch and a quarter long, but at the distal side coagulation had been entirely prevented by the reflux current of blood through a branch about as large as the human vertebral artery, which took origin as close to the ligature as possible. Under such circumstances secondary haemorrhage would certainly have occurred had a thread been applied in the manner then commonly employed. But in this specimen the artery appeared as strong at the part tied as elsewhere. The cul-de-sac showed some irregularity due to puckering of the internal and middle coats, but the surface appeared completely cicatrized, and presented the same character as the natural lining membrane of the vessel, and the ligature, which seemed as yet unaltered, was found lying dry in a bed of firm tissue. The tissue within the noose was apparently a new formation in place of the portion of external coat killed by the tightly tied thread; externally, the constriction, necessarily caused in the first instance by tying the ligature, had been filled in by a similar compact structure.

The success of this experiment justified the application to man of the principle upon which it was based. Accordingly, when a few weeks later (29th of January, 1868) Lister was called upon to tie the external iliac artery for aneurysm of the common femoral artery in an elderly lady, he made use of a silk ligature steeped in undiluted carbolic acid, used sufficient force to divide the internal and middle coats of the artery, cut the ends of the ligature short, and dressed the wound antiseptically. The aneurysm consolidated, the wound healed without suppuration, and the patient was out of bed in four weeks, and was able to take outdoor exercise in two more. Within a year she died suddenly from rupture of an aortic aneurysm. Careful examination of the iliac artery after death showed that the knot of silk was still in great part present, enclosed in a thin-walled capsule. Besides the remnant of the ligature, the tiny capsule contained a minute quantity of yellowish semi-fluid material, looking to the naked eye very like thick pus. Microscopic examination, however, proved that pus corpuscles formed but a small proportion of its constituents, which were principally rounded corpuscles of smaller size, and fibro-plastic corpuscles, together

[1] Vol. ii, p. 64.

with some imperfect fibres and granular material. There were evidences of the silk having been eroded by the action of the tissues around it, pieces of its fibres being present in the puriform fluid ; they had not been materially softened, but only ' superficially nibbled, so to speak. Indeed,' Lister added, ' considering the organic character of silk, the remarkable thing seems to be, not that it should be absorbed by the living tissues, but that it should resist their influence so long.'

The local result in this case was thus not altogether satisfactory, and Lister therefore turned his attention to other materials. Animal ligatures of various kinds, catgut, tendon, and leather, had long before been tried and abandoned as unsatisfactory, but there was good reason to expect that in the absence of sepsis very different results would ensue. Lister had been struck by the fact that the sloughs and clots produced by the injection into naevi of strong solutions of perchloride of iron or tannic acid, though impregnated with these substances, yet rapidly disappeared without suppuration. He had also learnt that portions of dead tissue and of blood-clot, free from sepsis, were absorbed, and that this process was in no way interfered with when carbolic acid had freely acted upon them. There seemed, therefore, to be no reason why carbolic acid should not be used for disinfecting the animal ligature.

In his next experiment, in which (on the 31st of December, 1868) he tied the right carotid of a calf at about the middle of the neck, he applied two ligatures separated from each other by a distance of about an inch and a half. One was composed of three strips of peritoneum from the small intestine of an ox, twisted into a cord, the other was of fine catgut. Both had previously been soaked for four hours in a saturated watery solution of carbolic acid. The wound healed by first intention, and the calf was killed a month afterwards. The result of the dissection of the vessel was at first disappointing, for the ligatures were still to all appearance present and as large as ever ; more minute examination showed that in reality they had been absorbed and replaced by bands of living tissue, ' the growing elements of which had replaced the materials absorbed, so as to constitute a living solid of the same form '. The fleshy bands so formed were continuous with the arterial walls, and so far from weakening the vessel at the point of ligature had rather strengthened and reinforced it, while by the early healing of the wound an immediate reconsolidation of the tissues detached from the vessel had taken place. The evidence of the organization of the ligatures, clear to the naked eye, was abundantly confirmed by the microscope. All these facts seemed to give sure promise, as indeed has proved to be the case, of security against secondary haemorrhage, so frequent and so justly dreaded up to that time, as well as of the absence of suppuration in connexion with such ligatures.

Lister subsequently gave much time and thought to the discovery of the best methods of preparing the catgut ligature so as to meet the various conditions which were required, and his latest contribution to the subject was in fact published so recently as the 18th of January, 1908.[1] The raw catgut as obtained from the shops was unsatisfactory, for the ligature as soon as it became soaked with fluid, and especially with serum, swelled up, and the knots became untied; further, it was absorbed too rapidly, a most serious drawback. The chief points to which he paid attention in the preparation of catgut suitable for general surgical use were the breaking strain, the solidity and permanence of the knot, the pliability of the material, and the rapidity of its absorption in the tissues; the papers in which he described the different methods devised for attaining these objects are reprinted in the second volume. At the present time, in the preparation of catgut attention is directed chiefly to its sterilization, without special reference to the other essentials on which so much stress was laid by Lister, but it may be doubted whether this is wise, and whether any better material than Lister's sulpho-chromic catgut has been introduced.

The adoption of absorbent dressings and absorbable ligatures marked a distinct stage in the development of antiseptic surgery; by simplifying the technique and rendering the results surer in the hands of other surgeons, it greatly contributed to bring about the general adoption of the system, and paved the way for the extraordinary extension of the field of surgery which the next quarter of a century was to witness.

At about the same time the metallic suture ceased to be the sole method of closing the wound, giving place to more convenient stitches of silk. In 1870[2] Lister gave an interesting account of the methods he employed in stitching up a wound, especially in those cases in which a portion of the skin had been removed, and where, therefore, there was considerable tension at the edges of the wound. The silk was rendered aseptic by being impregnated with a mixture of carbolic acid and melted bees-wax, and was kept in a five per cent. solution of carbolic acid until required. Catgut was also used in suitable cases for stitches, silver wire was employed where much tension existed, and silkworm gut and horsehair were utilized especially in septic cases. Later, waxed silk was replaced for most purposes by ordinary Chinese twist, rendered aseptic by having been steeped in 1 to 20 watery solution of carbolic acid.

It was at about this period also that Lister began to make use of the india-rubber drainage-tubes devised by Chassaignac early in the century for carrying off pus. Though no pus was formed in aseptic wounds, yet a considerable flow of blood and serum followed immediately upon the infliction of the wound, however

[1] Vol. ii, p. 119. [2] Vol. ii, p. 130.

managed. Pressure forceps, the use of which makes it possible to stanch by a few minutes' pressure, and, if thought necessary, to tie all bleeding-points, had not yet been introduced. Moreover, the stimulation of the wound by the antiseptic fluid, even though the endeavour was made to reduce this to a minimum, increased the flow of serum. To prevent the accumulation of these discharges, Lister had been in the habit of introducing and retaining for at least forty-eight hours, at one angle of the wound, a strip of lint soaked in a solution of carbolic acid and oil (1 to 4). The substitution of india-rubber drainage-tubes proved a valuable improvement in antiseptic technique. They were, of course, kept constantly immersed before use in a strong solution of carbolic acid.

Holding the view that the dust floating in the air was a potent source of infection, but recognising that the contact of carbolic lotion with the wound during the operation and at subsequent dressings was a source of irritation, Lister at about this period introduced the use of a spray of carbolic acid solution to play around the wound, with the view of destroying the germs floating in the air before they settled on the wound. He, however, eventually convinced himself, firstly, that the spray did not thoroughly disinfect the atmospheric dust, and secondly, that not only were the microbes in the air for the most part not pathogenic, but also that the tissues were capable of destroying organisms, provided they were neither very numerous nor very virulent. After full consideration of all the facts, and especially those constantly observed in the treatment of empyema,[1] Lister abandoned the use of the spray without reverting to the other precautions against the atmospheric infection which had formerly been deemed, and perhaps then were, essential.

Although carbolic acid had proved so conspicuously satisfactory as an antiseptic for use in surgery, it was open to two objections. The first was that it was irritating to the wound, and must therefore to some extent retard healing, and was poisonous if absorbed in quantity ; the second, that, being volatile, it was constantly being dissipated from the dressings, which it was therefore deemed advisable to change oftener than would otherwise have been necessary. Lister, consequently, was always seeking to find some substance which, while possessing adequate antiseptic properties, would yet be unirritating, non-poisonous, and non-volatile.

Among a large number of substances which were tested in practice, the following may be mentioned. In consequence of reports as to the value of boracic acid for the preservation of food, this substance was very extensively tried ; it was, however, found to be quite inefficient as an antiseptic for ordinary practice, but it did very well in the case of superficial sores and ulcers, and for

[1] Address to International Medical Congress, Berlin, 1890. Reprinted in vol. ii, p. 332.

those purposes it has continued to be used. At the present time, under suitable circumstances, boracic lotion (saturated solution of boracic acid in water), boracic lint, and boracic ointment are commonly employed. Salicylic acid was much praised by Thiersch, and was consequently carefully tested by Lister, but it was found to be open to many objections, especially that it was irritating to the wounds, and inefficient as an antiseptic. It is only used now in the form of salicylic wool and salicylic ointment. Thymol was for a time a favourite antiseptic with some surgeons, but after testing it in various ways it was rejected as being untrustworthy. Preparations of eucalyptus also failed to meet the requirements, and it only remains in use in the form of ointment, which is still occasionally employed, chiefly in the treatment of burns. Acetate of alumina was used to a considerable extent at one time, but on putting it to a careful test it also was rejected.

After the publication of Koch's earlier papers on disinfection, the various mercurial salts were examined, and they form a very essential part of the antiseptic equipment at the present time. A good deal of time was expended in testing the relative merits of lotions of the biniodide and perchloride of mercury: the conclusion reached was that, from every point of view, especially in respect to its efficiency as an antiseptic and lesser tendency to irritate the skin and the wound, the perchloride was superior to the biniodide. The strength of the perchloride lotions employed at an early period, 1–2000 and 1–4000, were the strengths used by Lister at the end of his work, and are still extensively employed. A great deal of labour was also expended on finding a suitable mercurial dressing which should, on the one hand, be non-irritating to the skin, and on the other would provide a sufficient store of antiseptic to obviate the necessity of frequent changing of dressings, even when the discharge was considerable. The record of several of these attempts will be found in the published papers: for example, we have [1] a description of an attempt to form a gauze with a combination of perchloride of mercury and albumen. This again, gave place [2] to a gauze containing the double chloride of mercury and ammonium (sal alembroth). Sal alembroth, however, had the defect of being very soluble in the serum of the discharges, and the solution so formed was very apt to irritate the skin; it eventually gave place to the double cyanide of mercury and zinc, which was quite unirritating, and while sufficiently soluble in blood to give to the gauze charged with it sufficient antiseptic power to inhibit the growth of microbes, was yet not so soluble as to be washed out of the dressing by the discharges, however copious. An aniline dye added to the salt was found to have the double advantage of fixing the double cyanide in the gauze, so that it did not shake out when

[1] Vol. ii, p. 303.

[2] Vol. ii, p. 306.

dry, and of indicating that the dressing had been uniformly charged. The use of this insoluble and non-volatile antiseptic allowed the macintosh covering to be dispensed with, and thus the discharges could dry up and the gauze became a dry dressing. In place of macintosh, a mass of antiseptic wool (double cyanide or salicylic) was applied outside, so as to add to the thickness of the antiseptic material through which the discharge had to pass.

Lister, as Cameron has pointed out,[1] was probably the first to use a dressing sterilized by heat, and not containing any antiseptic substance. This he did while still Professor in Edinburgh, and the material used for the purpose was absorbent cotton-wool. He did not, however, persevere in the practice, because he felt that it could only be safely adopted in such cases as furnished a comparatively small amount of discharge, for if the discharge came through the dressing without having acquired any antiseptic material in its passage, there was nothing to prevent putrefaction spreading into the wound. Hence in cases in which there was a considerable amount of discharge, it was necessary to change the dressings very frequently; and further, the successful employment of sterilized materials not containing antiseptics was a much more difficult and complicated matter than the use of antiseptic dressings, and implied considerable practical experience in bacteriological work. He therefore preferred to retain the use of antiseptics judiciously chosen and carefully used, so that, while their germicidal influence was retained, an irritating effect was avoided.

By the time he ceased active work as a surgeon, he had arrived at a method of wound treatment in which the maximum amount of protection against bacterial invasion was secured with a minimum amount of irritation to the wound. The result was that the frequent dressings formerly employed were given up, and usually one dressing, or at most two, sufficed for a clean case. At the same time also the irritation of the wound had been so much reduced that, in a great majority of cases, there was no necessity for drainage; in fact, his ideal of a subcutaneous injury had been more or less attained.

GENERAL SURGICAL ACTIVITY

Apart from the surgical improvements directly resulting from the prevention of sepsis, Lister published various articles on other surgical subjects. Attention may especially be directed to the article on excision of the wrist,[2] and to the essays on amputation and anaesthetics[3] written for *Holmes's System of Surgery*. The article on amputation differs from other articles on the same subject written at that date, in that it presents the reader with the principles

[1] loc. cit. [2] Vol. ii, p. 417. [3] Vol. ii, p. 378; vol. i, p. 135.

which should guide the surgeon in dealing with the several parts of each limb, and omits those tedious details which are often more confusing than instructive. One of the best amputations of the thigh is here described for the first time. The essay on anaesthetics set forth the methods then employed in Edinburgh, and supported them by scientific arguments in favour of their validity. The subject of anaesthetics was one in which Lister has always taken the keenest interest, and it is needless to add that his teaching has many followers at the present day.

Another very interesting paper was that on the effects of the position of a part on the circulation through it.[1] For years before the introduction of Esmarch's bandage, Lister had been in the habit, in operations on the extremities, of elevating the limb for a few minutes, and then, while it was still elevated, applying a tourniquet at the upper part; in this way he brought about a bloodless state of the limb. On the publication of Esmarch's paper, Lister adopted his elastic band in place of the tourniquet; but he continued to employ elevation of the limb, as a safer means of emptying it of blood in the first instance than the application of a bandage from below upwards, as advised by Esmarch. In the paper to which reference is made Lister explained his views as to the mode in which his plan brought about the desired exsanguine state.

As soon as it became evident that antiseptic methods protected the patient against septic diseases, a great change came over general surgical treatment, and from the very first there was not a case admitted into Lister's wards which was not considered from a fresh point of view. The dangers arising from the risk of wound infection being averted, the question arose in most instances whether something better might not be done in the way of treatment by operation than had been customary. The result of the treatment of compound fractures by the antiseptic principle was that instead of looking on amputation of the limb as an imperative procedure, in the great majority of cases that plan became relegated to a secondary place, and all the surgeon's energies were devoted to an attempt to save the limb. The result is that nowadays amputation is only very rarely performed in compound fracture, or compound dislocation. The method led also to a complete revolution in the treatment of spinal abscess and tuberculous abscesses of joints generally. Quite early the subject of ununited fractures was taken up, and instead of employing apparatus or inefficient subcutaneous operations, the bones were boldly cut down upon and repaired in any way which seemed mechanically advisable. From that it was but a step to operations on recent fractures,—the patella, for example—to operations for malunited fractures, and to osteotomy for knock-knee and other deformities.

[1] Vol. i, p. 176.

Operations on healthy and diseased joints were introduced—the bold removal of loose bodies from joints, drainage of chronic synovitis, incision into diseased joints, and so on. Extensive operations for cancer of the breast became justifiable, and his results as regards recurrence in those early days were very excellent. Were it necessary, it would be easy to enumerate many improvements and fresh operations which were carried out by him from the very first. Indeed much of the present operative work was directly initiated by Lister, although he published very little with regard to it, for as such innovations seemed to follow naturally from the altered course of wounds, Lister did not consider that the publication of improvements in individual operations was necessary. The great charm of Lister's hospital work and lectures in the early days was not only the way in which the wounds healed, and in which the patients operated on recovered without pain, or fever, or illness, but also the fresh point of view from which every surgical affection was considered, and the manner in which the ancient canons of surgical practice were one by one overthrown.

PART I. PHYSIOLOGY

OBSERVATIONS ON THE CONTRACTILE TISSUE OF THE IRIS

[*Quarterly Journal of Microscopical Science*, vol. i (1853), p. 8.]

Our knowledge of the cause of the movements of the iris was till within the last few years in a very unsatisfactory condition. That this organ possessed contractile fibres was a matter of inference, not of direct observation. In the third part of the last edition of Quain's *Anatomy*, published in 1848, we find it stated (p. 915) that the radiating and circular fibres of the iris are generally admitted to be muscular in their nature, but the grounds for that admission are not mentioned. Mr. Bowman's Lectures on the Eye, delivered in the summer of 1847, and published in 1849, show us that the then state of histology in this country did not enable that accomplished microscopical anatomist to identify the fibres of the iris with other plain (unstriped) muscular tissue. At p. 49 he says, 'The fibres which make up the proper substance of the iris are of a peculiar kind, very nearly allied to the ordinary unstriped muscle, but not by any means identical with it.' He afterwards goes on to argue that, as we know that the organ changes its form, and as its vessels are so distributed that it cannot be erectile, we have no other resource than to consider its fibres contractile, which conclusion he supports by reference to the striped fibres in the iris of birds and reptiles.

In 1848 Professor Kölliker announced to the world his grand discovery of the cellular constitution of all plain muscular tissue, in a full and elaborate paper in the *Zeitschrift für wissenschaftliche Zoologie*.[1] At p. 54 of the first part of the first volume of this journal, after speaking of the arrangement of the

[1] Professor Kölliker may almost be said to have been anticipated in this discovery by Mr. Wharton Jones. Through the kindness of that gentleman, I have now before me two original drawings, made by him about the year 1843, of plain muscular tissue from the small intestine. In one of these the muscular fibre-cells are characteristically shown, except that their nuclei are not apparent; one of them is wholly isolated. In the other drawing, the alternate disposition of the fibre-cells is seen after the addition of acetic acid. He also observed, as he informs me, that the unstriped muscle of the oesophagus and stomach, and also of the uterus and other organs, consisted of similar elements—a fact which he yearly communicated to his class in his public lectures at Charing Cross Hospital. He was led, from appearances in the embryo, to infer that striped muscular fibre is originally composed of similar elements, which, in the process of development, are enclosed in a sarcolemma common to many of them, and become split into fibrillae. He thus accounted for the nuclei of striped muscular fibre, which, according to this view, are the persistent nuclei of the primitive muscular fibre-cells.—J. L.

fibres of the ciliary muscle, the sphincter pupillae, and dilator pupillae, he makes the following statement: 'The elements of all these muscles are undoubtedly smooth muscular fibres. In man I have but seldom succeeded in isolating the individual fibre-cells, but I have had more frequent success in the case of the sheep, where I found them in the ciliary muscle, on an average, 1-600th of an inch in length, and 1-4000th to 1-3000th of an inch in breadth. In man, in all these muscles one sees, as a rule, only parallel fibres projecting to a greater or less extent at the edges of small fragments of the tissue, these fibres exhibiting in abundance the well-known elongated nuclei, either with or without the aid of acetic acid. In man, the muscle of the choroid (ciliary muscle) has broader and more granular fibres and shorter nuclei than the iris. In the former the nuclei measure from 1-2400th of an inch to 1-1333rd of an inch; in the latter as much as 1-1090th of an inch.'

Here, then, we have, so far as I know, the first and only recorded observation of tissue in the iris identical with ordinary unstriped muscle.

It is to be remarked that, where he alludes, in the passage above quoted, to having in rare cases separated the individual fibre-cells of the muscular tissue, Professor Kölliker speaks of the three muscles (ciliaris, sphincter, and dilator) collectively; in other words, that he does not tell us in plain terms that he has isolated the fibre-cells of the iris at all. Now, the ciliary muscle is confessedly easier to deal with than the iris. Mr. Bowman, who speaks so doubtfully of the fibres of the iris, says of the ciliary muscle, 'the fibres are seen to be loaded with roundish or oval nuclei, often precisely similar to those of the best marked examples of unstriped muscle' (op. cit., p. 53). Another very eminent microscopical anatomist has informed me, as the result of his experience, that it was easy to identify the tissue of the ciliary muscle with that of other organic muscle, but that this had not been the case with the iris. That Professor Kölliker's isolation of the fibre-cells of the muscles of the eye was in reality confined to the ciliary muscle is rendered probable by the fact that, while the whole article quoted from shows a manifest desire on the part of its author to give all available detail, yet regarding the iris he mentions no facts requiring isolation of the fibre-cells for their determination; while, on the other hand, he tells us that the fibre-cells of the iris are narrower than those of the ciliary muscle, and gives the length of the nuclei in the human iris—things which are very readily observed without isolation of the fibre-cells. His figures refer to the human ciliary muscle alone; and the only measurements given by him of muscular fibre-cells from the eye refer to the same muscle in the sheep.

It would seem, then, that with regard to the iris, Kölliker's proof falls short of the test of isolation of the fibre-cells.

An operation for artificial pupil, by excision, performed by Mr. Wharton Jones, at University College Hospital, on the 11th of August of the present year (1852), placed in my possession a perfectly fresh portion of a human iris, and, without knowing that Kölliker's observations had extended to the muscles of the eye, I proceeded to avail myself of this somewhat rare opportunity of investigating the muscular tissue of the human iris. On placing under the microscope, four hours after the operation, portions of the tissue carefully teased out in water with needles, I found that some of the muscular fibre-cells had become isolated, and presented very characteristic appearances. I accordingly made camera-lucida sketches of the finest specimens, which are reproduced on a smaller scale in the accompanying figures (see Pl. I, A, Figs. 7–11). I drew the last cell (Fig. 8) nine and a half hours after the operation. And here I may mention that I have not found the muscular fibre-cells by any means a very perishable tissue. After an iris has been soaking two or three days in water, the muscular tissue of the sphincter is still quite recognisable, not only by the nuclei, but also by the individual fibre-cells.

Of the figures above referred to, (7) and (8) are examples of the most elongated cells that I saw. By reference to the scale it will be found that the cell (7) is about 1-125th of an inch in length, and about 1-3750th of an inch in greatest breadth ; while (8) is a little shorter, but of about the same average breadth. Kölliker divides muscular fibre-cells into three artificial divisions, according to their shape, of which the third contains the most elongated and most characteristic cells. Of this third division, the cells (7) and (8) are good examples, and, in fact, correspond in their measurements to average fibre-cells of the muscular coats of the intestines. The cells (9) and (10), though less characteristic in respect of their length—(9) being about 1-333rd of an inch in length, and 1-3000th of an inch in breadth, and (10) 1-300th of an inch by 1-3000th of an inch—yet present the same peculiar delicate appearance and soft outline, and the same elongated nucleus, of not very high refractive power relatively to the contents of the cell, but clearly defined. All these cells have the same flat or ribbon-like form which is exhibited by the cell (8) at *a*, where one edge has become turned up by a folding of the cell ; at *b* there seemed a tendency to transverse arrangement of the granules of this cell, which tendency is more strikingly exhibited at *b* and *c* in the cell (11), which, though not isolated, is introduced on that account. This tendency to transverse arrangement of the granules was long since noticed by Mr. Wharton Jones, as that gentleman has since informed me, and is, indeed, indicated in the drawings which are alluded to in the note above. In the cells of this iris, however, it was not by any means constant. Some of them, as (7) at *a*, and (9) at *a* and *b*, exhibited something of a longitudinal arrangement of the granules, such as was noticed some years since in unstriped muscle by Mr. Bowman, who considered the rows of granules as an approach to the fibrillae of striped muscle. These cells are more granular than I have found those of the iris of the horse to be ; but I may here mention that, on comparing with these drawings the outline of a fine specimen of a muscular fibre-cell of the sphincter pupillae of this animal, which I had sketched by the camera lucida, I find it to be almost an exact counterpart of the cell (7) as regards the shape and size of both the cell and its nucleus. The nuclei of these cells measure from 1-1400th to 1-1110th of an inch in length, and about 1-9500th of an inch in breadth. They are not, however, the most characteristic that are to be found in the iris. Fig. 12 is from a camera-lucida sketch of a nucleus of the sphincter pupillae of a horse ; it measures 1-840th by 1-15200th of an inch, and exhibits in a very marked manner the true rod-shaped figure which appears peculiar to muscular fibre-cells. On the other hand, I found some instances in the human iris of fibre-cells with considerably broader nuclei than those in the figures. The iris that yielded these cells was a blue one, apparently perfectly healthy ; it was active and brilliant before the operation, which was performed on account of central opacity of the cornea, resulting from an attack of a severe form of ophthalmia fifteen months previously. I watched the case closely from the first, and there was no reason to suspect implication of the iris in the inflammation.

Having thus satisfactorily verified the fact of the existence in the iris of tissue identical with ordinary unstriped muscle, I was naturally led to inquire into its distribution in the organ : and, as this is a subject of great interest, and one about which much difference of opinion has prevailed, I may mention here the facts which I have hitherto observed, although there be not very much of actual novelty in them.

Kölliker, in the article above referred to (loc. cit., pp. 53 and 54), describes a sphincter and dilator pupillae, the former ‘ very readily seen in the white rabbit, or the blue iris of a man, from which the uvea has been removed, about a quarter of a line broad in man, exactly forming the pupillary margin, and situated somewhat nearer the posterior surface of the iris ’. Of the dilator he says, while confessing the difficulty of the investigation, that he believes it to consist of many narrow bundles, which run inwards separately between the vessels, and are inserted into the border of the sphincter.

Bowman, on the other hand, states (op. cit., p. 48) that, while in some instances a delicate narrow band of circular fibres exists at the very verge of the pupil, yet, in the majority of instances, he feels *sure* that no such constrictor fibres of the pupil exist. He ascribes the contraction of the pupil to the inner part of the radiating fibres, which, he says, are joined and knotted in a plexiform manner round the pupil. It is scarcely needful to observe that such a statement from such an authority could not but go far to impugn Professor Kölliker's assertion respecting the existence of a sphincter pupillae.

My experience, I must confess, accords with that of Kölliker, viz. that the sphincter is readily seen, while the dilator is that whose investigation alone presents very serious difficulty. In the first iris that I examined with a view to the distribution of the muscular tissue, I was struck, after removing the uveal pigment, with the appearance of a band on the posterior surface of the iris, near the pupil and parallel to its margin, quite evident to the naked eye, elastic and highly extensible. This proved to be the thickest part of the sphincter pupillae. I have examined six human irides with reference to the distribution of the muscular tissue, but in none have I had any difficulty in recognizing the sphincter, which I have also found equally distinct in some of the lower animals, viz. in the rabbit, the guinea-pig, and the horse. In man I find it about 1-30th of an inch in width, thickest towards its outer part, where it lies nearer the posterior surface of the iris than the anterior, and thinning off towards the pupil, where it forms a sharp margin, covered apparently on its anterior aspect only by some vessels and nervous threads and a delicate epitheliated membrane, which is thrown into beautiful folds when the pupil is contracted. The fibres of the sphincter are not absolutely parallel, and this deviation is probably produced in part by the dilating fasciculi sweeping in at various parts in a curved manner, and becoming blended with the sphincter. The reason for this supposition will appear hereafter. By teasing out under the microscope a portion of the actual pupillary margin, I found the sphincter to consist at this part of apparently unmixed muscular fibre-cells, without any connecting cellular tissue. Fig. 13 is a camera-lucida outline of the edge of a portion of the sphincter so prepared, which edge is seen to be formed of projecting fibre-cells, and similar appearances may be seen with great readiness under a high power, after stroking the pupillary margin with the point of a needle. Indeed, the great facility with which the tissue may be thus broken up appears opposed to the idea of the fibre-cells being united end to end into fibres, as the descriptions formerly given of unstriped muscle would lead one to suppose. The ends appear to separate as readily as the edges and surfaces, and it would rather seem as if the fibre-cells of a fasciculus were placed with their long axis in one direction, cohering generally to one another, but without the formation of longer fibres than each cell itself constitutes. I may here mention incidentally that in the circular coat of the aorta of the sheep, where the muscular tissue is disposed in thin layers among the elastic tissue, I have observed a distinctly alternate arrangement of the fibre-cells without any formation of fibres. Mr. Wharton Jones's drawing of alternately disposed fibre-cells in the small intestine has been alluded to in the note above. A portion of the outer and thicker part of the human sphincter pupillae proved also extremely rich in muscular fibre-cells. In the rabbit and guinea-pig the sphincter has much the same appearance as in man, whereas in the horse it forms a wide but very flat band.

The dilating fibres of the iris present a very difficult subject of investigation.

And here I must express my belief—a belief the result of repeated and very careful observations—that the fibres described by Mr. Bowman as probably the contractile fibres of the iris are in reality the outer cellular coats of the vessels. The outer coat is very abundant in the vessels of the iris, and indeed even in the blue eye towards the sphincter quite obscures the bore of many of the vessels, and prevents the recognition of their vascular character, which can only be determined by tracing them to their more external and more obvious vascular trunks. The distribution of these vessels, radiating between the sphincter and the circumference of the iris, and forming in the region of the sphincter a close and knotted plexus, corresponds accurately with Mr. Bowman's description of the distribution of the fibres of the iris. His account of the tissue of these fibres, which he considers as probably contractile, harmonizes with the characters of the cellular tissue that clothes the vessels. This is peculiar ; consisting of very soft looking fibres, whose fasciculi often require the best aid of a first-rate glass to resolve them into their constituent elements ; destitute apparently of yellow elastic fibres, as in the case of the cellular tissue of the uterus, but, like this, containing abundance of free nuclei, of roundish or elongated form. The fibres are completely gelatinized by acetic acid. Now such a tissue can hardly, in the present state of our knowledge, be regarded as contractile ; at any rate, if we can find any ordinary muscular tissue to account for the dilating action. On teasing out portions of the outer part of the human iris, I have found long delicate fasciculi, whose faint outline, absence of fibrous character, and possession of well-marked elongated nuclei parallel to the direction of the fasciculus, left no doubt in my mind that they were plain muscular tissue.

So far my observations regarding the dilator agree with Kölliker's, but whether or not these fasciculi are connected with the cellular coat of the vessels I have hitherto been unable to determine.

Among the lower animals the albino rabbit and guinea-pig appeared but little suited for the elucidation of this point. I have been most successful with the eyes of a horse, where, from the thickness of the iris and the abundance of pigment (for the eyes were black ones), I anticipated but little result from my examination. Having removed the uveal pigment from behind, I found that I was also able to strip off from the anterior surface a tough membrane, a portion of which, put under the microscope, appeared to be made up of peculiar short felt-like fibres, which were gelatinized by acetic acid. At and near the pupillary margin this membrane comes off in a continuous layer, leaving a delicate reticular structure, which contains the muscular tissue. It also contains vessels, as I proved by injection, and a black network, which consists of fine fibres, yellow, and highly refracting, more or less encrusted with pigment. I am uncertain whether or not this be a network of divided nerve-tubes with adhering pigment ; in some spots the pigmental crust was absent from a considerable length of the fibres. The sphincter pupillae is beautifully seen as a broad flat band, of extremely well-marked, unmixed, muscular fibre-cells ; but crossing this at right angles are found, here and there, other flat bands of fibre-cells, which are in so thin a layer that without isolation the width of the individual cells can be seen, and they are evidently of similar dimensions to those of the sphincter. On addition of acetic acid their nuclei are also seen to be exactly like those of the sphincter. These bands divide in their course towards the pupil into several fasciculi, some of which cross over the sphincter at right angles till very near to its pupillary margin, and then seem to blend with the sphincter by making a slight curve. Most of the fasciculi, however, arch away earlier from their first course and join the sphincter in more or less oblique lines. The bands from which these fasciculi diverge may be traced away from the pupil for some distance, continuing their course at right angles to the sphincter till they are obscured by other tissues. Hence I think the inference may fairly be drawn that these are the insertions of the dilating muscular bundles. In the horse, then, the dilating fasciculi appear to consist of precisely the same tissue as the sphincter, and to blend with it in their insertion. The flat bands of muscular tissue above spoken of seemed to have no special relation to the vessels, some of which were filled with injection. In the outer part of the iris of the same horse I found a delicate muscular fasciculus lying near but not intimately connected with one of the radiating vessels of this part. In the human iris I have seen a muscular fasciculus, as it appeared from the nuclei it contained, crossing the sphincter at right angles for a short distance ; this observation, so far as it goes, seems to imply that the same mode of insertion of the dilator occurs in man as in the horse.

The fibre-cells of the dilator appear to be held together much more closely than those of the sphincter, at least in the outer part of the iris ; for I have never been able to define the individual fibre-cells in a perfectly satisfactory manner in the dilator, though I have often teased out portions of the outer part of the iris. The dilating muscular tissue is also probably less abundant than the muscular tissue of the sphincter ; and this, if the fact, will help to account for the comparative difficulty in discovering it. I may here mention that both in the cat and in the rabbit, soon after death, dilatation of the pupils being present, exposure of one iris to the air caused it to contract at once, while the pupil continued dilated in the other eye, which was untouched. I do not know if this fact has been observed before, but it is interesting in two ways —first, as showing that the muscular tissue of the iris, like other muscular tissue, is obedient to the stimulus of exposure ; and, second, as proving either that the sphincter is in these animals a decidedly more powerful muscle than the dilator, which is equally exposed to the stimulus ; or else that the fibres of these two muscles have different endowments, as has been shown by Mr. Wharton Jones to be the case with the muscular tissue of the arteries and veins of the bat's wing ; where, although the veins are muscular, and even contract rhythmically, yet the arteries alone exhibit tonic contraction when irritated by mechanical stimulus.

A rich network of extremely fine fibres, seen readily in the blue human iris viewed from the anterior aspect, appears to represent the nerves of the organ. The fibres are of a yellowish colour, and are possessed of pretty high refractive power ; they present, if really nervous, a good illustration of the division and anastomosis of ultimate nerve-fibres ; the smallest divisions visible under a high power are seen only as fine lines.

I have not seen any nerves in the human iris presenting the double contour ; but in the iris of a cat, so fresh that the tissue contracted under the needles as I teased it out, the double contour of the nerve-tubes was already very strongly marked, showing the existence in this animal of the white substance of Schwann in these nerves. The double contour surrounded the ends of the nerve-fibres which I supposed to have been broken by the teasing process. This last fact seemed to confirm the general belief that the double contour is a post mortem effect, which, however, was in this instance a very rapid one.

I believe that a further investigation of the fresh blue iris in man, and of the horse's iris, would supply the means of finally settling the question of the distribution of the dilator pupillae.

My engagements do not allow me to carry the inquiry further at present ; and my apology for offering the results of an incomplete investigation is, that a contribution tending, in however small a degree, to extend our acquaintance with so important an organ as the eye, or to verify observations that may be thought doubtful, may probably be of interest to the physiologist.

OBSERVATIONS ON THE MUSCULAR TISSUE OF THE SKIN

[*Quarterly Journal of Microscopical Science*, vol. i (1853), p. 262.]

Among the abundant new matter contained in those parts of Kölliker's *Mikroskopische Anatomie* that are hitherto published, there is perhaps nothing more striking than the announcement that small bundles of unstriped muscle exist in all parts of the dermis that are provided with hairs, connected inferiorly with the hair-follicles, just below the sebaceous glands, and passing up obliquely towards the free surface of the skin.

The effect of the contraction of such little muscles must necessarily be to thrust up the hair-follicles and depress the intermediate portions of skin; in other words, to produce cutis anserina; and thus this condition, previously quite unaccounted for, received at the hands of Professor Kölliker a simple and beautiful explanation.

In March of the present year (1853) I made an attempt to verify this most interesting discovery; and although the somewhat arduous duties of a resident office in University College Hospital prevented me from making the investigation as extensive as I could have wished, yet I found myself able not only to verify, but in some slight degree to add to Kölliker's observations. And as the main fact of the muscularity of the skin had not previously, so far as I am aware, found confirmation in this country, I have been induced to publish my results in the hope that they may prove acceptable to the microscopical anatomist.

Kölliker originally described[1] these muscles of the skin as flat bundles of unstriped muscular tissue, from 1-120th of an inch to 1-75th of an inch in breadth, of which there appeared to be one or two in connexion with each hair-follicle: it seemed probable to him that they arose from the superficial parts of the corium, and he had clearly seen them passing obliquely downwards to their insertion into the hair-follicles, close behind the sebaceous glands which they embraced. In his *Handbuch der Gewebelehre*,[2] published in 1852, he gives in the text exactly the same account of these muscles, except that he no longer expresses any doubt regarding their origin from the superficial parts of the corium. He afterwards states in a note that these muscles had been very

[1] Vide *Mikroskopische Anatomie*, vol. ii, part i, p. 14.

[2] Vide *Handbuch der Gewebelehre des Menschen*, p. 82.

recently seen by two observers, Eylandt and Henle, both of whom, however, had found them narrower than he. Eylandt, who named them '*arrectores pili*', had never seen more than one bundle connected with each hair-follicle, and had failed to detect muscular tissue in the nipple and areola, and in the subcutaneous cellular tissue of the scrotum, penis, and perineum, where Kölliker had described it as existing. Henle had traced the muscles to the most superficial parts of the dermis, where they divided into numerous little bundles 1-3000th of an inch in diameter, which could be followed to immediately beneath the epidermis; he had also seen muscular tissue in the nipple, areola, and the other parts where Kölliker had described it, but, on the other hand, in the opinion of Kölliker, he had gone too far, inasmuch as he described bundles of plain muscular tissue as existing on the exterior of the sudoriferous glands and blood-vessels of parts destitute of hairs (such as the palm and sole). These Kölliker is unable to discover, and he believes that Henle has been misled by the use of boiled preparations, in which, as Henle himself states, fine branches of nerves are liable to be mistaken for muscle. Thus it appears that the confirmation furnished by these two observers is by no means a very satisfactory one, and that Henle, the only authority on whom we rest for the fact of the muscles taking origin immediately beneath the epidermis, cannot, in the opinion of Kölliker, be implicitly relied on with reference to this investigation. It appears remarkable that Eylandt should have failed to discover muscular tissue in the scrotum, for the dartos was long since proved to owe its contractility to unstriped muscle. Of the parts in question I have examined only the areola mammae, which, however, answered well to the description given by Kölliker, who states [1] that the bundles of muscle are there circularly disposed, forming a delicate layer in the deeper parts of the corium, and encroaching slightly on the subcutaneous cellular tissue. On dissecting a portion of an areola from the subcutaneous tissue towards the surface, I found on reaching the deepest part of the dermis a delicate reddish-yellow fasciculus circularly arranged; and a portion of this, teased out with needles, and treated with acetic acid, presented in a well-marked manner the nuclei of plain muscular tissue. A camera-lucida sketch of a small portion is given on a reduced scale in Pl. I, B, Fig. 6.

In enumerating the parts where he has met with muscles connected with the hairs, Kölliker does not mention the scalp, probably because the density of the tissue of this part rendered it unfit for investigation by the method in which he prepared his objects, viz. isolating a hair-follicle with its sebaceous glands and treating it with acetic acid. Its very firmness and consistence,

[1] Vide *Mikroskopische Anatomie*, vol. ii, part i, p. 14.

however, make the scalp better adapted for fine sections than any other part of the skin ; and as I succeeded better with sections than by the other method, the scalp has received most of my attention. By compressing a portion between two thin pieces of deal, and cutting off with a sharp razor fine shavings of the wood and scalp together, moderately thin slices may be obtained. Fig. 4 represents a perpendicular section made in this way, and treated with acetic acid ; the epithelium has become detached from the free surface *a*, *b* ; *b*, *c* is part of one of the muscles near its superficial attachment, and it illustrates pretty well the appearance presented by them under a rather low power. They are distinguished from the tissue around them by their transparent and soft aspect, and by the abundant elongated nuclei scattered through them. Under a higher power the characteristic 'rod-shaped' nuclei become fully brought out, and no doubt remains as to the nature of the tissue. A good example of nuclei so magnified, derived from a muscle connected with a hair-follicle of the pubes, is shown in Fig. 5. It will be observed in Fig. 4 that the muscle has been traced to within a very short distance of the surface, where the nuclei became obscured by other tissues.

But I afterwards found that much better sections could be obtained from dried specimens. A portion of shaved scalp being placed between the 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 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.

Fig. 1 is slightly reduced from a camera-lucida sketch[1] of such a section, made in a plane perpendicular to the surface of the scalp, and at the same time parallel to the sloping hairs. I find that such a plane always contains the muscles in their entire length, the reason of which will appear shortly. In this figure *d* is the corneous, and *e* the mucous layer of the epithelium ; *b*, *b* . . . are the hair-follicles with their contained hairs, both have been more or less mutilated by the process of section ; the second hair from the right being a short one, its bulk is seen : *c*, *c* . . . are the sebaceous follicles, also more or less mutilated : a_1, a_2 . . . a_6 are the muscles, which appear, under this very low power, merely as transparent streaks, and require a higher power to make out their tissue.

[1] In all the sketches from which the figures that illustrate this paper have been taken, I have used the camera lucida, which instrument has the great advantage of ensuring correctness of proportions.

The muscles are seen to arise in all cases from the most superficial part of the corium, and to pass down obliquely to their insertions into the hair-follicles immediately below the sebaceous glands. It will be remarked that the muscles are here all on the same side of the respective hair-follicles, viz. on that side towards which the hair slopes : and such I found in the examination of a large number of sections to be always the case. This is an interesting fact, as such an arrangement of the muscles is exactly that which is best adapted for erecting as well as protruding the hairs, which must be drawn by their contraction nearer to the perpendicular direction. That this erection as well as protrusion of the hairs does occur, I have proved by artificially exciting the state of cutis anserina upon my own arm and leg. Tickling a neighbouring part will often induce horripilation, and if the eye is kept on an individual hair at this time, it is seen to rise quickly as the skin becomes rough, and to fall again as the horripilation subsides. I have never seen more than one muscle to each hair-follicle in the scalp ; and in order that a single muscle may by its contraction simply erect a hair, it must be placed in a plane perpendicular to the surface of the skin and parallel to the hair ; this explains the fact before alluded to, that a section made in such a plane is sure to contain the muscles in their entire length if at all, while sections in other planes cut across either the muscles or the hairs.

Fig. 2 represents the superficial attachments of the two muscles a_1 and a_2 of Fig. 1 ; *a* being the upper end of a_1, and *b* that of a_2 ; *c* is the corneous, and *d* the mucous layer of the epidermis ; the intervening tissue between the muscles was omitted in the sketch to save time. *b* furnishes a good example of the subdivision of a muscle into secondary bundles near the surface, as observed by Henle, while in *a* the subdivision, if it has occurred at all, is certainly not carried so far : the muscle *b c* in Fig. 4 seems not to have undergone any subdivision : in some cases a simple bifurcation of a muscle near the surface is all that is seen : hence the splitting up of the muscles into smaller bundles near their upper attachment appears not to be a constant thing, and when it does occur, exists to a very variable degree in different muscles. Want of room in the plate has rendered necessary so great a reduction of the scale [1] from the original drawing, as barely to allow the nuclei of the muscles to be perceived ; by looking closely, however, it may be seen that at *e* and *f* nuclei exist immediately under the epithelium, and before introducing them into the sketch, I ascertained, by a higher power, that they were really of the same character as those in other parts of the muscles. At *g* it was impossible to trace the nuclei so far ; if any existed here, they were obscured by the fibrous

[1] Figs. 2, 3, and 4 have all been reduced one-half from the original sketches.

tissue of the scalp, which adheres to the muscles throughout their whole length, but appears to form special sheaths for the bundles of origin at the surface, and these sheaths interfere considerably with the examination of the muscular tissue enclosed by them. In some cases, however, they seem to be prolonged beyond the point to which the muscular tissue reaches, acting as tendons of attachment, and this may perhaps be the case at *g*: I have seen one striking instance of this mode of attachment, where a muscle having divided into two portions at some depth below the surface, a pretty long band extended like a cord to the surface from one of the divisions, and acetic acid having been added, nothing whatever but yellow elastic fibres could be seen in this band (the white fibres had been of course gelatinized). As a general rule, however, the muscular tissue extends to within a very short distance of the epithelium, and often, as above stated, can be detected immediately beneath it, as Henle has represented.

In Fig. 3 is shown the connexion of the muscle a_1, of Fig. 1, with its hair-follicle; so that were the muscle *a* of Fig. 2 continued far enough downward, it would join with *a* of Fig. 3. The hair and its follicle are seen cut across very obliquely: *b* is the hair, tilted somewhat out of its natural position in the inner root-sheath *c*; *d* is the outer root-sheath (corresponding to the mucous layer of the epidermis), whose outer cells are perpendicular to the hair-follicle; *e* is the 'structureless layer' of the hair-follicle; *f* is the circular layer of Kölliker; *g* the external longitudinal layer with which the muscle is seen to become blended. Several elongated nuclei appeared at g_1; whether these are derived from the muscle, which is evidently inserted a good deal into the part of the follicle that is hidden from view, or whether they are only the elongated nuclei that occur in all parts of the longitudinal layer of the follicle, is doubtful: their well-marked elongated character inclined me rather to the former opinion; *h* is a part of one of the sebaceous follicles, which appears to have no special connexion with the muscle that simply passes close by it without embracing it, as Kölliker implies, or sending any muscular expansion over it; and the same occurs in all cases, so far as I have seen; *i* is a portion of the fibrous tissue of the dermis, showing its connexion with the surface of the muscle.

Kölliker's description of the muscles of the skin (see above, p. 9) does not quite accord with what I have seen in the scalp, either as regards their shape or size. The muscles in this part had not, in sections parallel to their course, the appearance of flatness; and by cutting slices in the way above indicated, at right angles to their known direction, their transverse sections were readily seen, and proved to be often quite circular, sometimes somewhat elliptical or polygonal, showing their form to be that of more or less rounded bundles. Their average diameter is, according to my experience, 1-200th of an inch, which is less than half the average of Kölliker's measurements, but this discrepancy is probably due to difference of situation in the parts observed, Kölliker not having examined the scalp: for one muscle which I sketched from the pubes was very nearly 1-100th of an inch in diameter.

With regard to the statement of Henle, that muscular tissue exists in parts destitute of hairs, I have searched with diligence many good sections of both the palm and the sole, without having been able to discover any evidence of it on the exterior of either the sudoriferous glands or blood-vessels of these parts. In a section treated with acetic acid, the elongated nuclei of the internal coat of a small blood-vessel sometimes give it an appearance that might at first sight be mistaken for that of unstriped muscle; but this is an error easily avoided by care, and I cannot but agree with Kölliker in thinking that, in some way or other, his boiled preparations have led Henle into error.

In order to verify Kölliker's statement [1] that no unstriped muscle exists in connexion with the vibrissae of mammalia, I examined the feelers of a cat. These large hairs extend far down into the tissues beneath the skin, and have a more complex muscular apparatus than the small hairs of the human skin. Bundles of muscles extend from the lower part of the gigantic hair-follicle obliquely upwards to the inferior aspect of the skin, and, in addition to these, there is muscle surrounding the large nerve that enters the base of each hair-follicle. These muscles were all of the striped kind, but extremely soft and extensile, and among the fibres were a number of very elongated nuclei, but I saw no distinct evidence of the admixture of unstriped muscle.

In conclusion, I may state that this investigation has proved to me the general correctness of Kölliker's original observations, and also of the results of Henle's further inquiry, except in the case of the alleged muscularity of parts destitute of hairs; and I shall be happy if the little additional matter communicated in this paper shall be found to bear as well the scrutiny of others.

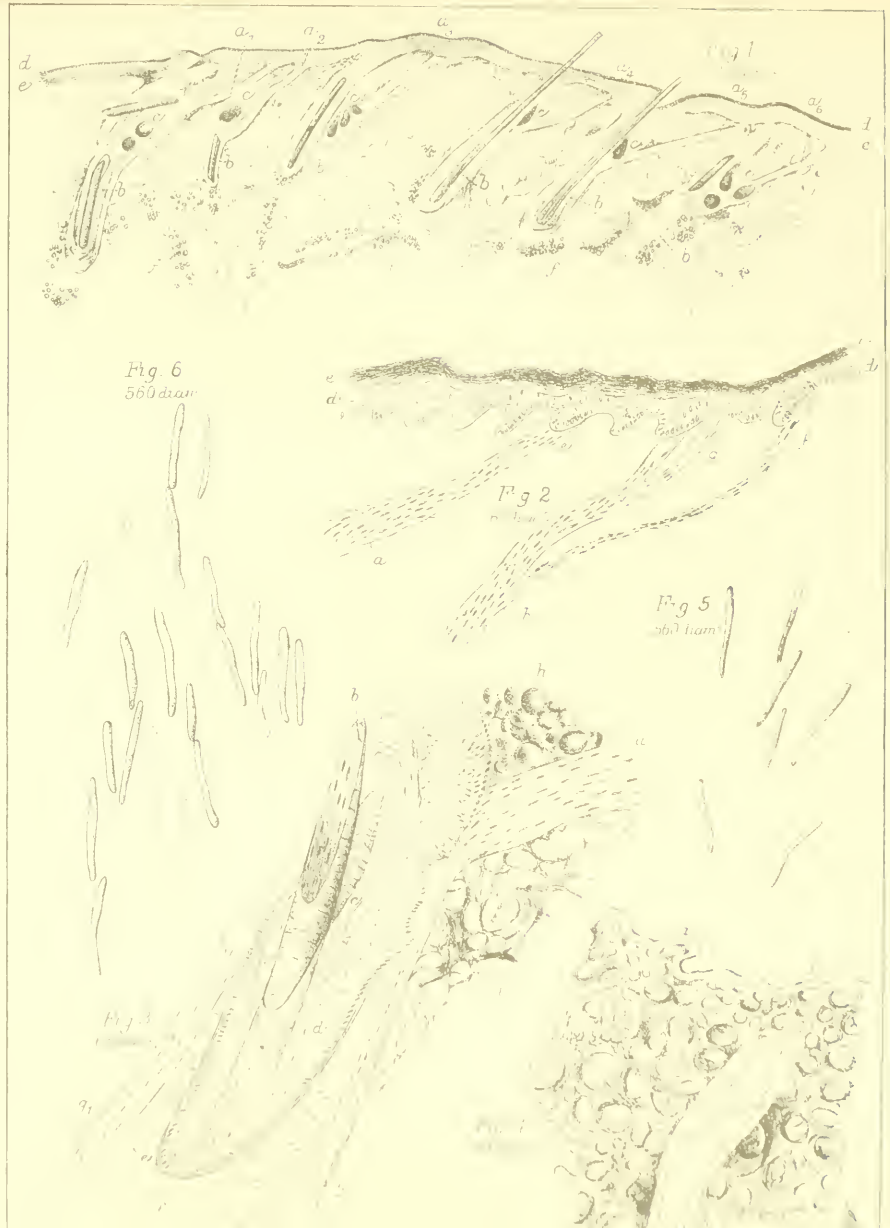
University College Hospital, June 1, 1853.

[1] Vide *Mikroskopische Anatomie*, vol. ii, part i, p. 15.

Plate I

A

P



ON THE MINUTE STRUCTURE OF INVOLUNTARY MUSCULAR FIBRE

[*Transactions of the Royal Society of Edinburgh*, vol. xxi, Part IV (1857), p. 549.]

Read December 1, 1856.

It has been long known that contractile tissue presents itself in the human body in two forms, one composed of fibres of considerable magnitude, and therefore readily visible under a low magnifying power, and marked very characteristically with transverse lines at short intervals, the other consisting of fibres much more minute, of exceedingly soft and delicate aspect, and destitute of transverse striae. The former variety constitutes the muscles of the limbs, and of all parts whose movements are under the dominion of the will; while the latter forms the contractile element of organs, such as the intestines, which are placed beyond the control of volition. There are, however, some exceptions to this general rule, the principal of which is the heart, whose fibres are a variety of the striped kind.

Till within a recent period the fibres of unstriped or involuntary muscle were believed to be somewhat flattened bands of uniform width and indefinite length, marked here and there with roundish or elongated nuclei; but in the year 1847, Professor Kölliker of Würzburg announced that the tissue was resolvable into simple elements, which he regarded as elongated cells, each of somewhat flattened form, with more or less tapering extremities, and presenting at its central part one of the nuclei above mentioned. These 'contractile' or 'muscular fibre-cells', as he termed them, were placed in parallel juxtaposition in the tissue, adhering to each other, as he supposed, by means of some viscid connecting substance. In the following year the same distinguished anatomist gave a fuller account of his discovery in the first volume of the *Zeitschrift für wissenschaftliche Zoologie*, and described in a most elaborate manner the appearances which the tissue presented in all parts of the body where unstriped muscle had been previously known to occur, and also in situations, such as the iris and the skin, where its existence had before been only matter of conjecture, but where the characteristic form of the fibre-cells, and of their 'rod-shaped' nuclei had enabled him to recognize it with precision. Confirmations of this view of the structure of involuntary muscular fibre were afterwards received from various quarters, one of the most important being the observation made in 1849 by Reichert, a German histologist, that dilute nitric or muriatic acid loosens the cohesion of the fibre-cells, and enables them to be isolated with much greater facility. In 1852 I wrote a paper 'On the Contractile Tissue of the Iris', published in the *Microscopical Journal*, in which I gave an account of the involuntary muscular fibre contained in that organ in man and some of the lower animals, stating that the appearances I had met with corresponded exactly with Kölliker's descriptions, and illustrating my remarks with careful sketches of several fibre-cells from the human iris, isolated by tearing a portion of the sphincter pupillae with needles in a drop of water. In 1853, another paper by myself appeared in the same journal, 'On the Contractile Muscular Tissue of the Skin,' confirming Kölliker's recent discovery of the '*arrectores pili*', and describing the distribution of those little bundles of unstriped muscle in the scalp. These and other investigations into the involuntary muscular tissue convinced me of the correctness of Kölliker's observations, and led me to regard his discovery as one of the most beautiful ever made in anatomy; and this is now, I believe, the general opinion of histologists.

Still, however, there are those who are not yet satisfied upon this subject. In Müller's *Archives* for 1854, is a paper by Dr. J. F. Mazonn of Kiew, in which the author expresses his belief that the muscular fibre-cells of Kölliker are created by the tearing of the tissue in preparing it, and denies the existence of nuclei in unstriped muscle altogether; but he gives so very obscure an account of his own ideas respecting the tissue, that his objections seem to me to carry very little weight, more especially as the appearances which he describes require, according to his own account, several days' maceration of the muscle in acid for their development. In June of the present year (1856), Professor Ellis of University College, London, communicated to the Royal Society of London a paper entitled 'Researches into the Nature of Involuntary Muscular Fibre'. In the abstract given in the *Proceedings* of the Society, recently issued, we are informed that, 'having been unable to confirm the statements of Professor Kölliker respecting the cell-structure of the involuntary muscular fibre, the author was induced to undertake a series of researches into the nature of that tissue, by which he has been led to entertain views as to its structure in vertebrate animals, but more especially in man, which are at variance with those now generally received.' In the 'summary of the conclusions which the author has arrived at', we find the following: 'In both kinds of muscles, voluntary and involuntary, the fibres are long, slender, rounded cords of uniform width. . . . In neither voluntary nor involuntary muscle is the fibre of the nature of a cell, but in both is composed of minute threads or fibrils. Its surface-appearance, in both kinds of muscle, allows of the supposition that in both it is constructed in a similar way, viz. of small particles or "sarcous elements", and that a difference in the arrangement of these elements gives a *dotted* appearance to the involuntary, and a tranverse striation to the voluntary fibres. . . . On the addition of acetic acid, fusiform or rod-shaped corpuscles make their appearance in all muscular tissue; these bodies, which appear to belong to the sheath of the fibre, approach nearest in their characters to the corpuscles belonging to the yellow or elastic fibres which pervade various other tissues; and from the apparent identity in nature of these corpuscles in the different textures in which they are found, and especially in voluntary, as compared with involuntary muscle, it is scarcely conceivable that in the latter case exclusively they should be the nuclei of oblong cells constituting the proper muscular tissue.'

Mr. Ellis, then, agrees with Mazonn in believing that the tapering fibre-cells of Kölliker owe their shape to tearing of the tissue; and he regards the nuclei as mere accidental accompaniments of the proper muscular structure, probably belonging to the sheath of the fibres, which, according to him, are of rounded form and uniform width.

The distinguished position of Mr. Ellis as an anatomist makes it very desirable that his opinion on this important subject should be either confirmed or refuted, and the object of the present paper is to communicate some facts which have recently come under my observation, and which, I hope, may prove to others as unequivocally as they have done to myself, the truth of Kölliker's view of this question.

In September last, being engaged in an inquiry into the process of inflammation in the web of the frog's foot, I was desirous of ascertaining more precisely the structure of the minute vessels, with a view to settling a disputed point regarding their contractility.

Having divided the integument along the dorsal aspect of two contiguous toes, I found that the included flap could be readily raised, so as to separate the layers of skin of which the web consists, the principal vessels remaining attached to the plantar layer. Having raised with a needle as many of the vascular branches as possible, I found, on applying the microscope, that they included arteries of extreme minuteness, some of them, indeed, of smaller calibre than average capillaries. A high magnifying power showed that these smallest arteries consisted of an external layer of longitudinally arranged cellular fibres in variable quantity, an internal exceedingly delicate membrane, and an intermediate circular coat, which generally constituted the chief mass of the vessel, but which proved to consist of neither more nor less than a single layer of muscular fibre-cells, each wrapped in a spiral manner round the internal membrane, and of sufficient length to encircle it from about one and a half to two and a half times. Fig. 18 (Plate II) represents one of these vessels as seen under a rather low power, and shows the general spiral arrangement of the fibres of the middle coat. Fig. 19 is a camera-lucida sketch of the same artery highly magnified, in which I have for the most part traced the outline of the fibres on the nearer side of the vessel only, but one fibre-cell is shown in its entire length wrapped round nearly two and a half times in a loose spiral. In some other vessels the muscular elements were arranged in closer spirals, as in Figs. 20 and 21. They are seen to have more or less pointed extremities, and are provided with an oval nucleus at their broadest part, discernible distinctly, though somewhat dimly, without the application of acetic acid. The tubular form of the vessels enables the observer, by proper adjustment of the focus, to see the fibre-cells in section; they are then observed to be substantial bodies, often as thick as they are broad, though the latter dimension generally exceeds the former. Here and there a nucleus is so placed in the artery as to appear in section with the fibre-cell, as shown in Figs. 20, 22, and 23. The section of the nucleus is in such cases invariably found surrounded by that of the substance of the fibre-cells, though occasionally placed eccentrically in it. From the circular form of its section the nucleus appears to be cylindrical. These fibre-cells are from 1–200th of an inch to 1–100th of an inch in length, from 1–2500th of an inch to 1–2000th of an inch in breadth, and about 1-2500th of an inch in thickness, measurements on the whole rather greater than those given by Kölliker for the human intestine, the chief difference being that in the frog's arteries they are somewhat broader and thicker.

Now, the middle coat of the small arteries is universally admitted to be composed chiefly of involuntary muscular fibre; but in the vessels just described it consists of nothing whatever else than elongated, tapering bodies, corresponding in dimensions with Kölliker's fibre-cells, and each provided with a single cylindrical nucleus embedded in its substance. Considering, then, that no tearing of the tissue had been practised in the preparation of the objects, but that the parts were seen undisturbed in their natural relations, it appeared to me that the simple observation above related settled the point at issue conclusively.

It was, however, suggested to me by an eminent physiologist, that the various forms in which contractile tissue occurs in the animal kingdom forbid our drawing any positive inference regarding the structure of human involuntary muscle from an observation made on the arteries of the frog. Being anxious to avoid all cavil, and understanding that Mr. Ellis's researches had been directed chiefly to the hollow viscera, I thought it best to examine the tissue in some such organ. For this purpose I obtained a portion of the small intestine of a freshly killed pig, selecting that animal on account of the close general resemblance between its tissues and those of man. The piece of gut happened to be tightly contracted, and on slitting it up longitudinally, the mucous membrane, which was thrown into loose folds, was very readily detached from the subjacent parts. I raised one of the thick, but pale and soft fasciculi of the circular coat, and teased it out with needles in a drop of water, reducing it without difficulty to extremely delicate fibrils. On examining the object with the microscope, I found that it was composed of involuntary muscular fibre, almost entirely unmixed with other tissue, reminding me precisely of what I had seen in the human sphincter pupillae, except that the appearances were more distinct, especially as regards the nuclei, which were clearly apparent without the application of acetic acid. Several of the fibre-cells were isolated in the first specimen I examined, each one presenting tapering extremities about equidistant from a single elongated nucleus. The fibre-cells were of soft and delicate aspect, generally homogeneous or faintly granular, with sometimes a slight appearance of longitudinal striae, such as is represented in Fig. 4.

I had now seen enough to satisfy my own mind that the involuntary muscular fibre of the pig's intestine was similarly constituted with that of the human iris and the frog's artery : but before throwing up the investigation, I thought it right to examine carefully some short, substantial-looking bodies of high refractive power, which at first sight appeared, both from their form and the aspect of their constituent material, totally different in nature from the rest of the tissue. Several of these bodies are represented in Figs. 10–15. Each is seen to be of somewhat oval shape, with more or less pointed extremities, and presents several strongly marked, thick, transverse ridges upon its surface ; and each, without exception, possesses a roundish nucleus whose longer diameter lies across that of the containing mass. Yet between these bodies and the long and delicate homogeneous fibre-cells above described, every possible gradation could be traced. Figs. 8 and 9 are somewhat longer than those just indicated, and are also remarkable for their regularity. In Figs. 5, 6, and 7 are represented fibre-cells of considerable length, marked here and there with highly refracting transverse bands, in the intervals of which they are of soft and delicate aspect. In several cells one half was short, with closely approximated rugae, the other half long and homogeneous. Hence it was pretty clear that the appearances in question were due to contraction of the fibre-cells, and that the shortest of these bodies were examples of an extreme degree of that condition ; their substantial aspect and considerable breadth being produced by the whole material of the long muscular elements being drawn together into so small a compass. The rounded appearance of the nuclei was accounted for by supposing either that they had themselves contracted, or that they had been pinched up by the contracting fibres, of which explanations the latter appears the more probable.

In order to place the matter if possible beyond doubt, I prepared two contiguous portions of the circular coat of a contracted piece of intestine in different ways; the one by simply cutting off a minute portion with sharp scissors, so as to avoid as much as possible any stretching of the tissue, the other by purposely drawing out a fasciculus to a very considerable length, and then teasing it with needles. In the former preparation, the fibre-cells appeared all of them more or less contracted, except in parts where the slight traction inseparable from any mode of preparation had stretched the pliant tissue, which in the fresh state appears to yield as readily to any extending force as does a relaxed muscle of a living limb. In the other object, where the tissue had been purposely stretched, most of the fibre-cells were extended, and possessed elongated nuclei. Here and there one would be seen of excessive tenuity, scarcely broader at its thickest part than the nucleus, looking, under the highest magnifying power, like a delicate thread of spun glass. To how great a length the fibre-cells admit of being drawn out in this way without breaking I cannot tell. Fig. 1 represents a portion of such a fibre with the contained nucleus. Among these extended fibres, however, there lay, here and there, an extremely contracted one, the result, I have no doubt, of the irritation produced by the needles upon the yet living tissue. In order to guard against this source of fallacy, I kept a piece of contracted gut forty-eight hours, and then examined two contiguous parts of the circular coat in the way above described. The muscle was much less readily extended than in the fresh state, and I found that, where stretching of the tissue had been avoided as much as possible, it was composed entirely of fibre-cells marked with transverse ridges of varying thickness and proximity; a minute fibril having, under a rather low power, the general aspect represented in Fig. 17. But I saw no distinct examples of the extreme degree of contraction so frequent in muscle from the same piece of intestine in the fresh state. This confirmed my suspicion that the latter had been induced by the irritation of the mode of preparation. On the other hand, a fully stretched fasciculus showed its fibres everywhere destitute of transverse rugae, so that the point was now distinctly proved. Kölliker, in his original article in the *Zeitschrift für wissenschaftliche Zoologie*, figured some long fibre-cells with transverse lines upon them,—'knotty swellings', as he termed them, which he supposed probably due to contraction, and he repeats this hypothesis in the part of his *Mikroskopische Anatomie* published in 1852. The *proof* of the correctness of this idea is now, I believe, given for the first time.

The bearings of these observations on the main question respecting the structure of involuntary muscular fibre are obvious and important. In the first place, if the short, substantial bodies were mere contracted fragments of rounded fibres of uniform width, we should expect them to be as thick at their extremities as at the centre, instead of which they are always more or less tapering, and often present a very regular appearance of two cones applied to each other by their bases. Secondly, the uniform central position of the nuclei in the contracted fibres, proves clearly that the former are no accidental appendages of the latter, to which it seems difficult to refuse Kölliker's appellation of *cells*.

The effect of acetic acid on the involuntary muscular tissue is to render the fibres indistinct, but the nuclei more apparent; and if this reagent be applied to a piece of contracted muscle, many of the nuclei are seen to be of more or less rounded form. The deviation of the nuclei from the 'rod-shape' has hitherto been a puzzling appearance, but is now satisfactorily accounted for.

In examining a fasciculus that had been fully stretched, forty-eight hours after death, I met with several good specimens of isolated fibre-cells, two of which are represented in Figs. 2 and 3. I would draw particular attention to the delicate, spirally twisted extremities of the fibre-cell 3, such as no tearing of a continuous fibre could possibly have produced. Though these fibres are very long, yet we have no reason to believe that anything near the extreme degree of extension has been attained in them, and we cannot but contemplate with amazement the extent of contractility possessed by this tissue.

In Fig. 16 is represented a portion of a fibre-cell curled up, which has been introduced for the sake of the clear manner in which it shows the position of the nucleus embedded in it. Just as in the case of the fibres wrapped round the arteries of the frog's foot, this cell might be seen in section by proper adjustment, and that section is observed to be oval; proving that the fibre is not round, but somewhat flattened. It happens that the nucleus appears at this point; its section is circular, and is surrounded on all sides by the substance of the cell.

The pig's intestine seems to be a peculiarly favourable situation for the investigation of unstriped muscle. Judging from Kölliker's measurements, the fibres appear to be of much larger size there than in the same situation in the human body. The length of the fibre-cell 3 is 1-37th of an inch. The fibre 2 is imperfect at one extremity; but, taking the double of the distance from its pointed end to the nucleus, its length is 1–33rd of an inch. These measurements are between three and four times greater than any which Professor Kölliker has given for the human intestine, and considerably exceed the length of the 'colossal fibre-cells' which he describes as occurring in the gravid uterus. The individual fibre-cells, with their nuclei and transverse markings, if they have any, are quite distinctly to be seen with one of Smith and Beck's $\frac{4}{10}$ object-glasses. But in order to examine their structure minutely, a higher power is required: that which I use is a first-rate $\frac{1}{12}$, made several years ago by Mr. Powell of London. All the figures in Plate II, except 17 and 18, are from camera-lucida sketches, reduced to the same scale. The principal measurements of the fibre-cells from the pig's intestine are as under:—

Length of fibre-cell, 3	$\frac{1}{37}$ inch.
Breadth of ditto	$\frac{1}{3300}$,,
Length of nucleus of ditto	$\frac{1}{1000}$,,
Breadth of ditto	$\frac{1}{8000}$,,
Breadth of fibre-cell, 16	$\frac{1}{3000}$,,
Thickness of ditto	$\frac{1}{4000}$,,
Length of fibre-cell, 13	$\frac{1}{750}$,,
Breadth of ditto	$\frac{1}{1250}$,,
Longitudinal measurement of nucleus of ditto . .	$\frac{1}{5500}$,,
Transverse, ditto	$\frac{1}{3500}$,,
Length of fibre-cell, 15	$\frac{1}{1000}$,,

Hence it appears that the length of the most contracted fibre-cell is the same as that of the nucleus of an extended one. The fibres vary somewhat in breadth, independently of the results of contraction. Thus, one in the extended condition which I sketched, but which is not here shown, measured only 1–4000th of an inch across. The nuclei of the uncontracted fibres are very con-constantly of the same length, and are good examples of the rod-shape to which Kölliker has directed particular attention. They always possess one or two nucleoli, and have often a slightly granular character; occasionally, as in Fig. 21, they present an appearance of transverse markings. One frequently sees near the nucleus of a fibre that has been artificially extended from the contracted state, an appearance of a gap in the substance of the cell, forming a sort of extension of the nucleus, as if the fibre generally had been stretched more completely than the nucleus: an example of this is presented by Fig. 7. Mr. Ellis lays great stress on a dotted appearance which he considers characteristic of involuntary muscular fibre. I must say I agree with Kölliker in finding the fibre-cells, for the most part, homogeneous when extended, or faintly marked with longitudinal striae.[1] No doubt dots are present in abundance; but these, so far as I have observed them in the pig's intestine, are distinctly exterior to the fibres, though adherent to their surface; and I suspect them to be little globules of a tenacious connecting fluid. That the fibre-cells do stick very tightly together may be seen by drying a minute portion of the tissue, after which they will be found shrunk, and slightly separated from one another, but connected more or less by minute threads.

To sum up the general results to which we are led by the facts above mentioned. It appears that in the arteries of the frog, and in the intestine of the pig, the involuntary muscular tissue is composed of slightly flattened elongated elements, with tapering extremities, each provided at its central and thickest part with a single cylindrical nucleus embedded in its substance.

Professor Kölliker's account of the tissue being thus completely confirmed in these two instances, and the description here given of its appearance in the arteries of the frog's foot being an independent confirmation of the general doctrine, there seems no reason any longer to doubt its truth.

It further appears, that in the pig's intestine the muscular elements are, on the one hand, capable of an extraordinary degree of extension, and, on the other hand, are endowed with a marvellous faculty of contraction, by which they may be reduced from the condition of very long fibres to that of almost globular masses. In the extended state they have a soft, delicate, and usually homogeneous aspect, which becomes altered during contraction by the supervention of highly refracting transverse ribs, which grow thicker and more approximated as the process advances. Meanwhile, the 'rod-shaped' nucleus appears to be pinched up by the contracting fibre till it assumes a slightly oval form, with the longer diameter transversely placed.

I will only further remark that these properties of the constituent elements of involuntary muscular fibre explain, in a very beautiful manner the extraordinary range of contractility which characterizes the hollow viscera.

[1] The longitudinal striae above referred to are probably due to a fine fibrous structure in the substance of the fibre-cells. When in London, last Christmas, I had, through the kindness of Dr. Sharpey, the opportunity of examining a specimen of muscle from the stomach of a rabbit, which he had prepared after Reichert's method. The nitric acid had not only detached the fibre-cells from one another, but also brought out very distinctly in each muscular element the appearance of minute parallel longitudinal fibres, which seemed to make up the entire mass of the fibre-cell except the nucleus. In a plate accompanying the paper on the Iris, before referred to, I gave figures of some fibre-cells with distinct granules arranged in longitudinal and transverse rows. This appearance, which, however, so far as my experience goes, is exceptional, and is hardly sufficiently marked to deserve the appellation 'dotted', is probably caused by unequal contractions in the constituent material.—April 2, 1857.

EXPLANATION OF PLATE II

Fig. 1 represents part of a fibre-cell from the pig's intestine, drawn out into a very fine thread.

Figs. 2 and 3, fibre-cells from the same situation, considerably extended.

Fig. 4, fibre-cells exhibiting faint longitudinal striation.

Figs. 5, 6, and 7, fibre-cells imperfectly contracted.

Figs. 8 and 9, small fibre-cells considerably contracted.

Figs. 10, 11, 12, 13, 14 and 15, fibre-cells extremely contracted.

Fig. 16, a fibre-cell curled up, showing the position of the nucleus embedded in its substance.

Fig. 17, part of a moderately contracted fasciculus of unstriped muscle from the pig's intestine, as seen under a rather low magnifying power.

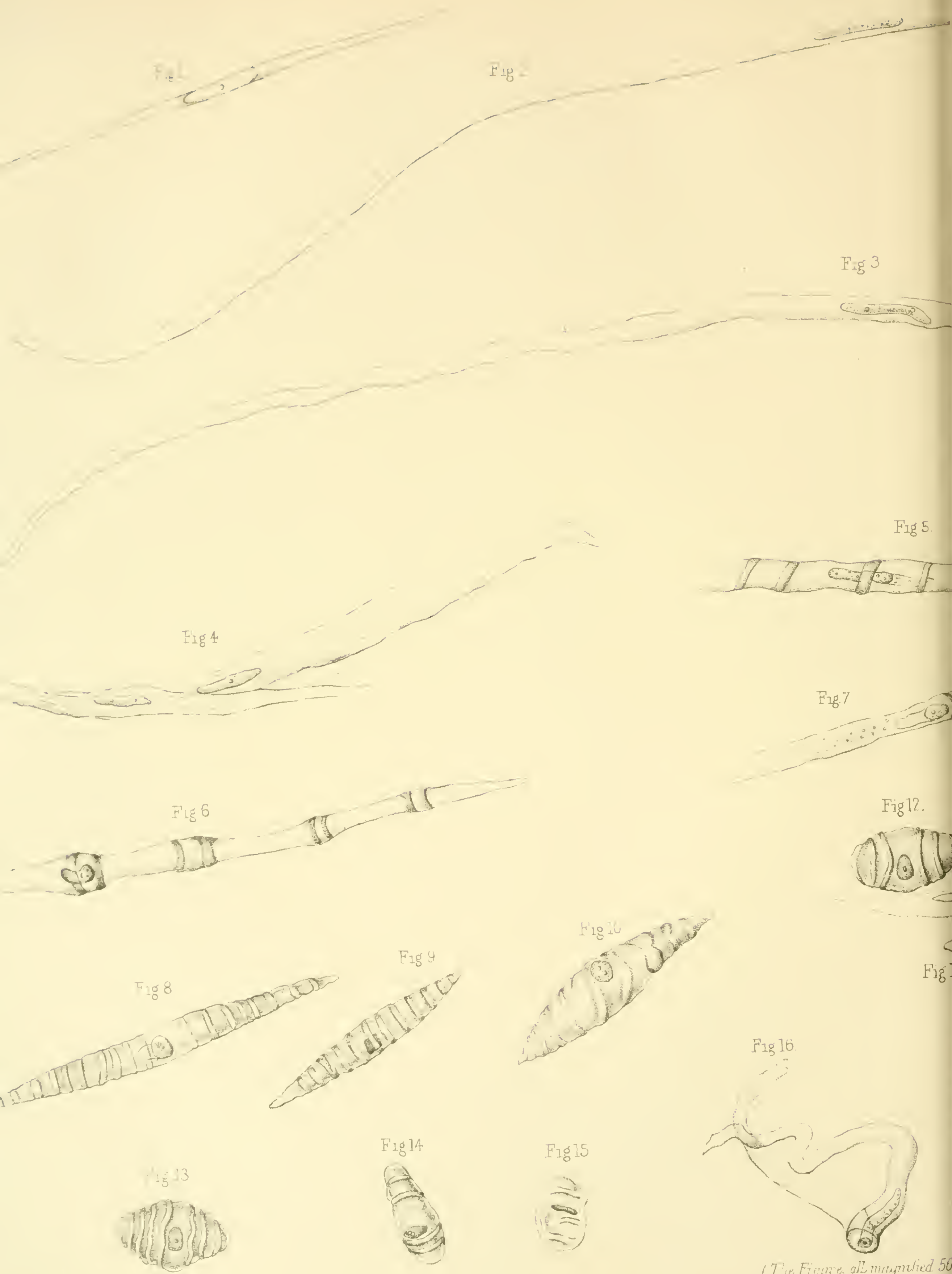
Fig. 18, a small artery from the frog's web, under a rather low magnifying power.

Fig. 19, part of the same vessel highly magnified, showing the spiral arrangement of the muscular fibre-cells.

Figs. 20 and 21, muscular fibre-cells from another artery. In Fig. 20, the spirals are much closer than in Fig. 19; and in Fig. 21, the spiral is quite close.

Figs. 22 and 23 represent some fibre-cells in arteries of extreme minuteness, and show the section of the nucleus surrounded by that of the fibre-cell.

Pl.



(The Figures all magnified 56

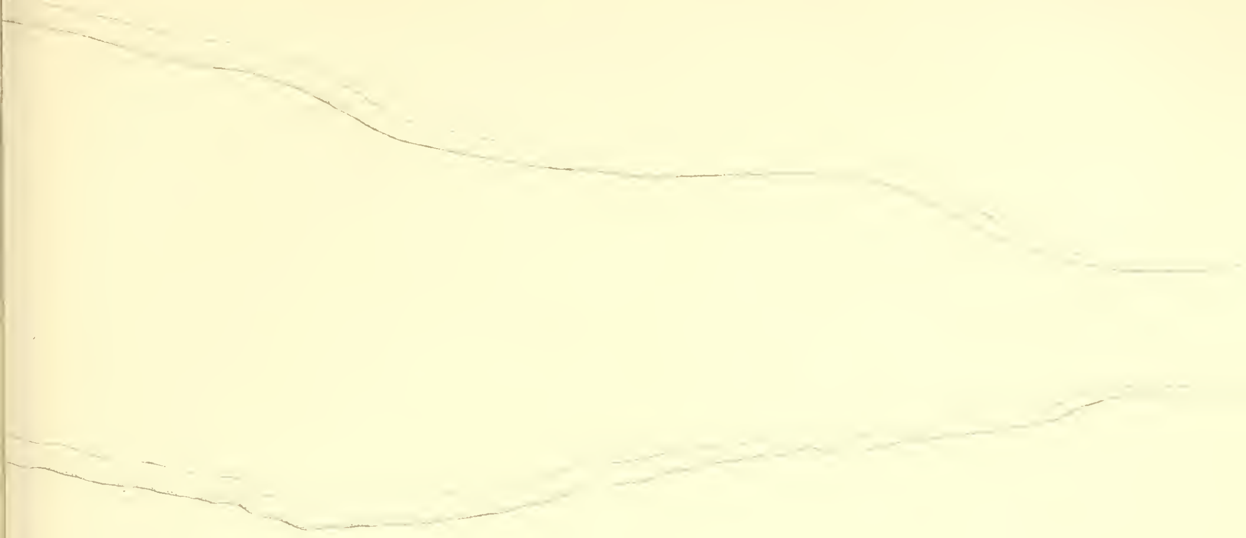


Fig 18

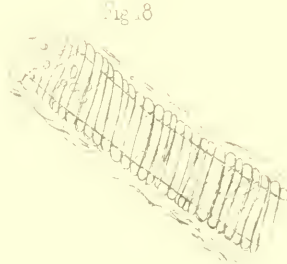
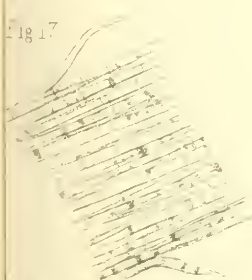


Fig 17



ON THE FLOW OF THE LACTEAL FLUID IN THE MESENTERY OF THE MOUSE

[*Report of the Meeting of the British Association, Dublin*, 1857, p. 114.]

THE objects of the experiments were twofold—first, to ascertain the character of the flow of the chyle under ordinary circumstances, which he believed had never yet been satisfactorily done ; and, secondly, to endeavour to throw some light upon the debated question, whether or not the lacteals were capable of absorbing solid matter in the form of granules visible to the human eye. In the first set of experiments,[1] a mouse having been put under the influence of chloroform an hour or two after partaking of a full meal of bread and milk, the abdomen was laid open by a longitudinal median incision, and a fold of intestine drawn out gently so that it might lie on a plate of glass under the microscope, the exposed part being occasionally moistened with water of the temperature of 100° Fahr. Under these circumstances, the lacteals were very readily visible as beautiful transparent beaded cords ; the beads corresponding to the situations of the valves, which were seen to be standing open, while chyle-corpuscles moved on through the tubes with perfectly equable flow, as a rule equal to about a quarter of that at which the blood moves through the capillaries. These observations were frequently repeated, and always with the same result. Hence it was clear that the lacteals, though known to be muscular, and richly provided with valves, do not, in the mesentery at least, promote the flow of the chyle by contraction, rhythmical or otherwise ; and that the source of the movement of the fluid is some cause in constant and steady operation. It was further observed that the chyle-corpuscles were, many of them, already of full size, although at so short a distance from the scene of absorption, proving the rapidity with which those corpuscles are elaborated.

The other set of experiments were performed in the same way, except that some coloured material, generally indigo, was mixed with the bread and milk. The animals took the mixture readily, and it passed freely along the intestines, but no indigo particles were ever seen in the chyle, although, had it been absorbed

[1] The experiments were made in 1853.

in the solid form, it would have been detected with the utmost facility within the lacteals. It might be supposed that the colouring matter had acted as a poison, and paralysed the function of absorption ; but there was no appearance of this, the chyle flowing just as rapidly as when the mice were fed with simple bread and milk. The facts, though not perhaps absolutely conclusive, seemed to throw great doubt on the possibility of absorption of solid matter by the lacteals.

AN INQUIRY REGARDING THE PARTS OF THE NERVOUS SYSTEM WHICH REGULATE THE CONTRACTIONS OF THE ARTERIES

[*Philosophical Transactions*, Part II for 1858, p. 607.]

Received June 18—Read June 18, 1857.[1]

GREAT light has been thrown in recent times upon the nature of the influence exercised over the blood-vessels by the nervous system. In 1852 it was shown by M. Bernard that division of the sympathetic nerve in the neck of a cat, or other mammalian, was followed by turgescence of the blood-vessels of the ear, and increased heat of that part and of the whole side of the face, together with contraction of the pupil. Early in the following year Mr. Augustus Waller performed the converse experiment of galvanizing the sympathetic above the point where it had been cut or tied, with the very striking result of rapid subsidence of the turgescence of the vessels, and fall of the temperature of the face; while the pupil became so extremely large, as to imply that the dilating fibres of the iris were thrown into a state of energetic contraction.[2]

From these experiments it appeared to follow pretty clearly that the sympathetic nerve in the neck presides over the contraction of the vessels of the face, which, becoming relaxed and dilated when the influence of the nerve was removed by its division, allowed the blood to flow through them in larger mass than before; but on the other hand, when excited to extreme constriction by the galvanic stimulus applied to the nerve, permitted but little blood to pass. This conclusion appears to be confirmed by the observation since made by Brown-Séquard, that the elevation of temperature which occurs in Bernard's experiment is never greater than is to be accounted for by the increased mass of warm blood which must be sent through the part, on the hypothesis that the turgescence of the vessels is simply the result of their dilatation. It was further shown by Messrs. Waller and Budge, that the same region of the spinal cord which they had previously ascertained to preside over dilatation of the pupil,

[1] This paper, and that on the 'Cutaneous Pigmentary System of the Frog' (p. 48 of this volume), were read as supplements to the 'Essay on the Early Stages of Inflammation' (p. 209 of this volume). The author has since extended his investigations into the subject of the present memoir, in accordance with a recommendation from the Council, and the results have been incorporated into the text, all new matter thus introduced being indicated as such either by date or by note at the foot of the page.

[2] *Comptes Rendus*, vol. xxxvi, p. 378.

namely, the part included between the last cervical and third dorsal vertebrae, also regulated the vessels of the face. When that part of the cord was removed, turgescence of those vessels occurred ; but galvanizing the anterior roots of the spinal nerves proceeding from that part produced the same effect as irritation of the sympathetic, namely, pallor with diminished temperature.[1] M. Schiff afterwards ascertained, that after destruction of the lower part of the cervical and upper part of the dorsal region of the cord in bats, there is an immediate dilatation of the small vessels of the wings,[2] and Brown-Séquard had previously shown that after transverse section of the spinal cord in the lumbar region in birds and mammals, an increase of 1°, 2°, or 3° Fahr. took place in the temperature of the paralysed parts.[3] All these facts tend to the same conclusion, namely, that the spinal cord is the part of the nervous centres which presides over the blood-vessels, and that one important action at least which it induces in them is constriction of the circular coat of the arteries. But there still remains, I believe, some difference of opinion with regard to the interpretation of Bernard's experiment ; and there might be some colour for the idea that the red and turgid state of the vessels seen after division of the sympathetic in the neck was due to a change in the blood, such as occurs in inflammation, and that the pallor ensuing upon galvanizing the nerve was the result of a return of the vital fluid to its normal condition after restoration of nervous influence. But all ambiguity of this kind seems to me to be removed by some observations made several years ago by Mr. Wharton Jones upon the frog. This animal is peculiarly adapted for investigations on this subject, because both the calibre of the vessels and the state of the blood as it flows through them can be observed with the utmost facility in the web ; and Mr. Jones found that division of the sciatic nerve was followed by dilatation of the arteries, but that this increase of calibre, so far from being caused by an obstruction in the progress of the blood, was accompanied with unusually free and rapid flow through the capillaries.[4] But with regard to the part of the nervous system which regulates the contractions of the arteries, some more recent observations by the same author are at variance with the conclusion above drawn from experiments by others upon mammalia. For he states that the division of the roots of the sciatic nerve within the spinal canal failed to produce dilatation of the vessels ; whence it was inferred that the sympathetic fibres of the sciatic trunk, as distinguished from those derived from the cord, are the channels through which

[1] *Comptes Rendus*, vol. xxxi, pp. 377, 575.

[2] *Gazette Hebdomadaire de Méd. et de Chir.*, 1854, pp. 421, 424.

[3] *Experimental Researches*, New York, 1853, p. 8.

[4] 'Essay on the State of the Blood and the Blood-vessels in Inflammation,' by T. Wharton Jones, Esq., F.R.S. *Guy's Hospital Reports*, vol. viii, p. 12.

the stimulus is transmitted to the arterial coats.[1] Waller and Budge's experiments, on the other hand, appear to show that it is from the cord that the sympathetic derives its controlling power over the arteries. This discrepancy upon a matter of such great importance in physiology appeared to me to demand further inquiry,[2] and I propose in the present paper to communicate the result to which this investigation has led.

The first experiment which I performed with reference to this subject (October 27, 1856), namely, division of the sciatic nerve on one side, gave somewhat puzzling results. Knowing how difficult it is to judge correctly of differences of calibre in the vessels by mere inspection, I tied out both feet of a frog (under chloroform), so that a slight movement of the stage of the microscope would bring either into view, and thus, after performance of the operation in one limb, the other foot might serve as a standard of comparison. I then selected a particular artery of the left foot for measurement with the eyepiece micrometer, and, having noted the limits between which its calibre varied during half an hour, isolated the nerve from surrounding parts by dissection, without any material change taking place in the diameter of the vessel. I next tied a piece of thread tightly round the nerve, with the effect of causing within the first few seconds distinct constriction of the artery, which then gradually expanded, and within two minutes had a larger measurement than I had previously observed. In other words, the effect of the ligature had been constriction speedily followed by dilatation. But on examining the web half an hour later, I found the artery had contracted again to about its usual proportions; after a few minutes the amount of constriction was very considerably greater, and continued so after division of the nerve above the ligature, and on looking at the other foot I found the arteries there similarly contracted. During the next twenty-four hours I made frequent careful comparisons of the conditions of the arteries in the two feet, and found that they presented exactly the same variations in calibre; being sometimes closely constricted, at other times fully dilated in both. The constrictions generally commenced a very short time before a struggle of the animal, and gradually subsided when it had become quiet. It was thus evident that the arteries had experienced no

[1] 'Observations on the State of the Blood and the Blood-vessels in Inflammation,' *Med. and Chir. Trans.*, vol. xxxvi.

[2] Since this paper was read, my attention has been called by Professor Goodsir to experiments recently performed by Pflüger. Operating upon the large edible frog of the continent (*Rana esculenta*), he succeeded in applying the galvanic stimulus to the anterior roots of the sciatic nerve within the spinal canal, with the effect of causing complete constriction of the arteries of the webs. Division of the same roots, on the other hand, was followed by full dilatation of the vessels (see Henle and Meissner's *Bericht*, 1857). Clear proof had thus been given, before my investigation of the subject commenced, that the spinal system does influence the arteries of the frog's foot.

permanent dilatation whatever from the division of the sciatic nerve, a result quite at variance with the experience of previous observers.

The explanation of this will shortly appear. On April 8, 1857, I laid open the spinal canal of a frog in its entire length, and divided, as I supposed, all the roots of the nerves coming off from the left side of the cord from the occiput to the sacrum, and immediately examined the webs of both feet, the frog being under the influence of chloroform. In the right limb the circulation was almost entirely arrested, while in the left it was going on freely. My attention was then diverted for half an hour, when the arteries of the right foot were found of medium size ; but in all the three webs of the left foot they were extremely dilated, appearing to have two or three times the diameter of those of the right limb.[1] This observation was of itself sufficient to prove that the spinal system, as distinguished from the sympathetic, does influence the contractions of the arteries of the frog's foot. Here, however, as in the case of the divided sciatic nerve, the effects were not permanent. Six hours later the arteries on the left side appeared smaller than they had been, though still bearing marks of the operation by remaining constant in calibre, whereas those of the right foot exhibited very frequent variations, from pretty full dilatation to almost absolute closure. Next day the same state of things continued, the vessels of the left foot being constant in size for four minutes together, while in the right foot an artery exhibited about eight distinct variations of calibre per minute as observed by micrometer ; but after three days more they had become both small and variable in the left foot, and seemed to have quite recovered. On the application of galvanism to the cord, however, both legs were thrown into violent spasm, showing that communications still existed between the left limb and the nervous centre ; and it appeared probable that the branches which remained undivided had come after a while to supply more or less perfectly the place of those which had been cut. A similar explanation seemed applicable to the speedy recovery of contractility in the vessels after cutting the sciatic, other nerves in the limb supplying the place of the divided trunk.

In another experiment, performed on the 11th of April, the roots of the nerves on the right side were divided within the spinal canal, beginning at the head and proceeding gradually backwards. No enlargement of the vessels of the webs occurred until the roots of the sciatic plexus were cut, when full

[1] In this and other cases of division of roots of the spinal nerves, I observed that the skin of the limbs supplied by the nerves cut became perfectly smooth, instead of being, as usual, rough with minute papillae. This appears to show that the unstriped muscular tissue of the skin is under control of the spinal system.

dilatation of the arteries of the right foot took place, one which had a few minutes previously varied from 1 to 2 degrees of the eyepiece micrometer being now $3\frac{1}{2}°$ in diameter, and remaining so for ten minutes together. Half an hour later, however, I was astonished to find the artery again contracted to 2°, and not quite constant in calibre. But next day, on dissecting the animal, I found that some branches of considerable size between the cord and the sciatic plexus remained entire.

This experiment, while confirming the proof of the influence exerted by the cord over the arteries of the feet, convinced me how difficult it is to make sure of dividing all the roots of the nerves for the hind legs within the spinal canal ; the operation being a very delicate one, while the parts are obscured by the bleeding which occurs in the living animal. At the same time the speedy recovery of function after partial division of the roots, pointed out a ready source of fallacy in such experiments. Had I deferred the examination of the web for half an hour in this case, there would have been no evidence of any effect produced on the vessels by the operation, and yet, had it not been for dissecting the frog, I should not have doubted that all the roots had been severed.

Dilatation of the vessels of the webs having been found to follow division of the roots of the spinal nerves, it appeared important, in order to complete the evidence on the point at issue, to observe the occurrence of contraction in the arteries on irritation of the cerebro-spinal centre. For this purpose, on the 14th I laid open the cranium of a frog under chloroform and thrust a very fine needle into the cerebral hemispheres, while one of the feet was stretched under the microscope : no effect was, however, produced upon the arteries ; one selected for micrometrical observation, the largest of the web, measuring, as it had done before, nearly 4°, which was a state of full dilatation. I then treated in a similar manner the posterior dark-coloured portion of the brain, including the optic lobes, cerebellum, and medulla oblongata, which were not distinguished from one another in the experiment. As I continued this treatment for a few seconds, keeping my eye over the microscope, the artery became contracted to 1°, which was the length of a red corpuscle. The leg then became spasmodically extended, and the artery was carried out of the field ; but when I next looked at the web after removal of the needle, the vessels had dilated again to pretty full size. Having selected a main artery of another web more conveniently placed, I repeated the experiment of thrusting the needle into the posterior portion of the brain. This vessel, which just before, though by no means at its largest size, measured $2\frac{1}{2}°$, became contracted to almost absolute closure, and remained so till the needle was removed, after which it gradually dilated, and in three minutes measured 2° ; forty seconds later $2\frac{1}{2}°$;

and about a minute afterwards 3°. The experiment was repeated several times with similar results, 'the invariable rule' (to quote from my notes) 'being contraction of the artery up to a certain point, and maintenance in the contracted state during the *whole* time, often several minutes, that the needle was stirred about in the brain; and then expansion, beginning almost immediately after withdrawal of the needle, and advancing to a certain point at which it remained till the needle was again introduced.' As the brain became more and more broken up, the contractions grew less and less energetic, and the dilatations were increased, till the needle failed to produce greater contraction than from 4° to 3°. I then thrust the needle into the spinal canal and withdrew it immediately. The hind legs started, and, after a few seconds, when I first caught sight of one of the webs, it was almost bloodless, and the arteries were invisible through extreme constriction. Four minutes later the artery before observed had begun to dilate and measured 1°, and after five minutes more it was 3°. A repetition of this experiment produced similar effects.[1]

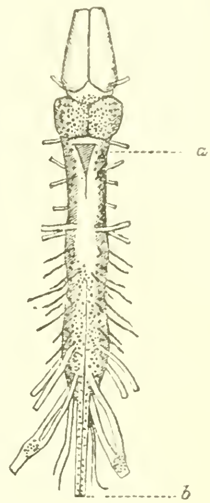
Abundantly sufficient proof had now been obtained that the cerebrospinal axis does contain a nervous centre for regulating the contractions of the arteries of the feet. But it was uncertain whether that centre were confined to any one part of the cord, or diffused extensively through it and the brain; or even whether a similar office might not also be discharged by some of the sympathetic ganglia. With a view to determining these points, which are of great physiological interest, several experiments were performed, some of which it will be necessary to relate; but in order to make their description intelligible, it will be well to say a few words regarding the arrangement of the spinal cord in the frog. It does not occupy the entire length of the spinal canal, but extends backwards only seven-tenths of the distance from the occiput

[1] The constriction of the arteries of the webs on irritation of the cord may be readily demonstrated in the following simple manner. The head of the frog being depressed so as to stretch the ligament between the occiput and first vertebra, a sharp knife is carried across the spinal canal immediately behind the head, so as to divide the cord from the brain. The toes may now be tied out and any observation made upon the web without the inconvenience generally produced by voluntary struggles on the part of the animal, while at the same time the use of chloroform is avoided; which is very desirable, on account of the irritating effect of its vapour on the web and the constant care required for its administration. If the webs be examined immediately after the operation, they will be found exsanguine from extreme constriction of the arteries; but in a few minutes this state will give place to dilatation with free flow of blood. If now a fine needle, curved at the end, be introduced through the wound into the spinal canal, so that its point may penetrate a short distance into the cord, while the eye of the observer is kept over the microscope, the arteries will be seen to become constricted to absolute closure, and dilate again after withdrawal of the needle. The experiment may be repeated as often as may be desired till the cord becomes disorganized.

I have lately found the above-mentioned mode of preparing the frog the best adapted also for experiments elucidating the nature of inflammation Little if any reflex action of the limb occurs when irritants are applied to the web; and if no great amount of blood have been lost in the operation, the creature will survive it a long while, e.g. eight days in one case.

to the sacrum, while the posterior three-tenths of the canal contain merely the cauda equina, including a slender filiform prolongation of the cord, which, though apparently composed in part of nervous matter, seems to give off no nerves.

In the accompanying sketch of the superior aspect of the brain and cord of a frog, magnified two diameters, the distance from *a* to *b* represents the length of the spinal canal. The principal nerves for the hind legs spring from the cord near its extremity, but other smaller branches with the same destination arise nearly as far forward as the middle of its length. There are also connecting filaments between these and some nerves for the abdominal parietes, taking origin slightly further forward than the middle of the cord. Thus the nerves for the posterior extremities are furnished chiefly, but not quite exclusively, from the posterior half of the cord. To expose the cord in its entire length without injury to it or any of its slender branches is troublesome, and also involves much loss of blood. It is therefore very desirable to be able to come at once on any part of the cord you may desire, without laying open the whole canal. This can be readily done from the data above given. The articulation between the occiput and first vertebra can be felt through the skin, as also can the commencement of the sacrum; and the distance between these points is the length of the spinal canal. This, multiplied by 0·7, is the length of the cord: the requisite fraction of this length is then measured from the occiput and gives the place required.



Assistance may also be derived from the circumstance that the posterior edges of the scapulae correspond very nearly with the mid-length of the cord, overlapping the posterior half by only about one-twentieth of the whole.

To proceed with the experiments. On the 16th of April, a large frog being put under chloroform, the entire brain was removed about 3 o'clock p.m. without injury to the cord. After this operation, the arteries, which had previously been of pretty full size and transmitting rapid streams of blood, were found completely contracted, so that the webs appeared bloodless except in the veins, and continued so for some minutes. At 3^{h} 10^{m} an artery selected for special observation was dilating, having already attained to a diameter of $1\frac{1}{2}°$, and the circulation was returning in the web. At 3^{h} 15^{m} the vessel measured $3°$, but two minutes later was $2\frac{1}{2}°$, and half an hour afterwards exhibited the spontaneous changes in calibre commonly seen in arteries in health, the limits observed being $1\frac{1}{3}°$ and $2°$. It thus appeared that the removal of the brain had had no further effect upon the arteries than the temporary constriction induced by the irritation of the anterior part of the cord in the operation, followed by a brief period of dilatation. At 4^h, a small part of the spinal canal having been laid open, the anterior sixth of the cord was removed, corresponding to the anterior third of the scapulae. At $4^h\ 3^m$, when the web was first looked at, the artery was contracted to absolute closure, and the web exsanguine; and this state of things continued till $4^h\ 7^m$, when the vessel began to dilate. At $4^h\ 8^m$ it measured $2\frac{1}{2}°$, and at $4^h\ 13^m$, $3°$. Four minutes later it was short of $3°$, and after five minutes more it was observed to be undergoing spontaneous variations of calibre from $2\frac{1}{2}°$ to $2\frac{2}{3}°$. Finally, at $5^h\ 30^m$ its condition was just as it was before the experiment was performed, varying from $1\frac{1}{2}°$ to $2°$, without any struggle on the part of the creature, the blood at the same time flowing rapidly through it.[1] At 6^h, another vertebral arch having been taken away, the subjacent portion of cord was removed, the canal being thus cleared as far back as the level of the mid-scapulae, corresponding to rather more than a quarter of the cord. The operation caused contraction of the artery to $1°$; but this passed off in half a minute, and was followed by no further dilatation than to $1\frac{1}{3}°$, and a few minutes later the artery was again spontaneously varying from $1°$ to $1\frac{1}{3}°$; at the same time the heart's action was somewhat enfeebled. At $6^h\ 15^m$ the portion of cord corresponding to another vertebral arch was cut away. The operation induced contraction from $1\frac{1}{3}°$ to $\frac{1}{2}°$, followed by gradual dilatation (in fifteen seconds) up to $1\frac{2}{3}°$, and this, in a few seconds, gave place to spontaneous contraction to $1\frac{1}{2}°$. By this last operation the vertebral canal had been cleared as far back as the posterior third of the scapulae, corresponding to between one-third and one-half of the length of the cord.

At $6^h\ 30^m$, having removed another vertebral arch, I divided the cord imperfectly, as far back as it was exposed, namely, at the level of the posterior edges of the scapulae, which is in the commencement of the posterior half of the cord; and on looking at the web twenty seconds later, found the artery undergoing oscillations in calibre, such as had never before been seen in it, contracting and dilating distinctly five times in a minute, from $1°$ to $1\frac{1}{3}°$ or $1\frac{1}{2}°$. At $6^h\ 32^m\ 20^s$ the cord was cut fairly through at the point indicated, without removal of the segment from the canal, and at $6^h\ 34^m$ the artery was found quite constricted and the web exsanguine. At $6^h\ 36^m\ 10^s$ the artery had somewhat dilated, and measured $1\frac{1}{3}°$, but the blood was moving very slowly through the vessels, the heart being exceedingly enfeebled. At $6^h\ 40^m$ the portion of the cord was

[1] The transient character of the effects produced upon the arterial calibre by these operations led me at first to conclude that the anterior parts of the cerebro-spinal axis did not contain any nervous centre for the arteries, and this view was expressed in the original manuscript. My opinions on this point have, however, been altered by the results of subsequent experiments, as will appear at the conclusion of the paper.

detached from the roots of the nerves which sprung from it and removed from the canal, immediately after which the artery was found dilated to $1\frac{2}{3}°$, but the blood had ceased to move in consequence of the feebleness of the heart.

The experiments upon this animal show that if the brain and anterior third of the cord act at all as nervous centres for the arteries of the feet, they are certainly not the only parts which possess that function ; and also, that irritation of any part of the anterior half of the cord gives rise to contraction of the arteries of the webs, followed by dilatation, varying much in extent and duration, but generally proportioned in both respects to the previous constriction. It is probable that the dilatation would have been greater after the last operations, had the heart been working more powerfully ; for it will hereafter appear that a certain amount of distending force on the part of the blood is necessary for the vessels becoming fully expanded.

And the 18th of April, having put a large frog under the influence of chloroform, I removed a vertebral arch opposite the junction of the middle and posterior thirds of the scapulae, and then cut across the cord in that situation, i.e. rather more than a line anterior to its middle ; a slight retraction of the two segments proved that the division had been thoroughly effected. This was at 10 o'clock a.m. A few minutes later the arteries had recovered from the effects of the irritation ; one selected for special observation, having measured $1\frac{2}{3}°$ just before the operation, now varied occasionally between $1\frac{1}{3}°$ and $1\frac{2}{3}°$, and the circulation was rapid through the vessel. The next vertebral arch posteriorly having been removed, the cord was divided as far back as it was exposed, at $10^{h}\ 23^{m}\ 50^{s}$; immediately after which the web was found exsanguine in consequence of complete closure of all the arteries, which continued almost in the same condition for ten minutes, at the end of which time the artery selected was still so small as to transmit single corpuscles with difficulty. At $10^{h}\ 35^{m}$ the portion of cord included between the points of section was detached from the roots of the nerves connected with it and removed from the canal. It measured nearly a line in length, and the posterior segment thus shortened proved afterwards to be only a very small fraction more than half the length of the cord. The vessels afterwards relaxed slowly, so that at $10^{h}\ 37^{m}$ the corpuscles were passing a little more freely through the artery. At $11^{h}\ 15^{m}$ the artery measured $1\frac{1}{2}°$, but transmitted the blood in a very languid stream ; and at noon the evidences of circulation were so equivocal, that I suspected the creature, which was weak to begin with, to be dead, though this afterwards proved to be a mistake. At $0^{h}\ 45^{m}$ p.m. the same state of things continued, and the artery still measured $1\frac{1}{2}°$, having remained unaltered in calibre for the last hour and a half ; but I determined to try the effect of irritating the posterior segment of the cord, and introduced the point of a needle a short distance into its anterior extremity and withdrew it immediately, keeping my eye over the microscope. The effect upon the artery was immediate constriction, causing a retrograde stream of the blood in it for about a second, and then absolute obliteration of calibre. At 0^h 49^m the artery allowed single corpuscles to pass through it with considerable difficulty. At 1 o'clock the arteries of the web were still small, but I noticed that they were undergoing very remarkable oscillations in calibre, just as occurred on one occasion in the frog last operated on, but in the present case they were more striking. I noted the variations for some time, and give in the following table a specimen of those which occurred during one minute :

	H.	M.	S.	
At	1	2	57	the diameter of the artery was $1\frac{1}{4}°$.
At	1	3	9	the diameter of the artery was $1°$.
At	1	3	20	the diameter of the artery was $\frac{1}{2}°$.
At	1	3	25	the diameter of the artery was $0°$.
At	1	3	38	the diameter of the artery was $\frac{1}{2}°$.
At	1	3	45	the diameter of the artery was $0°$.
At	1	3	50	the diameter of the artery was $\frac{1}{2}°$.

These oscillations continued for upwards of half an hour, but during the latter part of that time the extreme degrees of constriction were not observed.

At 1^h 43^m p.m. I raised the vertebral arches from the end of the spinal canal, and removed the posterior half of the cord together with the cauda equina ; immediately after which, the artery, which for the last hour had not exceeded $1\frac{1}{4}°$, became expanded to $2\frac{1}{4}°$, a dimension which it had never before been observed to attain, except during the secondary dilatation that ensued after the first division of the cord when the heart was in powerful action. All the other arteries of the web became dilated at the same time, and remained of perfectly constant diameter during the hour that I continued to observe them. Finally, at 2^h 40^m I introduced a needle into the anterior part of the spinal canal which had hitherto been undisturbed, and irritated both the anterior portion of the cord and the brain, but no effect whatever was produced upon the vessels.

The constriction of the arteries, which resulted in this case from irritation of the posterior half of the cord isolated from the rest, and the permanent dilatation which ensued on removal of the same part, prove that this portion of the cerebro-spinal axis certainly contains a nervous centre for regulating the contractions of the arteries of the feet. The frequently alternating contractions and dilatations which occurred in this animal, as well as in the last, after irritation of the posterior half of the cord, are curious, and may perhaps be considered analogous to rapid action of the heart under the influence of stimulus. The fact that the arterial contractions so constantly observed to result from irritation of the anterior part of the cord, while it retains its connexion through the rest of the cord with the roots of the nerves of the hind legs, fail to occur after removal of the posterior two-thirds of the cord, has been confirmed by subsequent experiments upon other frogs. It appears to imply that if the brain and anterior part of the cord discharge the functions of a nervous centre for the arteries of the feet, they do not exert that influence through the branches which connect them with the sympathetic, but only through the roots of the nerves given off from the more posterior parts of the cord.

On the 2nd of June, a large frog having been put under the influence of chloroform, the vertebral arches were removed, from the sacrum to the posterior edges of the scapulae, and at $0^h\ 30^m$ p.m. the cord was divided immediately behind the latter situation, i.e. a little behind its middle. The left foot being examined shortly after, the arteries were seen to be considerably constricted ; one of them, which appeared to be a principal trunk, permitting single corpuscles to pass with difficulty, and the contraction became extreme after irritation of the posterior segment of the cord with a needle. The whole of the exposed part of the cord and the cauda equina, including the chief branches of nerves for the hind legs, were then removed (at $0^h\ 56^m$), and when the foot was again looked at, at $1^h\ 10^m$, the circulation, which had been previously entirely arrested by the contraction of the vessels, was going on rapidly through dilated arteries, the one before mentioned now measuring 3°. This, however, proved not to be the extreme degree of dilatation of which the vessel was capable ; for a stream of water at about 120° Fahr., thrown for perhaps a second upon the foot, induced, after brief imperfect contraction, an expansion to nearly 4°, which again was followed after a few minutes by a return to 3°. This experiment was several times repeated. In the right foot, which had not been subjected to the hot water, though necessarily equally affected with the other by the removal of the portion of cord, the arteries were found of moderate size at $3^h\ 45^m$, having evidently recovered, to a considerable extent at least, their contractile power during the $2\frac{3}{4}$ hours which had elapsed since the operation. One which at this time measured $1\frac{2}{3}$°, became dilated on the application of hot water to 3°, and afterwards contracted spontaneously to 2°.

At $4^h\ 15^m$ an additional portion of the cord was removed, so as to clear the spinal canal as far forward as the anterior third of the scapulae. The arteries became at once dilated to some extent, notwithstanding that the heart's action was greatly enfeebled by this operation; and at $6^h\ 45^m$ they had [attained nearly the full diameters that the hot water had before induced, while the circulation had somewhat recovered. Next morning the arteries of the two feet, the dimensions of which were before given, measured 4° and 3° respectively, and they continued without the slightest variation until $5^h\ 25^m$ p.m.; the circulation meanwhile had continued to improve, and was healthy, though still languid. I then removed the remainder of the cord and the entire brain without producing any effect whatever on the size of the arteries, and they still measured precisely the same at $10^h\ 45^m$ p.m. The following morning the frog was dead, and the tissues of the web had become opaque by the imbibition of water.

In this case the arteries recovered their contractile power after the removal of the greater part of the posterior half of the cord, together with the chief roots of the nerves for the hind legs; but when the part which furnishes branches to the posterior extremities had been completely removed, the arteries became permanently dilated; and, though the circulation was then feeble, soon attained the full calibre which hot water had induced at a time when the heart was in powerful action.

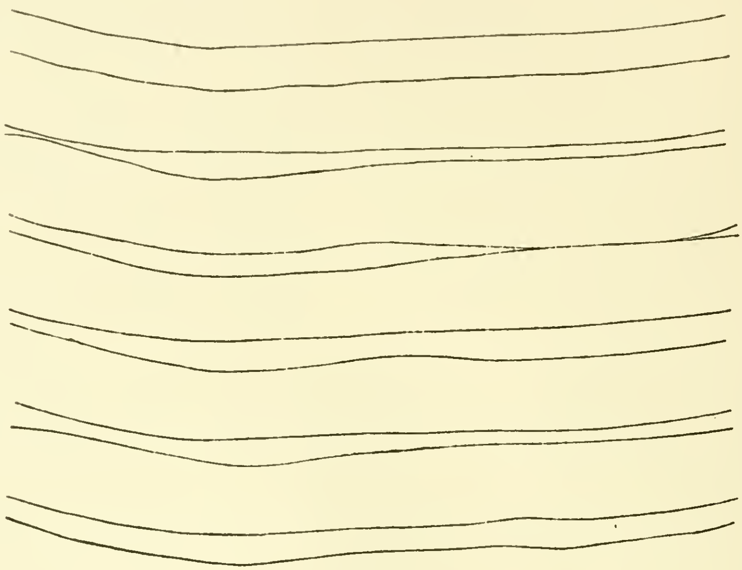
The perfect constancy with which the vessels observed maintained these dimensions for more than thirty hours after the operation, implied that they were not then at all acted on by the nervous system; and hence I was led at first to infer that there existed no other ganglionic apparatus for the arteries of the feet than that contained in the cerebro-spinal axis.[1]

I have since witnessed in other frogs the permanence of the dilatation of the arteries after removal of the brain and cord. The following case, however, appeared at first inconsistent with these observations. On the 23rd of October the brain and cord of a large frog were completely removed, and an operation was performed upon the right thigh, which, as it turned out, tended to interfere with the freedom of the circulation in the webs; so that after twelve hours, the blood, though not presenting the appearances of inflammation, was almost motionless in that foot. At the same time, two arteries in one of the webs, which had till then remained perfectly constant in calibre, as determined by micrometer, began to exhibit variations, and during the next twenty-four hours continued to change their diameter occasionally. There were, however, certain peculiarities about these changes such as I had never before seen. Generally speaking, all the arteries of a web are found in the same degree of contraction at any one time; but here, one of the vessels under observation

[1] This was the view expressed in the original manuscript, but it has been since modified by further experiments mentioned in the text, made, as their dates imply, subsequently to the reading of the paper.

was sometimes small, when the other, though in the same web, was large; and not only was there no proportion between the degrees of contraction in the two vessels, but in one and the same artery the amount of constriction was very different at different parts. The unusual character of these contractions implied that they were caused by some unwonted circumstances; and from their coincidence with the almost total arrest of the blood, as well as from the fact that in the left foot, where the circulation continued free, the arteries remained of full size till the animal was destroyed, I was led to conclude that the puzzling appearances in question must be in some way or other dependent on the cessation of the flow of the vital fluid through the vessels. If this were so, it seemed probable that the mechanism by which these irregular contractions were induced might be as local as their exciting cause, in which case they would be seen to occur in an amputated limb. In order to determine this point I made the following experiment. On April 2, 1858, having passed a knife between the brain and cord of a large frog so as to render the legs insensible, and having ascertained that the arterial constriction resulting from that operation had subsided, I placed a ligature round one of the thighs, and then amputated the limb at a higher point. The application of the ligature not only prevented the blood from escaping, but produced considerable tension in the soft parts of the thigh; and on examining the webs, I found the arteries fully dilated, one which I selected for special observation measuring $4\frac{1}{2}°$ in diameter. At 6^h p.m., an hour and a half after the amputation, the vessel still maintained the same calibre, but at $7^h\ 35^m$ it was slightly less, viz. $4°$, which was still its measurement at 11 o'clock. Hitherto no change distinctly referable to vital contractility had taken place, but on the following morning the vessel was reduced to $3°$ in diameter, and on the 4th of April it was of different sizes in different parts, viz. from $1\frac{1}{2}°$ to $3°$, and varied somewhat during the course of the day. Still more striking changes in the diameter of the artery appeared on subsequent days; thus the vessel was sometimes constricted to absolute closure in one part of its course, and dilated to a very considerable degree, e.g. $3\frac{1}{2}°$, in another part. More commonly, however, the artery, though never uniform in size as in health, had a general tendency either to moderate constriction or dilatation. The variations occurred frequently during the twenty-four hours, and on one occasion I saw the artery in the act of slow contraction at one part driving the blood into a dilated portion at a little distance. So late as the evening of the 10th of April, i.e. during the ninth day after amputation, far later than vital contractility is generally believed to last in a limb so circumstanced, variations of calibre continued to show themselves; but on the 11th of April the vessel had an almost uniform width of nearly 3°, and exhibited no variations, while, at the same time, other evidences of loss of vitality in the tissues began to show themselves. The accompanying outlines of the calibre of a limited portion of the artery, which was the subject of special observation, have been made from micrometrical measurements selected from among a large number daily registered. They will serve to convey an idea of the more striking varieties of appearance presented at different times. It may be mentioned, that the diameter of the vessel, when most dilated, was about 4½ times the length of a red corpuscle of the frog's blood.

H. M.
April 2 ...... 6 0 p.m.
April 5 ...... 3 15 p.m.
April 7 ...... 6 7 p.m.
April 7 ...... 11 20 p.m.
April 10 ...... 5 0 p.m.
April 11 ...... 11 10 a.m.



It must be added, that the limb was kept wrapped in clean wet lint in a cool place in the intervals of the observations, and that during the periods of examination care was taken to guard against warmth or dryness, or any other agency calculated to injure the delicate tissues of the webs.

Thus irregular contractions, precisely similar to those which accompanied local arrest of the circulation in the experiment of October 23, took place in consequence of amputation of the limb ; and as there could be no doubt that in both cases they were produced in the same manner, there was no longer any reason to suspect that sympathetic ganglia in the trunk might have had any share in their development in the former instance. Yet the circumstance above mentioned, that in the amputated limb the tendency to constriction usually affected a considerable tract of the vessel, and sometimes its entire length, to nearly the same degree, or in other words, that the muscular fibre-cells of the circular coat of the artery still contracted in concert with each other, seemed to imply the operation of a co-ordinating nervous apparatus contained in the limb. It appears probable that the means by which these concerted movements are induced are nerve-cells disseminated through the limb, in the same manner as Meissner has lately shown to be the case in the mammalian intestine.[1] The intestines also present a parallel to the arteries, in the fact that contractions of their unstriped muscular fibres result from arrest of the circulation in them; and I have lately shown[2] that these movements are not due to any influence exerted directly upon the contractile tissue, but that the intestinal nerves are essential to their production. Thus we have support from analogy for the view that the muscular contractions which occur under similar circumstances in the arteries are induced by nervous agency.

The fact that the contraction produced in an artery of the frog's web by pressure upon a particular point affects a considerable extent of the vessel, instead of being limited to the spot irritated, is also an argument for the existence of a local co-ordinating apparatus; for I find that this occurrence continues to take place in an amputated limb. The observation was made on August 4, 1858. One of the hind legs of a frog having been removed after a ligature had been passed round the thigh so as to prevent escape of the blood, pressure was made with a fine but blunt instrument over a particular point in the course of a large artery, whose calibre had previously been accurately determined by micrometer. The contractions which resulted affected the immediately adjacent parts of the vessel to an extreme degree; the effect, however, was not limited to these, but gradually shaded off in both directions; and even at a considerable distance, where by ordinary observation no change might have been detected, the micrometer showed a diminution from 6° to 5°,[3] occurring immediately upon the irritation and subsiding soon after. Similar results were obtained on repetition of the experiment.

From the analogy of the intestinal and cardiac movements,[4] it is probable that the local co-ordinating apparatus for the arteries comes into play in all cases of arterial contraction in the living animal, and is the medium through which the nerves which arise from the cord act upon the vessels. But it is very important to bear in mind that it is, under ordinary circumstances, in entire subjection to the spinal system, and only acts independently under special conditions of local irritation.

It remained as yet undecided whether the nervous centre for the arteries contained in the cerebro-spinal axis were extensively diffused or limited to

[1] Henle and Pfeufer's *Zeitschrift*, 2nd series, vol. viii, 1857

[2] Vide 'Preliminary Account of an Inquiry into the Functions of the Visceral Nerves, &c.' (p. 90 of this volume).

[3] These degrees have a different value from those mentioned in other parts of this paper, a different micrometer having been employed.

[4] See 'Preliminary Account, &c.', before referred to.

some particular region of it. The experiments hitherto related had revealed nothing absolutely irreconcilable with the hypothesis of a spot about the middle of the cord being the special regulator of the contractions of the vessels; a view indicated, though by no means proved, as regards the arteries of the face and fore-limbs in mammalia, by the observations of Waller and Budge and of Schiff, alluded to at the commencement of this paper. It appeared probable that this point might be readily determined by removing the middle third of the cord, and ascertaining whether or not the arteries still retained their contractility.[1] Accordingly, on August 26, 1857, having selected for measurement an artery in one of the webs of a frog, I divided the cord transversely at the distance of a quarter of its length from the posterior end, at $11^h\ 7^m$ a.m. During the next half-hour the diameter of the vessel was observed varying frequently from $\frac{1}{2}°$ to $1\frac{1}{2}°$. At $11^h\ 34^m$ the cord was again cut across opposite the middle of the scapulae, i.e. at a distance of a little more than a quarter of its length from the occiput. After this operation the artery was observed for about a quarter of an hour varying occasionally in calibre between 1° and 2°. At $11^h\ 53^m$ the portion of cord intervening between the two transverse incisions, and measuring very nearly half its entire length, was removed, immediately after which the artery measured $1\frac{1}{2}°$. At $11^h\ 55^m$ its diameter was 1°, the heart meanwhile continuing in good action, and twelve minutes later the vessel was again seen to change in calibre from 1° to $1\frac{1}{2}°$ and back again to 1°. The heart's action afterwards became very feeble, and the parts of the nervous centres concerned in regulating the arterial calibre appeared also to be failing in their functions, the vessel varying very slightly, and gradually increasing in diameter, till towards 1^h p.m. its measurements were from 2° to $2\frac{1}{4}°$. At $1^h\ 1^m$ the posterior end of the cord was removed, immediately after which the diameter of the artery was above $2\frac{1}{4}°$, or larger than ever seen before; at $1^h\ 4^m$ it was near $2\frac{1}{3}°$, and continued so at $1^h\ 10^m$. Soon after this the circulation ceased entirely.

In this case, notwithstanding the removal of the two middle quarters of the cord, the arteries were observed moderate in size and varying in calibre at a time when the heart was acting well. Hence it was evident that the middle portions of the cord are not essential to the regulation of the arterial contractions in the feet. The following experiment confirmed this important conclusion, and also furnished additional information.

On the 20th of October, a large frog having been placed under chloroform,

[1] In the original manuscript I was obliged to express my regret that time had not yet permitted me to carry out this idea. The dates in the text indicate that it has been done since the paper was read.

the cord was divided transversely at the distance of about one-fifth of its length from the posterior extremity. At 4^h 20^m p.m., just after the operation, an artery in the right foot measured $2\frac{1}{2}°$, the vessels appearing generally of pretty full size, and the flow of blood rapid through the web. At 4^h 25^m the cord was again cut across a little behind the mid-scapulae, at a distance from the occiput of somewhat more than a quarter of the length of the cord. At 4^h 33^m the diameter of the vessel was $1\frac{1}{3}°$. At 4^h 40^m the portion of cord included between the incisions was removed, without any interference with either the anterior or posterior segment. It was observed that a large branch for the hind legs, furnished by the middle segment, had to be divided during its removal, and immediately after the operation the artery measured $2\frac{1}{3}°$, and the flow of blood in the web was much more rapid than before. At 4^h 45^m the artery had contracted to $2°$, at 5^h 7^m it measured short of $2°$, and a minute later was again $2°$. At 5^h 11^m I introduced a fine needle into the anterior segment of the cord with the effect of causing convulsive movements of the fore legs, but no change whatever in the calibre of the artery in the hind leg. I afterwards repeated this experiment twice, and the last time carried the needle on into the brain, and stirred it up thoroughly, but no effect was produced upon the vessel. At 5^h 23^m the whole brain was removed, together with the anterior segment of the cord ; the artery, however, still continued to measure $2°$. At this time the circulation, though somewhat enfeebled, was still pretty good. At 5^h 53^m a complicated operation was performed upon the left thigh, to which I need not allude further than to mention that it no doubt involved exposure of the other foot to a higher temperature than before, in consequence of the vicinity of my hands, and this was probably the cause of the dilatation of the arteries observed immediately afterwards, that which had been previously measured being now $2\frac{2}{3}°$. Five hours later the artery was again $2°$, but the heart's action was excessively languid. Next morning the circulation was going on steadily, though somewhat slowly, the heart having obviously recovered to some extent during the night. The arteries were larger than ever seen before ; the calibre of that above noted being $3\frac{1}{4}°$, and there were a good many blood-corpuscles adhering to the walls of the vessels. It is probable that the small posterior segment of the cord had become impaired in its powers, but that it was still acting to some extent was evident from the circumstance that after its removal at 10^h 56^m a.m., the vessel was found increased to $4°$, and in consequence of the arterial dilatation, the stagnation of the red corpuscles, which existed in several parts of the webs, was almost entirely dispelled, although the action of the heart did not appear to have been changed. During the next half-hour the artery was measured four times, and was in every instance found to be still 4° in diameter. I may mention that I measured the posterior segment of the cord immediately after its removal, and found its length to be one-sixth of that of the whole cord ; it was in fact little more than the tip of it ; but allowing for a certain amount of contraction, it may be reckoned as one-fifth.

This case shows that the extremity of the cord acts as a nervous centre for the arteries. But the experiment of the 2nd of June proved that after the removal of the greater part of the posterior half of the cord, the vessels still remained under the control of the nervous system.[1] Hence it is clear that the nervous centre for the arteries is not confined to any limited region of the cord.

This experiment also indicates, in a very striking manner, how small a piece of the cord will suffice to regulate the calibre of the arteries, and how little effect may be produced, even in the first instance, by the removal of a large portion which also possesses that function. For it was shown, by the absence of contraction in the vessels when the anterior segment was irritated, and still more conclusively by the absence of dilatation when the anterior segment and the brain were removed, that the posterior segment was the only part capable of acting on the arteries after the removal of the middle segment ; or, in other words, that this operation deprived the arteries of the influence of the whole cerebro-spinal axis, except the posterior fifth of the cord. Yet, although the heart was acting powerfully at the time, the dilatation produced by this procedure was only moderate in amount, and very transient. Hence it follows that the mere fact of the speedy return of the arteries to their former state of contraction, after removal of an anterior portion of the cerebro-spinal axis, as seen in the experiment of April 16, 1857,[2] is no ground whatever for believing that such a portion does not act as a nervous centre for the arteries. This being clearly understood, the invariable occurrence of contraction, when the posterior part of the brain or the anterior half of the cord was irritated, in the experiments of April 14 and 16, 1857,[3] must be regarded as strong presumptive evidence, if not absolute proof, that they as well as the posterior half of the cord preside over the arterial contractions in the feet, although, as shown at p. 37, they appear to exert their influence only through those roots of nerves which take origin from the posterior regions of the cord. On the other hand, the cerebral hemispheres seem to take no part in this function, so far at least as it is safe to draw any inference from the negative evidence derived from a single experiment performed upon them, viz. that mentioned at p. 31.

The fact that the removal of a large portion of the cord is followed by

[1] Vide p. 37. [2] Vide p. 33. [3] Vide pp. 31, 33.

only temporary dilatation of the arteries, provided that a part remains which furnishes roots of nerves for the posterior extremities, is in harmony with the transient effects which were seen to be produced upon the vessels by partial division of the roots of the nerves within the spinal canal in the experiments of April 8 and 11, 1857.[1] In both these cases the arteries of the webs appeared to recover their contractile power completely, although the leg remained nearly, if not entirely, paralysed; which seems to indicate that a few fibres of the nerves for the blood-vessels of a part can supply the place of the rest more perfectly than is the case with the ordinary nerves of sensation and motion. This peculiarity of the 'vaso-motor' nerves is more strikingly illustrated by the first experiment mentioned in this paper[2], in which it may be remembered that the arteries of the webs completely recovered their usual powers of varying their calibre within half an hour after division of the sciatic, although this is an operation which abolishes for days at least all sensation and voluntary motion in the leg. I have since seen yet more remarkable instances of the same thing. On October 10, 1857, with the view of investigating the nature of the control exercised by the nervous system over the actions of the pigment-cells,[3] I divided all the soft parts in the middle of the thigh of a frog, except the main artery and vein. The first effect upon the arteries was full dilatation; but about twenty-four hours later they were again of moderate size, while the circulation was still active. After the death of the animal, I examined with the microscope the coats of the artery and vein, and also the periosteum, together with a very slight amount of muscular tissue adhering to it, but could detect no nerves in any of them, although from the method of examination I could hardly have missed branches containing more than very few nerve-tubes. Comparing the result in this case with the permanent dilatation which always occurred after removal of the spinal cord, so long as the circulation continued active, it was evident that the slender filaments contained in the coats of the vessels, or possibly in the bone, had served as an efficient means of communication between the cerebro-spinal axis and the arteries of the foot.

On the 13th of the same month I repeated the experiment upon another frog, operating in this case upon both thighs. In the first place, I divided thoroughly all the soft parts except the artery, vein and nerve, the circulation remaining unaffected. The nerves were then successively cut, full dilatation of the arteries and rapid flow through the capillaries being the immediate result. An hour and a half later, however, the flow was observed to be less rapid, no

[1] Vide pp. 30, 31. [2] Vide p. 29.

[3] Further information regarding this experiment, as respects the pigmentary system, will be found in the next paper (p. 48 of this volume).

doubt in consequence of slight contraction of the arteries, one of which, in the left foot, measured 3° by micrometer, and after sixteen hours more they were both moderate and variable in calibre in both feet ; that in the left limb before noted now changing between $1\frac{1}{2}°$ and 2°, and a principal artery in the right foot between 1° and $1\frac{1}{2}°$. The circulation meanwhile continued active, and remained so more than twelve hours longer ; from which circumstance as well as from the normal appearance of the contractions, it was evident that the arteries were still under the control of the cord ; and I may add, that in another animal in which the same operation was performed upon the thigh after removal of the brain and cord, the arteries remained of full size and without variation for thirty-four hours, after which circulation ceased.

From these facts it appears that there exists a very remarkable provision for ensuring the proper regulation of the arterial calibre in a part in spite of almost complete division of the nerves connecting the vessels with the nervous centre which presides over their contractions. It has been shown by recent discovery that sensation and voluntary motion are abolished in parts whose nerves have been divided, until repair has been effected by a process of fresh formation of the nerve-fibres. But the control of the flow of the nutrient fluid is not allowed to be interrupted in this manner, but continues to be exercised more or less perfectly, notwithstanding nearly absolute severance of nervous connexion.

Allusion has been more than once made to the circumstance that arteries do not dilate so fully when the heart is very feeble as when it is in powerful action. This was strikingly illustrated in the case of the frog which was the subject of operation on April 16, 1857. Immediately after the experiments recorded at p. 33, the heart having ceased to cause movement of blood in the web, I induced complete constriction of the arteries by irritating with a needle the posterior part of the cord, and then thoroughly cleared the spinal canal of its contents. The artery under special observation did not, however, become dilated to a greater diameter than $1\frac{1}{2}°$, although during the earlier experiments, when the heart was acting vigorously, it had been observed to attain sometimes a calibre of 3°. The heart never recovered its power, and the vessel maintained this medium width as long as I continued to examine the animal, namely, three hours.

From this and other similar observations, I infer that full dilatation of the arteries is a merely passive phenomenon as respects the parietes of the vessels. Contraction is effected by the muscular fibre-cells of their circular coat, on the relaxation of which the elasticity of the arteries tends to make them expand to a certain degree, beyond which they do not dilate, except in so far as they are distended by the blood.

It was observed by Wharton Jones,[1] that section of the sciatic nerve in the thigh of a frog was followed after a time by oedema of the limb and exfoliation of the epidermis. If this were dependent on the dilatation of the arteries produced by the division of the nerve, the fact would have a very important bearing upon the cause of inflammatory effusion. I find, however, that neither oedema nor exfoliation results from permanent full dilatation produced by operations upon the cord or the roots of the spinal nerves; while, on the contrary, both took place in the case of division of the sciatic, given in the early part of this paper, in which it will be remembered that the arteries recovered their contractility completely within half an hour, and presented, during the next twenty-four hours, precisely similar appearances with those in the other foot. Hence it is evident that the phenomena in question are not due to vascular relaxation, but to some other circumstances attending the operation performed upon the thigh.

It remains to be added, that, in a healthy state of the web, no change in the properties of the blood was ever observed to accompany the constriction of the arteries on irritation of the cord, or the dilatation which followed the destruction of the nervous centre. The exsanguine condition of the web in the former case, and the turgid state of the vessels in the latter, were simply the effects of the variations of calibre in the arteries, the blood flowing more freely in proportion to their width.[2]

To sum up the principal results of this inquiry, it appears—

1st. That, of the nervous centres usually recognized, the cerebro-spinal axis is the only part which regulates the contractions of the arteries of the webs; this function being apparently exercised by the whole length of the cord and the posterior part of the brain, operating through fibres which arise from the same region of the cord as do those through which sensation and motion are effected in the hind legs.

2nd. That there exists within the limb some means, probably ganglionic, by virtue of which the fibre-cells of the circular coat of the arteries may contract in concert with each other, independently of any ganglia contained in the trunk.

And 3rd, that the local co-ordinating apparatus, though capable of independent action in special conditions of direct irritation, is, under ordinary circumstances, in strict subordination to the spinal system; while a remarkable provision exists for the maintenance of this control, notwithstanding almost complete severance of nervous connexion between the cord and the limb.

[1] *Medico-Chir. Trans.*, loc. cit.

[2] The subject of the effect of variations in the calibre of the arteries upon the flow through the capillaries, will be found fully discussed in the paper 'On the Early Stages of Inflammation' (reprinted in this volume, p. 209).

ON THE CUTANEOUS PIGMENTARY SYSTEM OF THE FROG

[*Philosophical Transactions*, Part II for 1858, p. 627.

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THE fact that the skin of the frog is capable of varying in colour, has been for some years known to German naturalists. The first account of the mechanism by which these changes are effected, appears to have been given by Professor Brücke, of Vienna, in 1852,[2] and the subject has since been very carefully investigated by Dr. von Wittich of Königsberg,[3] and Dr. E. Harless of Munich.[4] All these observers describe the dark pigment as contained in stellate cells, each composed of a central part or body and several tubular offsets, which, subdividing minutely and anastomosing freely with one another and also with those of neighbouring cells, constitute a delicate network in the substance of the true skin. They describe the dark contents as sometimes concentrated in the bodies of the cells, at other times diffused throughout the branching processes, the skin of the creature being pale in the former case and dark in the latter. In the tree-frog the change from a dark to a pale state of the body generally was induced by bringing the creature into a bright light, by psychical excitement (as was supposed[5]), or by galvanizing the spinal cord; and a similar effect was produced on a particular portion of the surface by irritating it mechanically, or with oil of turpentine, or by galvanism applied either directly to the part, or through branches of nerves leading to it. After the source of irritation was removed, the skin returned somewhat slowly to its former colour; and von Wittich noticed that when the paleness produced by direct irritation had passed off, the tint became deeper in the irritated spot

[1] During the time that has elapsed between the reading of this paper and its publication, several new observations have been made, which it has been thought best to introduce into the text, distinguished by date or footnote from the matter of the original manuscript.

[2] 'Untersuchungen über den Farbenwechsel des africanischen Chamaeleons,' *iv. Band der mathemat.-naturwissenschaftl. Classe der Kaiserl. Acad. d. Wissensch. Wien.* This paper I have not yet had an opportunity of consulting.

[3] Müller's *Archiv*, 1854.

[4] *Zeitschrift für wissenschaftliche Zoologie*, vol. v, 1854.

[5] This rests on the authority of von Wittich; but, for anything stated to the contrary in his paper, the effects ascribed to psychical excitement may have been connected with the efforts of the creature in struggling, independently of any emotional change.

than elsewhere. The esculent frog exhibited similar phenomena, but was less sensitive. The concentrated state of the pigment is attributed by all the observers above named to contraction of the cells, while the diffused condition is supposed due to their relaxation. The contents of the cells are described as dark granules suspended in a fluid; and both von Wittich and Harless have distinctly seen the granules rolling along in the offsets during the process of concentration. All the authorities agree in the opinion that the fluid and granules move together from one part of the cell to another, the offsets being supposed empty of both when the pigment is accumulated in the body of the cell.[1]

In some respects the above description agrees with my own experience of the common frog of this country (*Rana temporaria*). I find that this well-known animal exhibits changes of hue almost as great as those of the chameleon, every specimen being capable of varying from a very pale to a very dark colour, the former being generally greenish yellow, but in some varieties reddish; and the latter brownish black, or sometimes coal black; while between these extremes any intermediate shade may be assumed. The depth of tint is generally proportioned to that of surrounding objects: thus a frog caught in a recess in a black rock was itself almost black; but after it had been kept for about an hour on white flagstones in the sun, was found to be dusky yellow, with dark spots here and there. It was then placed again in the hollow of the rock, and in a quarter of an hour had resumed its former darkness. These effects are independent of changes of temperature; for similar results may be obtained by placing a frog alternately in a vessel from which luminous rays are excluded, and in a white earthen jar covered with glass, in the same situation. Different examples, however, differ much in their sensitiveness to light. A violent struggle on the part of the animal is often followed by a speedy alteration from a dark to a pale state of the skin. It seems very doubtful whether psychical excitement has anything to do with this occurrence, any more than with the arterial contraction which invariably takes place under

[1] From the way in which von Wittich alludes to Brücke's description, it is clear that the latter supposed the cells to be contractile. Von Wittich himself in his first paper speaks of the movement of the pigment induced by galvanism as 'satisfactorily' showing 'that the stellate pigment-cells are contractile'. In his second paper (vide Müller's *Archiv*, 1854, p. 263), he expresses some doubt regarding the contractility of the *cell-wall*, but clearly speaks of the contents (fluid and granules) as moving together. Harless, after describing 'the rolling of the pigment-molecules towards the centre of the cell', goes on to say, 'that this rolling may be possible, there must be a fluid in the cells and offsets, *to which* the molecules owe their movement.' He takes it for granted that the movement of the fluid must be due to some contractile agency, and as he finds no apparatus of this nature around the cells, and as the unstriped muscular fibres of the skin have no special relation to them, he infers that the cell-wall is itself contractile.

such circumstances. Neither oil of turpentine nor galvanism, when applied to the integument, produces, so far as I have seen, any effect upon its colour; our species being little influenced in this respect by direct irritation. I have, however, frequently observed, after forcibly pinching a dark web, that a pale ring, about one-sixteenth of an inch in breadth, has formed around the area so treated; but this was very slow in appearing, being first noticed from half an hour to an hour after the pinch was given.

The webs of the hind feet, examined under a low power of the microscope, exhibit differences in the distribution of the dark pigment[1] according to the tint of the skin, such as will be understood by referring to Plate III (p. 68), where Fig. 1 is from a dark portion of web, and Fig. 2 from a pale part in the same animal. In Fig. 2 the colouring matter is seen to be collected in black spots of irregular angular shape. This, however, is not the state which exists when the colour is palest, for then the masses of pigment are in the form of round dots, as in the part to the right in Fig. 1, Plate V (p. 274). Neither does Fig. 1 of Plate III give the condition met with when the skin is darkest, in which case all that meets the eye on superficial observation is a reticular appearance, such as is represented in the stripe down the middle of Fig. 1, Plate V, and in the lower part of Fig. 2 in the same Plate. When the colour of the integument is about medium, the pigment is disposed in a truly stellate manner, as on the left side of Fig. 1, Plate V. It may be convenient for the purposes of description, to designate these various states as respectively the dotted, angular, stellate, and reticular conditions of the pigment.

When a higher magnifying power is applied in an extremely dark state of the skin, the chromatophorous cells, for such they seem to be, appear as depicted in Plate III, Fig. 3, where two of them are given, along with an adjacent capillary distended with blood-corpuscles. Each cell consists of a somewhat flattened central part with several irregular offsets, of considerable diameter near the central part, but speedily breaking up into small branches. The ultimate ramifications, some of which are of extreme minuteness, anastomose freely with one another and with those of neighbouring cells, constituting a very delicate and close-meshed network, which pervades the whole thickness of the

[1] Other kinds of pigment are also present in the skin of the common frog, generally of yellow colour, but sometimes red. My attention has not been much directed to these, but I have noticed that they are contained in receptacles of the same general form and structure as those which hold dark pigment; and on one occasion, since the reading of the paper, I observed the colouring matter disposed in a stellate manner with complex ramifications in one part of a web, and in another part collected into round spots; implying that these cells possess the functions of concentration and diffusion of the pigment. They do not, however, always act in harmony with the dark cells; and it is probably through their agency that changes in tint, such as I have seen to occur in one and the same frog, independent of mere lightness and darkness of shade, are produced.

true skin, and especially follows the course of the blood-vessels, entering into the composition of the cellular coat of the arteries and veins, and twining about the capillaries in a very remarkable manner. The walls of these cells and of their tubular offsets appear to be extremely delicate, and some attempts which I have made to isolate them from surrounding tissues have barely served to demonstrate their existence. The cells vary considerably in dimensions according to the size of the animal ; thus, those in Figs. 8, 9, and 10, which are from young frogs, though magnified 500 diameters, show in the drawing even smaller than those in Fig. 3, magnified only 250 times, the latter being from a full-grown specimen. In an average full-sized cell of a large frog, the middle portion was found to measure 1–330th of an inch in length by 1–670th of an inch in breadth, and 1–1500th of an inch in thickness. The last-named dimension was obtained by carrying the focus of an object-glass of high power, from the most superficial to the deepest part by the screw for giving slow motion, and reading off on its graduated circle the number of divisions traversed, these having a known proportion to the depth measured. Opportunities for testing the correctness of this measurement were presented by other cells which lay edgewise, so that their thickness could be observed directly.

Perhaps the strongest argument in favour of the cellular nature of these receptacles of colouring matter is afforded by the universal presence of a nucleus in the central cavity of each. In large frogs it is often difficult or impossible to discover clear evidence of it, but in small ones, in which the web is much thinner and its constituent parts therefore capable of clearer definition with the microscope, it can be quite distinctly seen in the reticular condition of the pigment. Its form and relations may be gathered from Figs. 8, 9, and 10. In 8 and 10 the bodies of the cells are viewed on the flat, and the nucleus appears as an oval colourless body, about 1–2500th of an inch long by 1–3300th of an inch broad. In Fig. 9 the body of the cell is seen edgewise applied to the wall of a capillary blood-vessel, which is embraced by its processes. The thickness of the nucleus is thus displayed, and is shown to be equal to that of the cell in which it lies, which in fact it causes to bulge slightly, and also nearly as great as the breadth of the nucleus in Figs. 8 and 10. In the cell of Fig. 10, the thickness of the nucleus, measured in the manner above described, was found about equal to its breadth. The nucleus in Fig. 8 is not centrally placed in the body of the cell, and I have in some other cases seen it still more eccentric.[1]

The contents of these cells are very minute dark granules or molecules sus-

[1] The precise relations and dimensions of the nucleus have been ascertained subsequently to the reading of the paper.

pended in a colourless fluid, in which I have often seen them moving freely: when in considerable mass they produce a jet-black appearance, but exhibit a brown tint when present only in small quantity.

When the skin of the animal is very pale, the colouring matter is all accumulated in the central parts of the cells. With regard to the method in which this change is effected, I am compelled to differ altogether from the before-mentioned authorities, who suppose that the granules and fluid are together forced by contraction from the processes into the bodies of the cells. They seem to take it for granted that the depth of tint of any one part of a cell depends simply upon the bulk of the contents situated there, and the consequent thickness of the coloured medium through which the light passes before reaching the eye. This, however, is by no means the case, as may be seen by referring again to Plate III, Fig. 3. The pigment is there represented fully diffused through the ramifications of the offsets, and some of the smallest of these are darker than the bodies of the cells and the adjoining broad parts of the processes; yet the former are far from being thicker than the latter: on the contrary, some of the branches, though conspicuous for their blackness, appear but as delicate lines which can be seen only at one focus when a glass of very high power is employed; while the bodies of the cells, as above mentioned, possess considerable thickness, and the processes are not flat, but subcylindrical. But the differences in tint are sufficiently accounted for by the circumstance that in the dark branches the colouring particles are closely packed together, whereas in the bodies of the cells and the paler parts of the offsets, the individual granules are separated from one another by considerable colourless intervals. Hence it is clear that the degree of darkness of any part of a cell does not depend so much on the bulk of its contents in the aggregate, as on the proportion which the pigment molecules in it bear to the fluid in which they are suspended.

If the whole contents of the processes were forced into the central parts during concentration of the pigment, and driven back again during diffusion, the bodies of the cells would be subject to great variations in capacity, becoming turgid in concentration and collapsed in diffusion; and the bulk of the central coloured mass would be great in the former case, but small in the latter. The very reverse, however, really takes place. Fig. 6 represents the appearance of the pigment in a concentrated condition, in one of the same cells which in Fig. 3 show it in full diffusion. During the time in which this change took place, the adjacent capillary had shrunk to about half its former size, but it will be recognized by its general form, and will indicate which of the two cells is that under consideration. Both the figures were drawn on the same scale with the camera lucida,[1] so that accuracy of proportion is ensured. The circular black mass into which the colouring matter is now all collected, measures less across than either the length or breadth of the body of the cell in the diffused state of the pigment. Further, the mass is not spherical, but of flattened form, and its thickness is only about that of the central part of the cell in diffusion. This we know from the appearances presented by the spots of concentrated pigment in other cells seen edgewise, as is the case with some in Fig. 7, which represents the outline of the wall of a large blood-vessel, and the pigment contained in its external coat in nearly complete concentration. Hence it appears that all the pigment-granules contained in the body of the cell and the minutely ramifying processes in the diffused state, have been brought together into a space considerably less than was then occupied by the pale contents of the body of the cell alone. The coloured particles have been concentrated into a dense disciform mass, but the fluid in which they were suspended has been left behind.

Fig. 4 shows the pigment in the same cells as Fig. 3 in an intermediate stage, in which the process of concentration is about half accomplished; the upper one being in the condition which would appear stellate under a low magnifying power. The greater part of the pigment is collected in the bodies of the cells, especially towards their central parts: in the middle of each dark mass, however, is a pale spot, doubtless due to the circumstance of the granules not having yet insinuated themselves between the cell-wall and the nucleus, which, as shown above, probably lies in contact with it. This appearance of pale central points was very general in the web at the time when Fig. 4 was drawn, but gradually disappeared as the aggregation of the pigment-molecules proceeded, and does not exist in Fig. 5, which represents the lower of the two cells in a more advanced state of concentration. The remote branches of the processes were then for the most part invisible, and those which did appear were generally pale, instead of dark, as they had been during full diffusion. This difference does not depend on contraction of the branches, but on the granules being absent from them, or sparsely scattered instead of closely packed; and I have often ascertained from some granules remaining widely separated in a process, that it was of large calibre, though, without careful searching, it would have seemed invisible Even in Fig. 6 concentration is not represented absolutely perfect; for a few molecules are to be observed near the black mass in the more circumferential parts of the body of the cell. The extreme delicacy of the cell-wall makes it very difficult to trace it among the surrounding tissues, and I have not attempted

[1] All the drawings in the plate which accompany this paper were made with the assistance of this very valuable instrument.

to give it in these figures, which, it must be clearly borne in mind, represent only the colouring matter. The external parts of the body of the cell and the principal processes may, however, be sometimes discovered, though perfectly colourless in consequence of concentration: they are then found to be of the usual dimensions met with in full diffusion, showing that they are still full of fluid though destitute of granules. In fact the only change of form to which the cells appear liable is a slight bulging of the central part at the seat of the black mass in the concentrated state, which I have detected in some cases by camera-lucida sketching, and which is consistent with the separation of the cell-wall from the nucleus, implied by the ultimate disappearance of the central pale points of Fig. 4.

The movement of the granules towards the centres of the cells may be seen without any great difficulty. The death of a healthy frog is always followed by complete concentration of the pigment for a time, however much diffused it may have previously been, and the process taking place gradually, its progress can be observed. If a frog with the skin dark, and the pigment therefore diffused, be killed and the web examined soon with a good glass of high power, the granules may be seen distinctly moving along the offsets of each cell to join the dark mass which is becoming accumulated in the central part. If the process is going on languidly, the individual molecules advance slowly with slightly dancing movements, indicating that they are free in the fluid and not confined in any way to the cell-wall. If concentration is taking place more speedily, the granules rush along so quickly that no time is allowed for observing their molecular movements, and often their motion is so rapid as to elude the eye altogether. In one instance a large-sized offset, which at first contained abundance of pigment, became gradually cleared in this way of its colouring matter without any change in its dimensions, till it was almost invisible on account of the very small number of molecules remaining in it.

It is thus a matter of direct observation, that the pigment-granules move along into the bodies of the cells during concentration, and leave colourless fluid behind them in the processes. It is clear that their motion cannot be explained by currents in the fluid; for streams proceeding towards the centre of a cell would necessarily be accompanied by a returning flow in the opposite direction, which would carry the pigment with it unless the molecules had a special tendency towards the centre. The circular form assumed by the mass of pigment when concentration is complete is strongly suggestive of a central attractive force acting on the granules. The occurrence of the central pale points, which are represented in Fig. 4, showing that the nucleus was there in the middle of the concentrating pigment, led me at first to suppose that this body was the attractive agent.[1] I afterwards took pains to ascertain whether the nucleus always has this relation to the mass, and found that such is not the case. On October 22, 1857, I watched three adjacent cells during the process of post mortem concentration; in two of them the nucleus ultimately projected by about a quarter of its length at one side from the black spot, while in the other cell the aggregated molecules covered only one-third of the nucleus, so that *no part* of that body lay in the middle of the mass. The point to which the granules appear to have a special tendency is the middle of the body of the cell, which seems always to correspond with the centre of the disc of molecules, whereas the nucleus is often eccentrically placed in the cell.

The diffusion of the molecules is not merely a passive result of the cessation of concentration, as has been hitherto supposed. In watching closely the occurrence of the phenomenon, I have seen[2] the granules start off suddenly from the central mass, with a velocity which implied that they were under the influence of forces very different from those which cause molecular movements in them when shed from their containing cells. That the process requires the vital forces of the cells to be in full operation is also proved by the fact that any agency, such as a galvanic shock, which temporarily paralyses their functions, arrests diffusion as well as concentration; whereas, if the former were merely passive, it would take place as soon as the concentrating power was set at rest.

I have already pointed out the sparsely scattered state of the granules in the central receptacles, compared with their accumulation in the branches of the offsets, in the fully diffused state shown in Fig. 3. This contrast is sometimes much more striking, so that the bodies of the cells are almost colourless, and require some experience with the tissue in order to detect them. This indicates a special tendency on the part of the granules to leave the middle of the cell. Yet to however great a degree diffusion be carried, there always remain some molecules in the body of the cell uniformly distributed throughout its thickness and not attached to the parietes, as they would have been had their dispersion been caused by attraction on the part of the cell-wall. This disposition of the granules, which obtains even in the immediate vicinity of the nucleus, appears also distinct evidence against the operation of a central repulsive force; for this would render the body and the adjoining parts of the processes as clear of pigment as the remote branches are made in concentration.

[1] This was the view expressed in the paper as it was read.

[2] This observation was made after the reading of the paper.

The hypothesis which would seem most consistent with the appearances described, is that of a mutual repulsion on the part of the pigment-granules, induced by some agency strongest at the centre of the cell and feeble in the remotest branches of the offsets.

On October 27, 1857, I was observing a cell in which post mortem concentration had occurred, the pigment being in the angular condition. At one of the angles movements of the granules were going on, of which I will content myself with giving two examples. At one time a number of molecules started off together with great rapidity from the black mass, but stopped after having proceeded a certain distance, some of them remaining in their new position, while others returned at various rates towards the centre. At another time an individual granule moved slowly away for a little space, and then came back by a circuitous route to a different part of the mass from that which it had left. What I then saw has led me to believe that the movements of the pigment-molecules are of a complex character that will perhaps never be fully explained. In the meantime it is clear that concentration and diffusion are both active vital functions, and that both imply peculiar relations of the centre of each cell to the pigment-molecules, as distinguished from the fluid in which they are suspended.

These conclusions invest the pigmentary changes with deep physiological interest. In the movements of the granules towards and from the centres of their containing cells, we now have ocular demonstration that a particular kind of material may have impressed upon it by vital action, independently of muscular contraction or ciliary motion, tendencies to rush energetically to or from certain fixed points in the tissues, through distances equal to nearly twice the thickness of a villus of the human intestine, and several times greater than the average breadth of a human capillary interspace. Whether we be able to explain the means by which such results are accomplished or not, it is obvious that forces of similar powers and range of operation, if suitably modified according to the circumstances of each case, would be more than adequate to cause the passage of particles of fat from the cavity of the intestine into the central lacteals of the villi, or the transit of the material required for a particular secretion or act of nutrition out of a capillary into a neighbouring gland cell or other portion of tissue; and, again, for the discharge of an elaborated product of secretion into a duct, or the return of waste matter into the blood-vessels or lymphatics. We thus obtain a basis of fact for what has hitherto been merely conjectural, in the explanation of the processes of absorption, secretion, and nutrition generally.

The functions of the pigment-cells are under the control of the nervous system,[1] as is evident from the effects produced on the colour of the skin by a struggle on the part of the animal.

Much attention has been devoted by von Wittich to the inquiry, by what ganglionic centres this control is exercised. He found that division of the sciatic nerve in the thigh, or of cutaneous branches in the dorsal region, did not prevent the parts of the skin supplied by them varying in colour along with the rest of the body under the influence of light; and, supposing that in such operations all connexion was severed between the portions of integument concerned and the central organs of the nervous system, he inferred that the pigmentary changes induced by light were effected independently of either the cerebro-spinal axis or the usually recognized sympathetic ganglia. He nevertheless regarded such variations as probably reflex in their nature, and attributed them to a peripheral ganglionic apparatus in the skin itself; and this opinion appeared confirmed by the circumstance that direct irritation operated in the same manner upon the colour of a detached piece of integument as upon that of the living animal. At the same time, as he observed paleness of tint to result from irritation of the cord, or of the nerves distributed to a particular part of the surface, he concluded that the spinal system was also capable of acting on the pigment-cells, and so accounted for the supposed influence of psychical excitement upon the tint of the skin. Thus, according to his view, the cutaneous pigmentary system was circumstanced like the heart or intestines, which, though possessing the faculty of independent action by virtue of their intrinsic ganglia, may also have their movements affected by mental emotion.[2]

In the course of some experiments performed in April 1857, with reference to the influence exerted by the cord upon the calibre of the arteries, I noticed on two occasions that partial division of the roots of the nerves for one of the hind legs within the spinal canal was immediately followed by increased paleness of the limb, of transient character, after which the leg assumed precisely the same colour as the other, this result being in accordance with von Wittich's description. But I further observed in two cases in which such operations had been performed, that when a considerable time had elaspsed, viz. nine hours in one instance and two days in the other, the limb whose nerves had been cut was decidedly darker than the rest of the body. Similar results were once obtained from the division of the sciatic nerve in the thigh. When the operation was performed, viz. at 4^{h} 30^{m} p.m. on April 4, 1857, the pigment was in

[1] The part of the paper devoted to this branch of the subject has been entirely rewritten; and the dates in the text imply that most of the observations with reference to it have been made since the reading of the manuscript before the Society.

[2] Vide Müller's *Archiv*, loc. cit., p. 56.

the stellate condition in the webs, the tint of the skin being moderately dark; and this state of things continued unchanged in both limbs for the next six hours. On the following day, however, the leg operated on was seen to be very dark, and the pigment in its webs was reticular; while in the rest of the body the colour remained as before, and the pigment was still stellate. This striking contrast continued unaltered for two days, when it was destroyed by the body generally assuming the darkest possible tint.

The diffusion of the pigment in consequence of division of nerves appeared to be the counterpart of the concentration by their irritation, and it seemed probable that the want of constancy in the results in the former case was caused, like the variable amount and duration of arterial dilatation after such operations,[1] by the place of the divided trunks being supplied by other branches; and that, if the nerves of a limb were all completely severed, diffusion would necessarily take place. With the view of testing the truth of this idea, the following experiment was performed. In the afternoon of October 10, 1857, I divided in a pale frog all the soft parts in the middle of the right thigh, except the femoral artery and vein and the sciatic nerve; and late in the evening, having ascertained that the circulation was going on freely in the webs, I cut the nerve also, no effect having been hitherto produced upon the colour of the limb. Next morning the body generally was still pale, but the right leg was black from the wound downwards. The same remarkable appearance continued till the evening, when circulation ceased in the limb. On the 13th I performed the same experiment upon both thighs of another large pale frog, leaving the sciatic trunks entire in the first instance, until I had ascertained that the circulation in the feet had not been interfered with. Three hours after this had been done I divided the nerve in the left thigh, and in about forty minutes observed that the leg was decidedly darker below the seat of operation. After another hour I found the pigment stellate in the left webs, whereas it was in the dotted condition in the right foot. I then cut the nerve in the right limb, and within a quarter of an hour the leg was already considerably darker below the wound, and the pigment in the webs had become stellate. Next morning the body was still pale, but the legs were very dark, and they continued to deepen in tint, although the animal was kept in a white earthen jar covered with glass in a bright light, till at about 3 p.m. they were almost absolutely black, while the pigment was diffused in the webs to the extremest degree, the body meanwhile and the upper parts of the thighs retaining their former light colour. The tint of the legs remained unaltered till the death of the animal, which took place several hours later.

[1] See p. 31.

The natural interpretation of these results appeared to be, that there exists a constant tendency to diffusion of the pigment in a limb so soon as it is liberated from the influence of the usually recognized nervous centres. It afterwards occurred to me, that if this were really true, diffusion of the pigment might, by proper management, be observed in an amputated limb before the supervention of the tendency to post mortem concentration : for I knew, from reasons to be mentioned hereafter, that this effect of death depended on the cessation of the flow of blood through the vessels, and, from what I had seen of arterial contractions in the frog's web, and vermicular movements of the mammalian intestine from a similar cause, I felt sure that, if the blood were retained within the vessels, the arrest of the circulation could not be instantaneous in its effects upon the pigment, but that some minutes would probably be required to develop them ; during which time the diffusion resulting from liberation of the pigment-cells from the influence of the ganglia in the trunk would proceed unchecked. Accordingly, on September 3, 1858, having tied a string tightly round the ankle of a pale frog, I immediately amputated above the ligature, and, avoiding the loss of time involved in tying out the toes, placed the foot at once on a plate of glass with a drop of water, two adjacent toes being kept apart by morsels of moistened lint. Within a minute and a half of the application of the string, the pigment in the web was observed to be in the angular condition, with short simple projecting processes, i.e. approaching stellate, and two minutes later two contiguous cells were sketched in that state. About a minute after this it was evident that diffusion was taking place, and it continued to develop itself during the next ten minutes, at the end of which time the rays of the stellate pigment had shot out complicated offsets. Within the following five minutes, however, it was arrested by post mortem concentration, which gradually carried the pigment back to the angular state. This experiment, therefore, furnished confirmation of the view, that, in the ordinary circumstances of the animal, the influence of the central organs of the nervous system is required for the maintenance as well as the development of concentration of the pigment in the limbs.

Supposing this to be established, it would follow that the accommodation of the tint of the skin to that of surrounding objects is certainly not the result of direct action of the rays of light upon the pigment-cells, but a reflex phenomenon ; and it was an interesting question whether the afferent nerves concerned were the optic pair, or branches in the skin sensitive to luminous impressions. With a view to determining this point, I completely removed the eyes of a pale frog on September 13, 1858, at 1 p.m., and then placed it in a dark cupboard. During the first hour after the operation it became even paler than before, no doubt in consequence of the injury which had been inflicted,[1] assuming apparently the lightest possible shade; and this continued with very little change till night, although the animal was still kept in the dark. Next morning it was decidedly darker, and the tint was still deeper at $2^h\ 25^m$ p.m. The glass containing the frog was now placed in a bright light, and surrounded on all sides by white objects; but this change produced no difference in the colour of the skin, which continued till $7^h\ 30^m$ p.m. of a peculiar dingy hue. It was then put back into the dark place, and at $11^h\ 40^m$ p.m. was still exactly the same. On the following day, at 8 a.m., the animal seemed a little paler, and was even lighter at 10 a.m., though still in the dark; so that it was evident that no difference whatever was produced upon its colour by admission or exclusion of light. But that the nervous system generally was in a state quite disposed for acting upon the pigment-cells when subjected to appropriate irritation, was shown by the following circumstances. At the hour last mentioned, the animal, having escaped from the vessel in which it was contained, struggled violently during my attempts to secure it, and in the short time thus occupied changed to almost the palest possible tint. It was then placed at once in the bright light, as before, but, in spite of this, was within ten minutes already decidedly darker, and, half an hour later, was almost coal black, though still subject to the full influence of white light. Just after this observation was made, the frog again escaped, and having again struggled considerably before it was replaced in the glass, it was seen to be within four minutes as pale as when first observed in the morning, but after the lapse of another half hour it was again almost as dark as ever, and continued so till $2^h\ 30^m$ p.m., though all the while exposed to the same light. The observations were continued for two more days, during which period the same complete indifference to the brightness or obscurity of surrounding objects was still evinced.

These facts indicated pretty clearly that the eyes are the only channels through which the rays of light gain access to the nervous system so as to induce changes of colour in the skin. But for the sake of confirmation I thought it worth while to perform the following experiment. Two very dark frogs having been obtained, I put a hood of black cloth on the head of one of them, leaving the body and limbs uncovered, an aperture being made in the cloth below the throat for the purposes of respiration, and then placed them both in the same glass vessel exposed to white light. The struggles of the animal while the covering was being adapted and secured had the effect of making it grow much paler, so that it was of about medium tint when introduced into the

[1] Probably from the irritation of the optic nerves.

glass ; while the other, which was from the first the darker of the two, still retained its original coal-black appearance. Half an hour after this had been done, the contrast between them was much diminished, partly in consequence of the dark one having become slightly paler, but much more from the paler having grown darker. After another half hour they were of precisely the same colour, and when another similar period had elapsed, that which was the darker to begin with was distinctly the paler of the two, being much lighter than at first, though still considerably darker than medium. A hood was now placed upon this animal, and that upon the other was removed, and both were replaced in the same light as before. This procedure occupied about ten minutes, and within seven minutes of its completion the creature which had the head uncovered was already the paler of the two, having grown decidedly lighter in colour ; while that on which the cap had been last placed seemed somewhat darker ; and after another hour, while the latter was still of much the same dark shade, the former, with the head exposed, was very much paler, being about midway between the medium and the palest possible tint. An experiment of the same kind was performed upon another pair of frogs with very similar results, the details of which it is not necessary to mention. I afterwards found that the presence of the hood tends to check diffusion, or even in some cases to give rise to concentration of the pigment, probably by making the animal struggle to throw it off ; so that in one instance a frog which was put in a perfectly dark place, immediately after the cap had been put on, grew much paler in the course of two hours. This circumstance prevents the skin from becoming as dark on the application of the hood as it would do if the head could be covered without exciting the animal. This, however, only renders the facts above mentioned more striking, so that they afford of themselves sufficient proof that the direct action of light upon the integument is incapable of affecting the pigmentary functions ; and thus the conclusion before arrived at receives complete confirmation from these experiments.

There is of course nothing new in the fact that other functions besides vision may be excited in a reflex manner through the optic nerves ; the contraction of the pupil, and the sneezing experienced by many persons on coming suddenly into bright sunshine, being well-known examples of such phenomena. On the other hand, the view that the cutaneous nerves are sensitive to luminous impressions was destitute of any support from analogy.[1]

[1] In the chameleon, a part exposed to the sun becomes dark, while the rest of the body remains unaffected. I have little doubt, however, that this is due to the calorific, not the luminous rays. That heat does produce such an effect was lately demonstrated to me by Professor Goodsir upon a living chameleon, which, when held in broad daylight before a dull-red fire for a short time, grew much darker on the side that was warmed, but retained elsewhere its former pale green colour.

From the part taken by the second pair of nerves in bringing about the changes in the tint of the skin under the influence of light, and also from the darkening of the hind legs observed to occur after dividing within the canal the roots of the branches which supply them,[1] we learn that the cerebro-spinal axis is chiefly, if not exclusively, concerned in regulating the functions of the pigment-cells. Considering that those functions have probably a close affinity with the processes of secretion and nutrition, it is interesting to find that they are thus subject to the control of the spinal system.

The circumstance before alluded to, that a dark frog always becomes pale after death, is mentioned both by von Wittich and Harless, but without any discussion of its cause. This post mortem concentration takes place in a limb in spite of amputation, and therefore cannot be due to the agency of any ganglia contained in the head or trunk. Neither can it be the result of failure in action on the part of such ganglia; for if the circulation be artificially arrested in a part of a living frog without interfering with the nerves leading to it, a similar change in the pigment to that which results from death comes on before the nerves have become, so far as we can judge, at all impaired in their functions. This was proved by the following experiment:—On June 7, 1858, having tied the right femoral artery of a moderately dark frog in the middle of its course, I divided it below the ligature, and also cut through, in the same situation, all the soft parts of the thigh except the sciatic nerve with a little adherent muscle. The operation was completed at noon, when the animal was put into a dark place; and at 1^{h} 40^{m} p.m. the body generally was darker, but the right leg from the wound downwards was decidedly paler than before; the animal, however, still moved it freely. At 6^{h} 20^{m} p.m. the general surface was as dark as ever, but the right foot presented the extreme degree of pallor; yet the creature still moved the leg both spontaneously and when the toes were pinched, showing that the motor and sensor nerves retained their functions. Sensation, however, was not so acute as in the left foot; in the latter a touch sufficed to induce movements in the body generally, whereas in the former a pinch was necessary to produce the same effect. At 10^{h} 15^{m} p.m. the same contrast in colour continued, but no movement could be induced in any manner in the pale limb, although obscure indications of a certain amount of sensibility remaining in it were still elicited by forcible pinching.

In this case, concentration of the pigment came on in the limb in consequence of arrest of the circulation through it, several hours before its nerves concerned in sensation and motion had lost their powers, and therefore at a time when we cannot doubt that the ganglia in the trunk had full opportunity

[1] See p. 57.

for acting on the pigment-cells, which, as we know from experiments before mentioned, are capable of being influenced through the sciatic trunk. Hence it appears that post mortem concentration is the result of the cessation of the flow of the blood through the vessels, and that it is a purely local phenomenon developed in some manner quite independent of the central organs of the nervous system.

The period at which it occurs varies a good deal in different cases. This seems to depend partly upon whether the blood is retained in the vessels or not. Thus in one instance in which a piece of web was cut out, so as to ensure complete escape of the vital fluid, the process was already considerably advanced within nine minutes ; whereas in the case above related, in which the blood was retained in the limb by a ligature, concentration did not commence till full a quarter of an hour after amputation. The season of the year also seems to have a great effect. In a cold room, in the depth of winter, I have known some hours elapse before the pigment began to change in an amputated limb : this is probably owing to greater languor in all the vital processes during the period in which the creature naturally hibernates.

The dead frog, if previously healthy, assumes after a while a nearly uniform pale colour, concentration being carried to the extreme degree in all parts. It does not, however, remain in this condition ; for when a variable time has passed, the skin becomes again somewhat darker, and on microscopic examination the pigment is found pretty uniformly angular or stellate. Nor are these the only changes to which the pigment is liable after death, as I first became aware in April 1858, when examining an amputated limb with reference to the post mortem contractions of the arteries, the blood being retained in the vessels. In that case, after complete concentration followed by slight diffusion had taken place, irregular changes began to appear ; some tracts of the web under observation becoming affected with more or less full diffusion of the pigment, while in others it became more concentrated. Then after the lapse of some hours its state was found reversed, being concentrated in parts where it had been diffused, and vice versa. These curious variations continued till so late as the tenth day after amputation, becoming more frequent after the first few days ; so that sometimes a considerable alteration was observable within half an hour.

These facts appeared to me of great importance, as proving the continuance of vital actions for a much longer time than had been previously supposed possible in a severed portion of the body. They seem also valuable with reference to the influence of the nervous system over the pigmentary functions ; for the circumstance that considerable patches of the web usually had the pigment in the same condition throughout at one time implies that a large number of pigment-cells were acting in concert, and therefore probably under the control of the nervous system, although, as the leg had been amputated, they were of course freed from the influence of the central ganglia. Hence we are led to suspect the existence in the limb of an apparatus, probably ganglionic in structure, co-ordinating the actions of the pigment-cells, just as we know that the muscular contractions in the mammalian intestine are harmonized by a local mechanism of that nature, while we have reason to think that the same thing holds regarding the arteries in the frog's web.[1] Such a view is in accordance with the results of recent anatomical discovery, which has revealed nerve-cells in many parts where their occurrence had not previously been conjectured. But in the absence of more positive evidence, we must be careful not to trust too much to analogy on such a point ; for it by no means necessarily follows, that, even if muscular fibre-cells are incapable of acting in mutual harmony without the aid of the nervous system, the same must be the case with pigment-cells, which, it is to be remarked, resemble ganglion corpuscles in being connected together by anatomosing offsets. The nerve-cells, if such be really the means by which the harmonious actions of the pigment-cells in an amputated limb are induced, must be disseminated among the tissues of the web itself ; for both post mortem concentration and secondary diffusion occur in a piece of web cut out and placed in a drop of water on a plate of glass. This was ascertained on September 4, 1858, in the case already alluded to as an instance of rapid occurrence of concentration. About half an hour after removal from the body, the pigment, previously reticular, was in the dotted state, and three hours later it was found to be again stellate.

The case of the pigment-cells is analogous to that of the arteries in this respect, that, so long as circulation is going on, they are generally in entire subjection to the central ganglia, and act only when stimulated by their influence. But as, in the arteries, it appears to be by the independent action of the local nerves that a contraction caused by direct irritation spreads to a considerable distance from the part operated on, so it is probably by local means that the pallor induced by pinching the web affects a circle of surrounding tissue. If this be true, the case of direct irritation will be an exception to the general rule, that, while circulation continues healthy, concentration always implies the operation of the central organs of the nervous system.

Comparing the changes in the pigment in an amputated limb with those which take place under similar circumstances in the arteries,[2] it appears that

[1] See the preceding paper 'On the Parts of the Nervous System which regulate the Contractions of the Arteries', p. 41.

[2] See the preceding paper before referred to, p. 39.

the first effect of removal from the influence of the nervous centres in the head and trunk is arterial relaxation and pigmentary diffusion, followed in a variable time by contraction of the vessels and concentration of the dark molecules, giving place again to relaxation and diffusion, after which succeed irregular alternations of contraction and dilatation in the one case, and of concentration and diffusion in the other. Here, though the vascular and pigmentary changes do not at all correspond with one another in point of time, yet there is an evident parallel between them ; and, admitting that in each case the variations are the result of alternate action and inaction of the appropriate local nervous system, it is evident that concentration of the pigment corresponds to contraction of the muscular fibres of the arteries ; these being both the results of nervous action, while diffusion of the pigment, like arterial relaxation, takes place when the nerves cease to operate. It will be remembered that a similar conclusion was derived from the study of the influence exerted upon the pigment-cells by the central ganglia. Hence it appears that the tendency to diffusion of the pigment-molecules is in constant operation in the cells, but kept in check by an antagonistic concentrating agency varying in obedience to nervous influence.

It is an interesting circumstance, that two functions seemingly so totally distinct as muscular contraction and pigmentary concentration, should both be thrown into a state of activity in consequence of arrest of the circulation. It is to be remembered, however, that there is no evidence that either the involuntary muscular fibre or the pigmentary tissue is directly influenced by the cessation of the flow of blood, the effect being apparently produced through the medium of the local nervous system. This we know with certainty in the case of the post mortem movements of the intestines ; and we have seen reason to think it likely that the same is true regarding the contractions of the arteries after death, and the concentration of the pigment under similar circumstances. It is a curious question how the arrest of the circulation causes these actions of the local nerves. The idea suggested by the facts is that the tissues begin to suffer from the want of fresh supplies of the vital fluid, and resent the injury, as it were, by a struggle.

Rich in results of general physiological interest as the study of the pigmentary system of the frog has proved, it has yielded fruit of not less value in a pathological point of view. Indeed, what induced me to investigate the functions of concentration and diffusion, was the unexpected light thrown upon the nature of inflammation by the effects produced by irritants upon those processes. For information on this subject I beg to refer the reader to my paper 'On the Early Stages of Inflammation'.[1]

[1] See p. 209 of this volume.

The pigmentary system also promises to render good service in toxological inquiry. Hitherto, in experiments performed upon animals with that object, attention has been directed chiefly, if not exclusively, to the effects produced upon the actions of the nervous centres, the nerves and the muscles. In the pigment-cells we have a form of tissue with entirely new functions, which, though apparently allied to the most recondite processes of the animal economy, yet produce very obvious effects, and thus afford great facilities for ascertaining whether or not they have been destroyed by any poison that may have been administered.

An experiment of this kind which I once performed, though with a different object, may be mentioned by way of example. Being desirous of confirming the conclusion to which I had been led by experiments above related, viz. that diffusion always tends to take place when the influence of the nerves is withdrawn from the pigment-cells, it occurred to me that the urari poison might be brought into requisition for that purpose: for it has been shown by Professor Kölliker of Würzburg, that this substance paralyses in the first instance the extremities of the motor nerves without affecting the contractility of the muscular tissue; and supposing the nerves concerned in regulating the pigmentary changes to be similarly deprived of their powers, while the pigment-cells themselves remained intact, diffusion should take place after exhibition of the drug, provided my view were correct. Accordingly, at $2^h\ 10^m$ p.m. on December 21, 1857, I introduced beneath the skin of the back of a pale frog a portion of urari extract, for which I was indebted to the kindness of Dr. Christison. At $2^h\ 25^m$ reflex action was entirely abolished, the creature being to all appearance dead, so far as could be judged by the naked eye, although the microscope showed that circulation continued in the webs. The pigment meanwhile had become stellate, but did not continue in that condition, being, half an hour later, found fully concentrated. Soon after this, however, diffusion again commenced, and continued to advance steadily till circulation ceased early the following morning, at which time the integument was almost black. In the course of a few hours, however, it was brought again back to the palest possible tint by post mortem concentration.

The diffusion which ultimately took place in this case was no doubt due to loss of function on the part of the central ganglia or the nerves connecting them with the pigment-cells. But from the occurrence of concentration half an hour after the faculty for reflex action had ceased, we learn that these nerves, like the intrinsic motor nerves of the heart and intestines, remain unaffected by the urari poison for a considerably longer time than those which excite the contractions of the voluntary muscles. We further learn from the fact that post mortem concentration came on as usual, that the pigment-cells retain their powers, and also their capability of acting in mutual harmony after the rhythmical contractions of the heart have been abolished by this poison.

Such experiments are so readily performed, and the effects produced upon the pigment-cells or the nerves which govern them are so obviously indicated by the changes of colour in the integument, that I venture to recommend this method of investigation to those who are occupied in studying the action of poisons.

PLATE III

illustrates the anatomy and physiology of the cutaneous pigmentary system of the frog.

Figs. 1 and 2 are sketched from webs of different feet of the same animal. The creature was dark when it was killed, but one of the legs afterwards underwent the usual post mortem change to a pale colour, and such was its state when Fig. 2 was drawn. The other limb was deprived of the power of thus altering by immersion for half a minute in chloroform ; and Fig. 1 shows the appearance of the colouring matter in the permanently dark condition of the integument.

Fig. 3 represents two chromatophorous cells with the pigment-granules fully diffused, the animal having been at the time coal-black. The bodies of the cells are seen to be pale, containing chiefly colourless fluid, while some of the finest branches of the offsets are quite black, in consequence of the dark molecules being closely packed together in them. In the same figure a capillary fully distended with blood-corpuscles is also given.

Fig. 4 represents the colouring matter in the same two cells during the progress of the process of concentration. The dark molecules are already for the most part collected about the middle of the body of each cell ; but in the very centre of each cell is a pale point, where the granules seem not yet to have insinuated themselves between the cell-wall and the nucleus. The same capillary is here seen much reduced in calibre.

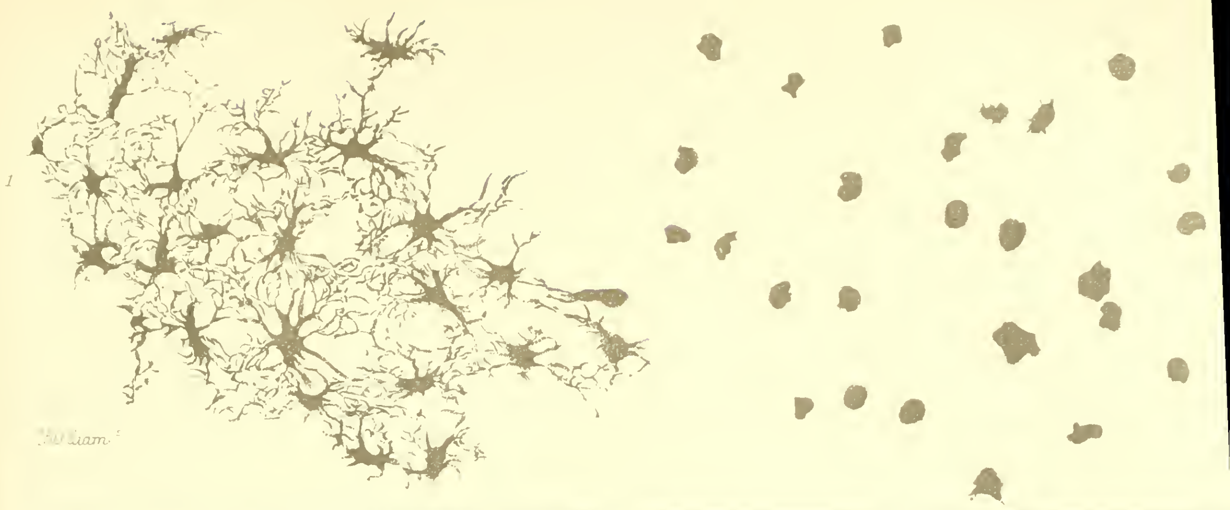
Fig. 5 shows the pigment in the lower of the two cells, concentration being still further advanced.

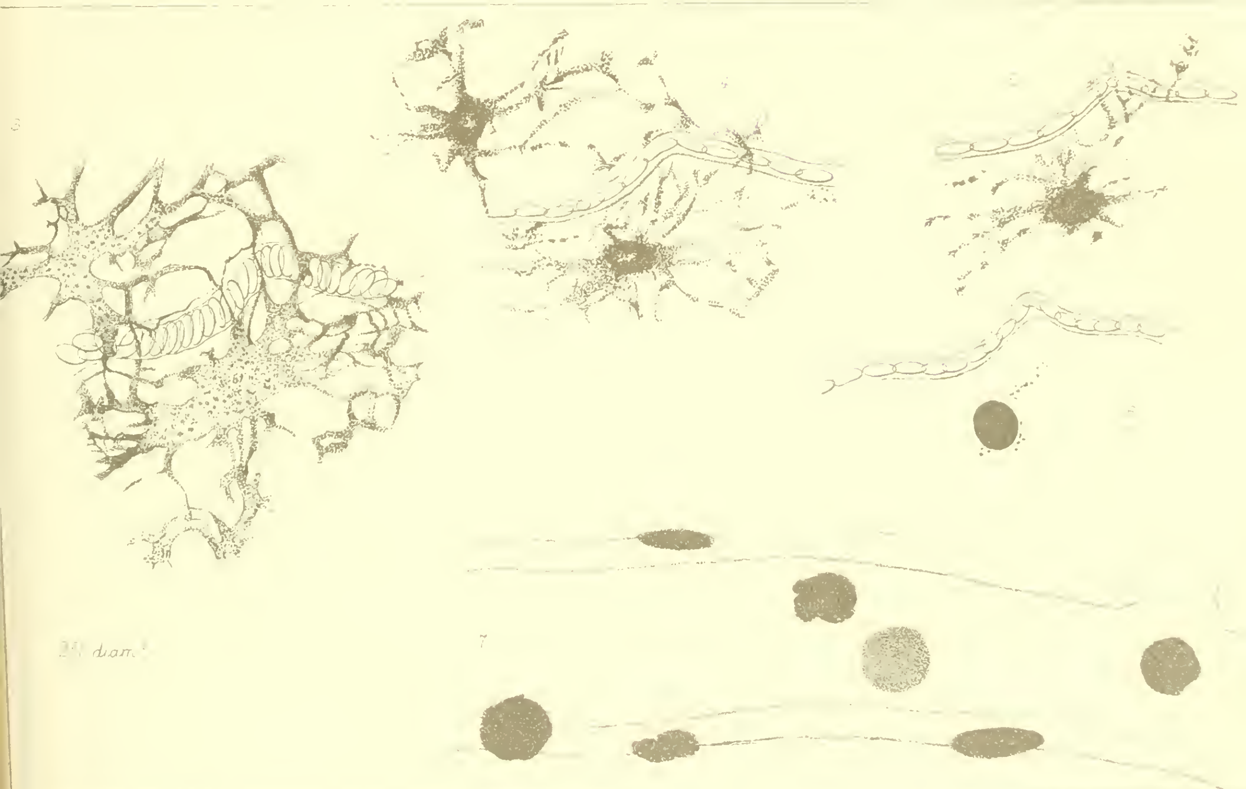
In Fig. 6 the process is seen to be almost absolutely completed, the molecules being almost all of them aggregated into a black circular mass, occupying the middle of the body of the cell, the more circumferential parts of which contain only colourless fluid, and are therefore invisible.

Fig. 7 is an outline of the wall of a large blood-vessel, with chromatophorous cells in its external coat. The pigment is almost completely concentrated, but the form of the section of the black masses, where they are seen edgewise, shows that they are not spherical, but disc-shaped.

Figs. 8, 9, and 10 are drawn, with a much higher power, from young frogs, with small pigment-cells : they exhibit especially the form and relations of the nucleus.

In Fig. 10 the pigment is shown in an unhealthy state, the molecules being irregularly aggregated.





ON SPONTANEOUS GANGRENE FROM ARTERITIS AND THE CAUSES OF COAGULATION OF THE BLOOD IN DISEASES OF THE BLOOD-VESSELS

Read before the Medico-Chirurgical Society of Edinburgh, March 17, 1858.

[*Edinburgh Medical Journal*, April 1858.]

Mr. President and Gentlemen.—The case which I have the honour to bring before you this evening is one of spontaneous gangrene in a child. The patient was a girl, six years old, who, having had scarlet fever nine months previously, and afterwards suffered severely from dropsy, was seized about the middle of July last with deadly whiteness and coldness of both lower limbs up to a little above the knees. Her mother describes them as having resembled wax in appearance. She and her neighbours rubbed the legs perseveringly, and, after an hour or two, the left limb recovered its warmth and usual aspect, but the other continued in the same state for about two days, when the mother observed some pale blue discoloration between the ankle and the calf. This increased, spreading downwards to the foot ; and, at the same time, undergoing various changes of tint to pink, red, and green, till, at the end of four weeks, the limb presented the appearance depicted in this sketch. [Not here reproduced.] At this time she was brought to the Royal Infirmary, and was admitted into one of the senior surgeon's wards, where, in the temporary absence of Mr. Spence, she came under my care. Her general health appeared remarkably good, considering all that she had gone through : her tongue was clean and moist, and her appetite good, and though her pulse was very quick, viz. 148, this was not to be regarded as a serious symptom in one so young, with such a source of irritation present. Accordingly, three days later, a line of demarcation having distinctly declared itself, I performed amputation immediately above the knee. Very little blood was lost in the operation, which did not accelerate the pulse or impair the appetite even for a day. Three days later, the constitution was evidently experiencing relief from the removal of the disease : the pulse was reduced to 112, and her general aspect improved. The stump healed kindly, and the result was in all respects satisfactory.

The amputated limb having been laid open on its posterior aspect, the gangrene was found to have extended somewhat higher in the deep parts than in the skin ; the mortified tissues, including the posterior tibial nerve, were congested in a manner closely simulating inflammation, but of a duller tint, and exactly as far as this congestion extended, the posterior tibial venae comites were turgid, and evidently contained coagulated blood. In the upper part of the limb the veins were flaccid and empty, and all the tissues appeared healthy, except that the popliteal artery, for an inch and a half from its lower end, was the seat of intense congestion, which also implicated slightly the cellular tissue about the vein and nerve. [These appearances were represented in a coloured drawing.] On laying open the vessels, the vein was found pervious and healthy, except that its coats seemed a little thicker than natural, but the artery was filled at the congested part with a coagulum, an inch and a quarter in length, partly pinkish and partly dark in colour. There was no appearance of any inflammatory exudation having taken place into the interior of the vessel, but the clot lay everywhere in contact with the internal coat, to which it was firmly adherent, so much so, as to tear away a portion of it when removed. Beneath the lining membrane were to be seen transverse red streaks, which appeared due to congestion of the circular coat of the vessel. [A sketch of the vessel and its contained clot was now exhibited.] The coagulum extended down the anterior tibial artery as far as to the commencement of the gangrene, but the companion veins were empty and perfectly natural in appearance, as also was the posterior tibial artery.

These pathological appearances clearly indicate that the primary disease was inflammation of the arteries, accompanied by coagulation of the blood within them, obstructing the supply of the nutrient fluid, and so inducing death of the lower part of the limb. This conclusion is in harmony with the previous history, which was from the first that of arterial obstruction.

This case is of practical interest, as illustrating the principle that spontaneous gangrene may be entirely local in its cause, and that in such cases the greatest benefit may be anticipated from removal of the mortified part, provided the constitution be in a state fitted, as regards age and in other respects, for bearing the operation.

But my chief reason for bringing the case now before the Society is because it appears a distinct example of inflammation of the coats of a vessel determining coagulation of the blood within it, without the exudation of lymph into its interior. Not that there is any novelty connected with such an occurrence, but because this effect of arteritis and phlebitis, long recognized by all sound pathologists, appears to be of peculiar interest at the present juncture, in connexion with the recent publication of the last Astley Cooper Prize Essay, in which Dr. Richardson of London propounds the theory, that the coagulation of the blood is due to the escape of a minute quantity of ammonia, which he believes holds the fibrine in solution. I propose, therefore, on the present occasion, to consider how far this new theory accounts for this phenomenon of coagulation in inflammation and other diseases of the blood-vessels.

So short a time having elapsed since the publication of the volume alluded to, it may be well to mention, as briefly as possible, the main facts by which the arguments of the author are supported:—And first I may relate the startling observation made by Dr. Richardson, that if a current of air is passed through two successive portions of freshly drawn blood, contained in two Wolfe's bottles, while that in the first bottle, as might have been expected, has its coagulation accelerated, that in the second bottle is prevented from coagulating for several minutes after the time at which it would have solidified, had it been left in the vessel without interference. In other words, the air has had its properties so modified in passing through the first mass of blood, that it afterwards retards instead of promoting coagulation; whence Dr. Richardson infers, that it has obtained in its passage some volatile solvent of the fibrine. Secondly, Dr. Richardson has discovered that a very minute quantity of ammonia added to freshly drawn blood keeps it fluid for an indefinite period in a stoppered bottle, but that if exposed to air it coagulates as usual, though at a later period, in proportion to the amount of ammonia employed. He also finds that, by careful management, a fresh clot may be redissolved by means of ammonia, and that after the escape of the ammonia it will again coagulate, and afterwards contract in the usual manner, though more feebly. Next, he finds that ammonia is always to be obtained from the halitus of freshly drawn blood, and although the alkalinity of the blood through soda renders the ammonia excessively prone to escape, so that a good deal is necessarily lost from unavoidable exposure to air, yet he has succeeded in collecting about a third by weight of the smallest amount which he has found sufficient to keep the blood permanently fluid outside the body. Lastly, he has observed that all those circumstances which are known to promote the coagulation of blood outside the body, such as an elevated temperature, free admixture with air, a vacuum, &c., also hasten the process in blood mixed with ammonia, or, in other words, favour the escape of the volatile alkali; while, on the other hand, those things which check coagulation, such as cold and occlusion from air, prevent or retard the evolution of the gas. To the latter class he has added the remarkable fact that blood remains fluid for many hours under a high mercurial pressure, but coagulates when relieved from it. I confess that, although I was by no means prepossessed in favour of this theory, these facts appear to me to prove irresistibly that the cause of the fluidity of blood, after it has been drawn from the body, is a minute portion of free ammonia holding the fibrine chemically in solution, and that the coagulation of such blood is the result of the escape of the alkali. The only point on which the evidence appeared deficient was the effect of occlusion from air in tubes of dead matter, and this defect I endeavoured to supply by the experiment which I mentioned at the last meeting of the Society, by which I succeeded in keeping the blood of a sheep fluid for three hours within a vulcanized india-rubber tube, the blood coagulating in about two minutes when let out just as if freshly drawn from the veins of the animal.[1] Hence it appears to me that the medical profession is deeply indebted to Dr. Richardson for his laborious and able investigations, which have, as I think, removed much mystery from this long vexed question.

But Dr. Richardson aims at much more than the explanation of coagulation outside the body. He believes that the fluidity of the blood within the healthy living vessels is due simply and solely to the presence of free ammonia, which he supposes to be generated either in the systemic or pulmonary capillaries, and he denies that the walls of the arteries or veins have any effect on the blood by virtue of their vitality, or exercise any other influence upon it than that of checking the evolution of ammonia, just as would be the case were they tubes of dead matter of the same degree of permeability. And all cases of coagulation within the living body are supposed, by him, to be explicable on simple chemical principles. Here, however, I find myself quite unable to follow him. Thus, he believes that the coagulation in an aneurysm is the result of the blood which is at rest in the tumour giving up its ammonia to the current which is flowing past the mouth of the sac. This theory was suggested to him by the following circumstance :—In one of the experiments of transmitting air through successive portions of blood, the longer tube in the last Wolfe's bottle was

[1] This experiment was performed in the following manner :—One of the jugular veins of a sheep having been exposed, it was emptied of blood by passing the finger along it while pressure was applied by an assistant at its anterior part. The vessel was then opened at two places about three inches distant from each other, and into each opening was tied one end of a piece of vulcanized india-rubber tube, a quarter of an inch in diameter, and about eighteen inches long, filled with water, to prevent the introduction of air into the circulation. The pressure was then removed from the upper part of the vein, so as to allow the blood to flow through the tube. It was now easy to ascertain, by observing the collapse of the lower part of the vein, when a part of the tube was momentarily obstructed by pressure, that the circulation was going on freely through the new channel. This having been determined, ligatures of waxed string were tied as tightly as possible round the tube, at intervals of about two inches, beginning at the end next the head and proceeding backwards, so as to avoid all tension upon the enclosed blood, which was, of course, displaced freely in the direction towards the thorax. By this means a number of portions of blood were obtained enclosed in receptacles nearly, though not absolutely, impermeable to gases. The various compartments were opened at different intervals, and up to three hours some of them contained fluid blood which coagulated on exposure, whereas there was in others a considerable portion of coagulum. After four hours, coagulation was almost complete, but a slender thread of fibrine was still obtained from the fluid part in one of the divisions a few minutes after it had been let out.

accidentally too short, so that it did not reach farther down than to about an inch from the bottom of the vessel. The result was, that while the upper part of the blood in this last bottle was retained fluid for a considerable time, that below the level to which the tube reached speedily coagulated. Dr. Richardson infers that the lower portion of blood gave up its ammonia to the air which was bubbling through the upper part sufficiently charged with the alkali to retain that part in a state of fluidity. But, surely, this implies a mistake in chemistry. The lower portion of blood coagulated, I imagine, for the same reasons that it would have done had it been put in a stoppered bottle [1] after passing through the air, though probably not quite so rapidly, while the other part was prevented from coagulating by the ammoniacal vapour bubbling through it.

But if the ammonia theory fails to explain the coagulation that occurs in aneurysm, still more inadequate does it appear to account for the phenomenon in arteritis or phlebitis. How can the fact that the wall of the vessel is inflamed determine, on simply chemical principles, the evolution of ammonia from the blood within it ? Being convinced that in these and other cases of coagulation of the blood in local diseases of the vessels something remained quite unexplained, I have, during the last fortnight, made several experiments, with a view to throwing further light upon the subject, and will now communicate to the Society the results at which I have arrived.

In reflecting upon the matter, some circumstances in physiology and pathology appeared to me to indicate that, on the hypothesis that the blood does contain free ammonia in the living body, the healthy vessels must have a special power of preventing its escape. Thus, the blood in the capillaries of the lungs is separated from the air in the air-cells only by an excessively thin partition of permeable living tissue ; yet Dr. Richardson's experiments have shown that there are times in the day, as, for instance, early morning, in which not a trace of ammonia is given off in the breath. Again, in surgical emphysema, the tissues of the body may be enormously distended with air, without any special tendency to coagulation of the blood in the vessels, such as might be anticipated unless their parietes have a special power of preventing the escape of ammonia. It is true that in this case, the blood being in constant circulation, a perpetual supply of lost ammonia might be maintained from the capillaries ; but it occurred to me that some information might perhaps be gained upon the point in question, by producing emphysema artificially in a limb in which the circulation had been arrested. For this purpose I applied a tourniquet firmly to one of the fore legs of a sheep, just above the elbow, and then injected

[1] This occurrence I have frequently observed.—J. L.

air, by means of a condensing syringe, into the tissues of the lower part of the limb. The struggling of the animal, however, caused repeated displacement of the tourniquet, which I did not succeed in retaining in position for longer than an hour at a time. But, though the experiment was so far a failure, it yielded fruit in an unexpected manner. Having amputated the limb and preserved it, though with little expectation of learning anything from it, I was surprised to find, on examining it six hours later, that, although the cellular tissue about the vessels was still fully distended with air, the blood within them was perfectly fluid, and coagulated in about two and a half minutes, when shed into a saucer. Still greater was my surprise on finding next day, sixteen hours after the amputation, that the blood was still fluid in the vessels ; and though it took longer to coagulate when let out from them, viz. five minutes, did so as fully as before. The muscular irritability, as tested by a powerful galvanic battery, had been found, on the previous evening, to be entirely lost. I next obtained four other feet, with the veins turgid with blood, by applying bandages firmly to the limbs below the joints where the butcher removes them, and amputating above the constricting band, after the sheep had been killed in the usual manner, by the knife. I examined veins in these limbs, day after day, till all the vessels were exhausted, and found at the end of the sixth day after their severance from all connexion with the vascular and nervous centres, that the blood from a deep vein was still perfectly fluid, and coagulated when shed, though the time occupied by the process was now half an hour,—the length of the period having gradually increased, from day to day, since the time of the amputation. The feet, in the meantime, continued perfectly sweet, the coldness of the weather at the time being very favourable for the experiments. Some blood from a subcutaneous vein of the same foot, where decomposition might be expected to occur somewhat earlier, contained, at the same period (the end of the sixth day), some minute portions of coagulum. The fluid part of this blood remained liquid for an hour, but then coagulated well. Hence it was evident that so long as the tissues retained their freshness, the blood within the vessels was kept in a state of fluidity by some agency utterly inexplicable by the ammonia theory. I also found that the same thing occurs in the cat. In one such animal, killed under chloroform, by a knife passed into the great vessels of the neck, the blood in the veins of the extremities remained perfectly fluid after forty-eight hours, and coagulated when shed. In another cat, killed by asphyxia, the same was the case as regards the posterior extremities ; but the veins of the fore legs contained particles of coagulum, like the subcutaneous vessel of the sheep's foot. This difference I am inclined to attribute to the fact that the animal made violent and protracted exertion with the fore legs during the death struggle, thus exhausting their vital energies more than those of the other limbs. After four days, however, the blood in the hind legs, though still fluid, with the exception of very minute particles of coagulum, had lost its power of coagulation. This increasing slowness and final absence of coagulation in blood long kept within the vessels is curious, and must, I imagine, depend upon some gradual change in the properties of the fibrine.

We have seen that in two classes of the higher animals, differing from one another as widely as the carnivora and herbivora, and after modes of death so various as haemorrhage, asphyxia, and an operation performed under chloroform, the blood remains fluid in the vessels, though perfectly at rest, for days after death. It may appear almost incredible that a fact of such fundamental importance, and at the same time so easy of demonstration, should have escaped the observation of all the eminent men who have made the coagulation of the blood a subject of special study; yet such appears to be the case. Dr. Richardson speaks of occasional instances of fluidity of the blood after death, and coagulation on exposure, but considers it quite essential for such an occurrence that the vascular system should not have been opened by wound, though it is difficult to see how such a circumstance could affect the question, according to his theory, except on the supposition that the blood-vessels were impermeable to gases in solution. Again, Dr. Davey, in his *Researches*, writes as follows :—'The blood, after death, I have often found liquid, and that many hours after death, when cold, but still retaining its power of coagulating'; but he had no idea of fluidity and coagulability lasting for days after death, or even for hours, except in rare instances. The nearest approach which I have been able to find to such an observation is contained in that inexhaustible treasury of original observation and profound reflection, the works of John Hunter, where the following passages occur :—'As a proof that blood will not coagulate in living vessels, in a perfect and natural state, and ready to act when powers were restored to it, I found that the blood of a fish, which had the actions of life stopped for three days, and was supposed to be dead, did not coagulate in the vessels, but, upon being exposed or extravasated, soon coagulated. . . . The blood of a lamprey-eel, which had been dead to appearance some days, was found fluid in the vessels, because the animal was not really dead: there had, however, been no motion in the blood, as the heart had ceased acting; but upon its being exposed, or extravasated into water, it soon coagulated' (Palmer's edition, vol. iii, p. 32). Hunter, however, does not seem to have drawn any inference with regard to the higher animals from these cases. He speaks of 'the very speedy coagulation of the blood which usually takes place in all the vessels after death' (vol. iii, p. 27); and though he believed that 'where there is a full power of life, the vessels are capable of keeping the blood in a fluid state', he also supposed that some motion, though 'very little, is required to keep up its fluidity' (ib., p. 32). Indeed, the expression, 'full power of life,' just quoted, is quite inconsistent with the state of a sheep's foot, six days after muscular irritability has been lost. I had myself frequently made experiments on inflammation upon the amputated limbs of frogs, and observed that the blood remains fluid for more than twenty-four hours after death; but muscular irritability, ciliary action, &c., also last in those creatures to a very much later period than in the higher animals, so that I never ventured to infer that fluidity of the blood was likely to continue long after death in mammalia.

Further observations on the feet of the sheep and limbs of the cat proved even still more strikingly the influence of the vessels upon their contained blood. If the skin be reflected from over a subcutaneous vein full of blood, and lightly replaced, so as to protect the subjacent parts from evaporation, without excluding the air, the vessel will be found, in two or three hours, changed from a dark venous colour to a scarlet arterial tint; yet no coagulation will occur in the blood, although the oxygen of the atmosphere has evidently penetrated freely through the coats of the vessel, showing that abundant opportunity has occurred for evolution of ammonia, provided any tendency to such an occurrence existed. Again, if such a vein be cut across with fine sharp scissors, without disturbing its connexions, or inflicting much injury on its coats, the blood will be found, after about six hours, perfectly fluid in the vein, up to within perhaps 1-20th of an inch of the wound, where a small clot is perhaps seen, utterly insufficient to obstruct the progress of ammoniacal vapour. Hence it appears to me to follow, as a matter of demonstration, that, if free ammonia really exists in the blood within the vessels, the circumstance of its being in those vessels deprives it entirely of its volatility; and that, whether the ammonia be free in the blood or not, its chemical tendencies, such as it exhibits outside the body, are in some manner entirely modified by the vicinity of the vascular tissue. With regard to the nature of the modifying influence, no other explanation appeared to offer itself than that it depended upon residual vitality in the tissues.

In order to prosecute the investigation of the cause of coagulation in arteritis or phlebitis, I endeavoured to produce artificially, as nearly as practicable, in a living animal, the condition in which the vessels are when inflamed. Having proved, as I think I may venture to say—by investigations, an account of which will shortly appear in the *Philosophical Transactions*[1]—that inflammation consists in an impairment of the vital energies of the tissues of the part

[1] See p. 209 of this volume.

affected, I resolved to destroy the vitality of a vein, and then permit the blood to flow through it for some time, and ascertain whether coagulation would occur in spite of the current, as it must do in phlebitis.[1] The agent which seemed best adapted for inflicting the lesion was strongest liquor ammoniae, both on account of its rapid action, and also from the circumstance that, as Dr. Richardson has shown, its chemical effect upon the blood, whether applied concentrated or diluted, is to prevent coagulation. On the 8th inst., having exposed one of the jugular veins of a sheep, and isolated it from surrounding connexions for six inches of its length, carefully avoiding even momentary obstruction of the flow through it, I placed a plate of glass beneath the vein, to protect the neighbouring tissues from the action of the alkali, and at 3^h 13^m p.m. emptied the portion of vein of its blood, by stroking the finger along it, while an assistant exerted gentle pressure on the anterior part, and then at once applied the liquor ammoniae thoroughly, with a camel's hair brush, to all sides of the vessel throughout the length exposed. The application of ammonia occupied three-quarters of a minute, and three-quarters of a minute later the blood was again allowed to flow through the vessel, having been arrested altogether a minute and three-quarters. A short time having been allowed for the evaporation of the ammonia, the edges of the wound were brought together with stitches. At 4^h 58^m, or an hour and three-quarters later, the wound having been opened, the flow was again obstructed as before, and the vein was rapidly slit up. A small amount of dark coagulum escaped with the fluid blood. The interior of the vessel was now immediately examined. A valve with three flaps, about the middle of the opened portion, was rendered conspicuous from the fact that a black coagulum existed between each of the flaps and the wall of the vessel ; and on careful observation of the lining membrane of the vein in other parts, it was seen to be dotted over in patches with fine granular deposits of pink fibrine, which could only be detached by firmly scraping with the edge of the knife, reminding me precisely of the close adhesion of the clot which occurred in the popliteal artery in the case which I related at the commencement of this paper, and which is known to be characteristic both of arteritis and phlebitis. Here it is clear that the coats of the vessel having been deprived of their vitality, the blood flowing through it assumed

[1] Sir Astley Cooper performed experiments to show the effect of mechanical injury of the coats of a vein upon the coagulation of the blood at rest within a portion of the vessel contained between two ligatures ; and he came to the general conclusion, that loss of vitality in the vessel greatly accelerated the process of coagulation. Dr. Richardson alludes to these experiments, but says they have been invalidated by subsequent investigations by Scudamore. I have not as yet seen Sir Astley's own account of his researches on the subject, but, from a notice of them by Palmer, in his edition of Hunter's works, I suspect that they do not deserve to be set aside so lightly.

the same chemical tendencies as we have seen it to possess when removed from the body; and those parts of the fluid which remained at rest under these conditions, namely, the motionless layer of liquor sanguinis next to the lining membrane, and the portions of blood in the sinuses of the valve, underwent coagulation, yielding up their ammonia through the permeable coats of the vein. And I think we need not hesitate to admit that similar occurrences take place in the early stages of arteritis and phlebitis, the coats of the vessels being in those cases not dead, but impaired in vital energy by inflammation.

A similar explanation appears to account for the early formation of coagula in the vicinity of a ligature placed upon an artery. It has been seen how utterly the usual explanation, that of the quiescence of the blood, fails to account for the phenomenon; but the fact that lymph is afterwards exuded from this part of the vessel shows that the case is really one of limited traumatic arteritis.

But if the coagulation within inflamed vessels thus receives a solution from the results of the last-mentioned experiment, still more unequivocally, at least to most of my hearers, is the coagulation in gangrene explained, such as occurred, for instance, in the case which has been described.

Again, it is well known that contused wounds bleed very little, the ends of the divided arteries becoming speedily plugged with a long coagulum. The only explanation which Sir Charles Bell could offer of this remarkable provision of nature was, that the living vessels had a special faculty of preventing the blood from exercising friction upon their lining membrane, but that the contused artery, having lost its vitality, the blood became arrested by friction and coagulated. We now see that there was much more truth in this theory than has been generally supposed, though the loss of vitality in the vessel does not operate in the manner which Sir Charles imagined.[1]

It has been found difficult to understand why the fact of the arteries being converted into calcareous tubes should impress upon the blood within them a tendency to coagulate in atheromatous degeneration of the vessels. The impairment, or entire loss of vitality connected with such a condition, will now be found a sufficient explanation.

The coagulation in aneurysm is now equally comprehensible, the walls of the sac consisting either of degenerated or torn coats of the vessel, of inflamed surrounding tissues, or of layers of fibrine, each of these constituents being in a state of very low vitality.

The rapid coagulation of lymph, which appears to be neither more nor less

[1] I find I have not done justice to Sir C. Bell's views upon this subject. In his later works he expresses the opinion that the lining membrane of the living vessels possesses the power of 'preserving the blood fluid', and that the cause of coagulation in a contused artery is the loss of this power in consequence of the injury.—Vide Sir C. Bell's *Institutes of Surgery*, vol. i, p. 52, and vol. ii, p. 277.

than the fibrine of effused liquor sanguinis, contrasts, in a very striking manner, with the lengthened period during which blood extravasated into the cellular tissue may retain its fluidity. But the fact that the liquor sanguinis is exuded among tissues that are in a state of inflammation, and so impaired in their vital energies, renders the circumstance in question easily intelligible.

With regard to the nature of the influence exercised by the living vessels upon the blood within them, it might be conceived to be either of a positive or negative character. It might be imagined, either that the blood has a natural tendency within the vessels to comport itself as it does when outside the body, and that this tendency is counteracted by an active operation of the living tissues, or, that the vital fluid tends to no such change except when prejudicially acted on by surrounding objects, which in that case might be supposed to exert upon it attractive forces such as tend to group the molecules of dead matter together in aggregation, while the living tissues were destitute of such action, and simply neutral in their conduct towards the blood. Of these, the former has always appeared to me the more likely, *a priori*, but I had not expected to have met with any facts to give distinct evidence either in one direction or the other upon a subject so recondite. A simple observation, however, made on the sheep's foot, appears to throw clear light on the matter. I have frequently observed that when a vein has been opened and has remained patent, the blood has continued fluid in the aperture for a very much longer time than is necessary to produce coagulation of a portion of that blood placed in a saucer. When the wound in the vein has been a narrow one, I have seen the blood remain fluid between its lips for three hours together, though perfectly at rest. I have even observed where a portion of fluid blood has been pressed from a vein into a groove in the tissues, formed by muscle below, periosteum on one side and tendon on the other, this portion of blood has remained fluid for an hour, while another drop removed into a saucer at the same time from the same vein, has coagulated in a quarter of an hour. Now, in all these cases the blood was fully exposed to the influence of the atmosphere; and if the air had been an active agent, promoting the tendency to coagulate, and the tissues merely neutral in their operation, coagulation must have occurred rapidly. On the other hand, if we admit that the tissues exert an active influence on the blood, and that air, oil, and other inorganic matter is inert with regard to it, the retarded coagulation follows naturally.[1] Here, then, it appears to me, we

[1] Since this paper was read, I have obtained further evidence which will, I trust, appear quite conclusive regarding the entirely negative influence of the atmosphere upon the blood, with respect to promoting the tendency to coagulation. Just forty-eight hours after the death of the sheep which furnished preparations exhibited to the Society, I exposed a vein of one of the feet and injected air forcibly into it, by means of a condensing syringe with a fine injection pipe adapted to it. Seven hours

have a sure, though imperfect glimpse, of the operation of mysterious but potent forces, peculiar to the tissues of living beings, and capable of reversing the natural order of chemical affinities ; forces which I suspect will never be fully comprehended by man in the present state of his existence, and the study of which should always be approached with humility and reverence.

Having thus obtained evidence of the active operation of the living tissues upon the blood, it occurred to me that the walls of the vessels might probably act to greater advantage upon their contents when of small than of large calibre, and that, in that case, the blood might be found fluid in the small vessels of the human body after death, although coagulated in the heart and large vessels. Accordingly, I have examined three human bodies with regard to this point, and in every case have found my idea confirmed. One of these was a woman, aged seventy, who had been a patient under Dr. Gillespie's care at the Infirmary, with senile gangrene. The right cavities of the heart were full of blood, and contained large clots buffed on their upper surface, and the large vessels also contained abundant soft coagula, but a small vein from one of the thighs yielded fluid blood, which coagulated slowly in a saucer. The body was examined about thirty-six hours after death. The other two had been patients under Dr. Gairdner's care, also in the Royal Infirmary. One of these was a man about thirty, who had died of meningitis. The heart had been removed before I saw the body, but the large vessels, such as the external iliac vein, contained coagula, whereas all the small veins which I observed contained perfectly fluid blood, which, however, had lost the power of coagulation. The third case was that of a young man, aged twenty-one, who died of a complication of medical and surgical complaints, nearly forty-eight hours before the body was examined. The corneae were perfectly clear, and there was no appearance of any incipient decomposition. This case was investigated very carefully ; and as the subject is novel, it may be well to give the results in detail :—I was not present

later I again examined the foot, and on reflecting the skin from the opposite aspect of the limb, found there a large subcutaneous vein distended with a mixture of blood and air ; the latter, which had evidently passed through an anastomosing channel, being present in the form of very numerous large and small bubbles. Having secured the ends of a long piece of this vein, I dissected it out and shed its blood into a saucer. Not a particle of clot existed in the vein, and complete coagulation took place within a quarter of an hour. The vein which had been exposed, in order to inject the air, contained here and there portions of clot in the exposed part, the vitality of the vessel having doubtless been impaired by the mechanical violence to which it was subjected in the dissection, or by the drying influence of the atmosphere.

In order to illustrate the effect of mechanical violence applied to a vessel in promoting the coagulation of the blood within it, I pinched a vein of the same foot severely with dissecting forceps in about an inch of its length, at the same time that I injected the air into the other vein. On examining the foot, seven hours later, the vein which had been pinched contained coagulum in the part which had been so treated, but fluid blood in the rest of its extent, both above and below the injured portion.—J. L., March 19, 1858.

when the heart was removed, but Dr. De Fabeck (resident physician under Dr. Gairdner) informs me that the cavities contained coagula buffed on their upper surface. The vena cava, the right iliac veins (common, internal, and external), and the femoral vein for about four inches down the thigh, contained soft coagula, mixed with thick dark fluid blood. The upper part of the axillary vein and the internal jugular of the same side, also contained some soft dark coagula, but the deep epigastric, the femoral vein below the part before mentioned, the internal saphena, and a smaller venous branch in the thigh, the axillary, except at the upper part, the cephalic, and a subcutaneous vein of the throat, all contained fluid blood, which coagulated in about half an hour after being shed ; and I noticed in the thigh that the blood from a small venous branch coagulated more quickly than that from the saphena. In the veins of the lower limb, both large and small, there were curious strings of highly elastic tawny fibrine, but these had evidently been deposited long before death. Similar threads were also present in the veins of the neck and in the aorta, external iliac, and femoral arteries, which, however, contained but little blood, and no post mortem coagula. I did not test the coagulability of the blood in the arteries, nor in a branch of the internal iliac vein, which also contained fluid blood.

I am aware of one source of fallacy in these experiments, namely, that the abdominal viscera are subject to decomposition before the limbs ; and as soon as decomposition does set in, the blood coagulates in the parts which are the seat of it ; as, for example, in small veins of the intestines. This cause of error was, however, I think, guarded against in the last case ;[1] and considering the

[1] Through the kindness of my friend Mr. John Gamgee, of the New Veterinary College, I have had the opportunity of making further observations regarding this point, upon an animal with very large blood-vessels, so soon after death as to avoid the risk of incipient decomposition. A healthy horse having been killed by pithing, at 11.30 p.m. on the 22nd inst. (March 1858), I examined the body just twelve hours later, while it was still warm. The cavity of the thorax, when opened, smelt perfectly fresh. Both auricles contained large masses of coagulum, buffed on their upper surface. There were also soft dark clots in both ventricles, together with a good deal of fluid blood, which, however, scarcely coagulated at all, a considerable portion from the right ventricle yielding, after many minutes, only a minute thread of fibrine. I suspect this was chiefly serum and corpuscles, which had passed in from the auricles on relaxation of the ventricles. There was a considerable amount of firm coagulum in the aorta, and the large veins at the anterior part of the chest were loaded with firm buffed clot. A small branch beneath the pleura, where it is reflected over the pericardium, contained perfectly fluid blood, as also did a coronary vein of the heart, about as large as the saphena of the human thigh ; whereas the concomitant artery, which was very large (bigger than the human femoral), had the blood a good deal coagulated. That from the coronary vein, having been shed into a saucer, yielded, after some time, threads and lumps of fibrine. An intercostal vein, from beneath the pleura, as big as a crow-quill, furnished fluid blood, which coagulated. The superficial veins of both fore-legs yielded perfectly liquid blood, which began to coagulate in about four minutes, and set into a solid mass. But, just below the axillary, small portions of coagulum made their appearance in the vessels, which here attained a size about equal to the femoral in man ; and both the axillary trunks were plugged with firm clot.

almost universal occurrence of coagulum in the heart of the human subject twenty-four hours after death, compared with the universal absence of it in the small veins of healthy parts, so far as I have yet examined them, both in man and the lower animals, I think the fact must be admitted, that where a large mass of blood exists within a cavity of the heart or a blood-vessel, it experiences coagulation sooner than if in a small vessel of the same body. If this be admitted, it becomes a strong argument in favour of the active operation of the tissues, for the blood is more exposed to the influence of the air in a subcutaneous vein than in the heart, and the only conceivable reason for the greater persistence of fluidity in the latter than in the former is that the influence of the tissues operates to greater advantage upon the smaller mass of blood.

Again, supposing it to be admitted that free ammonia exists within the blood-vessels, maintaining the fibrine in solution, a hypothesis which, I confess, appears to me very probable,—granting the ammonia theory, I say, as far as it can possibly be granted, it is clear that no merely neutral action of the tissues could check the evolution of the alkali in the manner above described ; and nothing can tend to convince us more of the potency of the vital forces than to consider what new powers must be impressed upon the chemically inert constituents of the tissues, in order to enable them securely to chain down the alkaline gas, in spite of its excessive volatility.

There is one other experiment upon the sheep's foot which I do not like to omit mentioning. Having exposed a subcutaneous vein, six hours after the death of the animal, I pressed out the blood from an inch of it, and treated the empty part with caustic ammonia, the adjacent parts being protected by olive oil. When the smell of ammonia had passed off, I let the blood return, and, two or three hours after, found that the portion which had had its vitality destroyed by the ammonia, was full of clot, while the blood in the adjacent parts of the vein was fluid, and coagulated on exposure.[1]

This, however, was not the only result of the application of the ammonia. The surrounding tissues had not been thoroughly protected from its action by the oil, and next morning all the parts on which it had acted were the seat of the most intense congestion, accompanied with exudation of glairy matter into the cellular tissue ; in fact, there were all the appearances of the most severe

[1] Two feet of a sheep, killed six hours before the Society met, were exhibited in illustration. One of these was prepared in the manner described in the text. The portion of vein which had been treated with ammonia contained a cylindrical coagulum, while the blood in the adjacent parts of the same vessel was fluid. The other foot was for the purpose of showing the fluidity of the blood so many hours after death. A considerable amount having been shed into a saucer in the liquid state, soon assumed the solid form.

inflammation. Some of the exuded matter had trickled down on a board beneath, and had there coagulated, showing that genuine exudation of lymph had been the result of this post mortem inflammation, then, I believe, for the first time observed in one of the mammalia.[1] I cannot avoid expressing the satisfaction that it has given me to find what I had inferred from other circumstances, in my investigations on inflammation, now established as a matter of observation. I had found that the blood-corpuscles, both red and white, were perfectly free from adhesiveness within the vessels of a healthy part, but that in an inflamed region they stuck together just as they are seen to do between two plates of glass. Having thus observed that the corpuscles of the blood comport themselves in an inflamed part in the same manner as in blood drawn from the body, I inferred that the liquor sanguinis was, in all probability, similarly affected, although coagulation is not observed in the capillaries, in consequence of the movement of the blood ; and I gave the same explanation of the speedy coagulation of lymph, and of the formation of clots in inflamed vessels, as has been substantiated by independent facts this evening. In the paper before alluded to, the following passage occurs :—‘ The non-adhesiveness of the red and white corpuscles, and the fluidity of the blood, seem to be due to one and the same mysterious and wonderful agency—the tissues of a healthy body appearing to extend over the blood near them, a part of the same influence by which they are themselves protected from the action of chemical affinities tending to their decomposition.’ We now see that when an agent capable of producing inflammation acts upon a part in which the blood is at rest, coagulation of the blood does really occur in the vessels.

There is an error of observation into which Dr. Richardson has unaccountably fallen, which it appears important to correct. In speaking of the coagulation of a portion of blood enclosed between two ligatures in the jugular vein of a dog or cat, he mentions the formation of a large bubble of air within the vessel, a little prior to the occurrence of coagulation. I have frequently seen the pellucid appearance he describes, but find that it is in no way connected with coagulation, but is due to the subsidence of the red corpuscles, leaving a layer of clear liquor sanguinis at the top. If two ligatures be applied, about an inch apart, upon a subcutaneous vein of one of the legs of a cat, care having been taken not to disturb the connexions of the vessel, or inflict injury upon it, and the leg be suspended by the paw in the vertical position, the clear appearance will begin to show itself below the upper ligature within five minutes.

[1] Tension upon the blood in the vessels, resulting from the bandage, supplied, I imagine, the place of the force of the heart in squeezing out the liquor sanguinis through the walls of the capillaries, deprived of their usual power of retaining it.

If now the limb be left for several hours, the skin having been carefully replaced so as to prevent evaporation, the clear colourless upper layer will be found to occupy nearly two-thirds of the length of the portion of vein, and to be sharply defined from the black lower layer which contains all the red corpuscles. If now the upper part be punctured, the clear liquor sanguinis will flow out, and coagulate upon any object held to receive it.[1]

Some of the observations above described will have a bearing upon medico-legal inquiries, showing, as they do, that not only ecchymosis, which some have denied, but even inflammation may be developed post mortem, provided that the return of blood by the veins is in some way prevented.

There are other bearings, both upon pathology and practice, to which I cannot even allude on the present occasion ; but I thought it best to place the facts at once before my professional brethren, confident that they will receive from them all the attention that they may deserve.

In conclusion, I have to express my thanks to my friend, Mr. Craig, for the kind and able assistance which he has afforded me throughout this investigation, and also to my friends, Drs. Gourlay and Hill, who have on several occasions lent me most valuable aid.

[1] Post mortem congestions simulating inflammation are, I suspect, due to this gravitation of the red corpuscles of the still fluid blood into the vessels of dependent parts.

A CASE OF LIGATURE OF THE BRACHIAL ARTERY, ILLUSTRATING THE PERSISTENT VITALITY OF THE TISSUES

[*Edinburgh Medical Journal*, vol. iv, p. 119, August 1858.]

On the 28th of May last I was requested to see a case at Balfron, in Stirlingshire, under the care of Mr. Burgess, who stated that on the 10th of April the patient, a man about fifty years of age, inflicted a suicidal wound with a razor on the front of the left arm about three inches above the elbow, severing the biceps completely and dividing both the main superficial veins of the limb. The bleeding was very profuse but chiefly venous, and was readily controlled by pressure, and the wound was afterwards lightly dressed without anything unusual occurring for several days, when haemorrhage again took place to a very alarming extent. It was treated as before by compression, but recurred twice at intervals of a few days, after which for a period of more than three weeks the healing process appeared advancing favourably. On the 24th of May, however, there was another discharge of blood from the wound, and this was repeated at frequent intervals and with increasing violence in spite of compression, until the 27th, when it became imperative to have recourse to other measures. Inconvenience in the arrangements of the railway delayed my arrival nearly a day, and in the meantime it had been found necessary to apply bandages at the seat of wound with all possible force, so as completely to arrest the flow of blood through the vessels of the limb, which had thus been entirely devoid of circulation for about thirty hours before the time at which I first saw the patient, viz. 2 p.m. on the 29th. At this time he was lying in bed pale and weak from loss of blood with the left arm somewhat swelled below the bandages, livid in tint and quite cold. Chloroform having been administered I removed the bandages, after which arterial blood gushed from the wound as soon as the pressure of the fingers over the brachial artery was relaxed. With the assistance of Mr. Burgess I proceeded to expose the bleeding-point, and after a somewhat troublesome dissection among the tissues, densely matted together with inflammatory deposit, discovered a small wound in the brachial artery, and having cleared the vessel sufficiently to avoid the risk of including either of the adjacent nerves, passed ligatures around it above and below the aperture, with the effect of removing all tendency to haemorrhage. Before I left in the afternoon the limb had already recovered its warmth and Mr. Burgess has since informed me that feeble pulsation was soon after perceptible at the wrist. In his last letter, written on the 21st of June, he stated that the ligatures had come away several days previously, the wound was healing kindly, and there was good sensation in the limb, though not quite so acute as in the other arm, while the patient was regaining health and strength.

This case is an example of the practical application of the principles sought to be established in a paper lately published in this journal,[1] in which it was shown that tissues previously healthy retain their vitality for a much longer period than had been before supposed after complete withdrawal from the influence of the centres of circulation and innervation ; and that by virtue of this persistent vitality the blood continues fluid for several days within the vessels of an amputated limb. In the present case the appearances of the arm and the previous history were such as would, I believe, have induced most surgeons not conversant with these principles to have resorted at once to amputation.

[1] Vide a paper by the author 'On Spontaneous Gangrene from Arteritis and the Causes of Coagulation of the Blood in Diseases of the Blood-vessels'. *Edinburgh Medical Journal*, April 1858 (p. 69 of this volume).

PRELIMINARY ACCOUNT OF AN INQUIRY INTO THE FUNCTIONS OF THE VISCERAL NERVES, WITH SPECIAL REFERENCE TO THE SO-CALLED 'INHIBITORY SYSTEM'

In a Letter to Dr. Sharpey, Sec. R.S.

[*Proceedings of the Royal Society of London*, vol. ix, No. 32 (1858).]

Received August 13, 1858.

My dear Sir.—The fact that the irritation of visceral nerves sometimes causes arrest of the movements of organs supplied by them, as shown by Edward Weber's experiment of stopping the action of the heart by stimulating the vagus, and by Pflüger's more recent observation that the application of galvanism to the splanchnic nerves produces quiescence of the small intestines, appears to me to have an intimate bearing upon the question how inflammation is developed through the medium of the nervous system at a distance from an irritated part; and as the nature of the inflammatory process has lately engaged my special attention, I have been led to make an experimental inquiry into this 'inhibiting' agency, the true interpretation of which is, as you are aware, still *sub judice*. I now propose to state the principal results at which I have arrived, reserving further details for a more extended communication which I hope soon to offer the Royal Society.

The view which has been advocated by Pflüger,[1] and I believe very generally accepted, viz. that there is a certain set of nerve-fibres, the so-called 'inhibitory system of nerves' (Hemmungs-Nervensystem), whose sole function is to arrest or diminish action, seemed to me from the first a very startling innovation in physiology; and you may possibly recollect my mentioning to you in conversation, when in London last Christmas, my suspicion that the phenomena in question were merely the effect of excessive action in nerves possessed of the functions usually attributed to them. On further reflection upon the subject, the consideration of the contraction produced in the arteries of the frog's foot by a very mild stimulus, as compared with the relaxation of the vessels caused by stronger irritants acting through the same nerves, confirmed my previous notions. For I could hardly doubt that the cause of the

[1] Eduard Pflüger, *Ueber das Hemmungs-Nervensystem*, 1857.

quiescence of the heart or intestines on irritation of the vagus or splanchnic nerves was analogous to that of arterial dilatation in the web, and that, provided a sufficiently mild stimulus were applied to the so-called 'inhibitory nerves', increased action of the viscera would occur, corresponding to the vascular constriction.

To test the truth of this hypothesis, I made several experiments between the 17th of June and the 14th of July of this year, with regard to the movements of the heart and intestines. The means used for stimulating the nerves and spinal cord were sometimes mechanical irritation, but more commonly galvanism, applied with a magnetic coil battery of a single pair of plates, the strength of which could be regulated in a rough way, with great facility, by the height at which the acid solution stood in the jar and the extent to which the rods of soft iron were inserted in the helix. The mildest action employed was such as was but just perceptible to the tip of the tongue, placed between the fine silver-wire extremities of the poles, when the rods were fully in the helix, but inappreciable after their complete withdrawal; the spring carrying the magnetic bar being made to vibrate by a touch with the finger: the greatest action of the battery, on the other hand, was so powerful as to elicit sparks when the poles were applied to the tissues.

My attention was first directed to the intestines, and it may be well to mention first all the results obtained with reference to them. The animals operated on were generally rabbits, they being very easily managed, and also favourable for the purpose on account of the large amount of movement which occurs in their intestines. Chloroform was generally not administered, on account of its depressing effect upon the action of the nervous centres.

In the first experiment, the ends of the poles having been fixed to the spinous processes of the ninth and twelfth dorsal vertebrae, according to Pflüger's original method, and the intestines allowed to protrude through a wound in the abdominal parietes, a series of interrupted currents were transmitted, a very small amount of acid being in the jar, and the rods fully in the helix. The effect was complete relaxation and quiescence of the small intestines, which had been previously in considerable movement, while the muscles of the limbs were thrown into spasmodic action; but on the discontinuance of the galvanism the previous intestinal motion returned. The rods were then removed from the helix, and the battery, thus diminished, was applied on several occasions, with markedly increased action of the intestines in every instance during the first twenty-five minutes. In the next half-hour the increase of action from the galvanism, though still distinct, was less strongly marked; and at the end of that period, the rods having been reintroduced, the inhibiting influence was also found to be much less complete than before, indicating that the parts of the nervous apparatus concerned were in a less active condition, no doubt in consequence of exhaustion. The arches of the tenth and eleventh dorsal vertebrae having been removed before the experiments with galvanism, I subsequently introduced a fine needle into the exposed part of the cord, with the effect of causing in repeated instances increased movements of the intestines, which were especially striking on account of the occurrence of peculiar local contractions not seen at other times. Further observations upon this animal tended to confirm those which have been mentioned, as did an experiment of the same kind performed the next day upon another rabbit.

I afterwards found that the best mode of proceeding was to remove the skin and one or two layers of muscles from a portion of the abdomen till the parietes were sufficiently thinned to permit the intestines to be distinctly seen through them ; by this means the complication produced by exposure of the intestines to the atmosphere was avoided, and the most satisfactory results were obtained ; the increase of the peristaltic movements during the transmission of extremely feeble shocks being strikingly apparent and constant on every occasion. During the experiment performed in this way I noticed several times that a violent struggle on the part of the rabbit, when the intestines were in pretty free movement, was followed by absolute and universal quiescence of those organs for several seconds ; this appeared to me of great interest, as proving that the inhibitory influence is certainly sometimes exerted in the natural actions of the animal, and is not merely the result of artificial stimulation.

In the course of the above experiments several other observations were made. In the first place I verified the statement of Pflüger, that if, when the intestine is lying relaxed under the inhibiting influence of galvanism applied to the spine, a particular part be irritated, local contraction occurs, but is not propagated to neighbouring parts. This fact is of fundamental importance, since it proves that the inhibitory influence does not operate directly upon the muscular tissue, but upon the nervous apparatus by which its contractions are, under ordinary circumstances, elicited.

Another point which seemed to require investigation was the well-known increase of peristaltic action which takes place after death, and which continues in spite of cutting off the mesentery close to the gut. Those who believe in a constantly restraining function of certain nerves during life might argue that the intestine has always a tendency to such active movements, but is kept in check by the 'inhibitory nerves', and released from their control when they have lost their power after death. A different explanation, first suggested, I believe, by Bernard, is that the increased action of the intestines is the result of failure of the circulation in the part ; and to this view I felt disposed to agree, in consequence of having noticed curious irregular contractions in the arteries of the frog's foot from a similar cause. In order to decide the question, I tied three adjoining arterial branches in the mesentery of a rabbit, thus depriving about three inches of the intestine of its circulation, the parts so affected being accurately defined by the extent of absence of pulsation in the minute vessels close to the gut. In about a minute and a half, vermicular movements commenced in this part, the rest of the intestines being at the time very quiet. Powerful interrupted galvanic currents were then transmitted through the posterior dorsal region of the spine, with the effect of causing perfect quiescence of the whole of the intestine, including the part whose arteries had been tied. After cessation of the galvanism the movements recurred in the portion devoid of circulation, while elsewhere they were almost entirely absent. This experiment was repeated on another occasion with similar results. In one of the cases I divided the mesentery close to the gut, after ligature of the vessels, but no change took place in the character of the movements which had been previously induced, indicating that the increased action in these cases had been of the same nature as that which results from death. The arrest of the movement on the application of galvanism proved that the delicate operation of ligature of the mesenteric vessels had been performed without injury to the adjacent nervous branches; and it therefore followed that the movement in the parts supplied by those vessels was not due to any injury of the nerves, but simply to the arrest of circulation. It further appears from these experiments, that, in whatever way the cessation of the flow of blood through the vessels operates in increasing the peristaltic action, it does so through the medium of the nervous apparatus, and not by directly influencing the muscular tissue. For, in the latter case, the movement would have continued in spite of the inhibiting influence, which, as we have seen, has no effect upon muscular irritability.

The fact that the movements continue in a portion of gut deprived of its mesentery, proves that the nervous apparatus by which the muscular contractions are induced and co-ordinated in post mortem peristaltic action, is contained within the intestine.

The distinction between the co-ordinating power and muscular contractility was very strikingly shown in the further progress of one of these experiments. The peristaltic movements of the portion of gut supplied by the ligatured arteries ceased entirely about twenty minutes after the vessels were tied, and the surface of the gut became there perfectly smooth and relaxed, contrasting strongly with the wrinkled aspect of other parts. But muscular irritability had outlived the co-ordinating power, as was shown by energetic, purely local contraction taking place in a part pinched. Similar observations confirmatory of this point were afterwards made upon a rabbit which had died of haemorrhage an hour before.

The mechanism by which the muscular contractions are regulated is, doubtless, the rich ganglionic structure lately demonstrated in the submucous tissue by Dr. Meissner of Bâle.[1] Professor Goodsir gave me the first information of the anatomical fact on my mentioning to him the foregoing physiological proofs of the existence within the intestines of a co-ordinating apparatus distinct from the muscular tissue. I have since verified Meissner's observations, and found abundant well-marked nerve-cells in the submucous tissue of the ox, exactly corresponding with his descriptions.

But while muscular irritability outlives the co-ordinating power in the intestines, the latter lasts much longer than the inhibiting property in the spinal system, for I find that Pflüger's experiment does not succeed in a dead animal, unless performed soon after death, although the intestines may continue to move for a long time.

In another experiment I divided with fine scissors, at a little distance from the intestine, all the visible branches of nerves in a portion of mesentery corresponding to an inch and three-quarters of the gut, leaving the vessels uninjured. No effect was produced on the peristaltic movements, which happened to be pretty active at the time, and continued the same at the seat of the operation as elsewhere. To ascertain whether the division of the nerves had been thoroughly effected, I now transmitted powerful galvanic currents through the spine, as in former experiments, when all movements ceased in the intestine, except in the small piece whose nerves had been cut, which continued in vigorous action as before. The persistence of the vermicular motion after complete division of the mesenteric nerves shows that the movement which occurs during life, like that which takes place post mortem, is effected by a mechanism within the intestine; and its continuance in the portion of gut so treated, while other parts were relaxed, on the application of galvanism to the spine, proves that the inhibiting influence acts through the mesenteric nerves, whose integrity is necessary to the effect.

This being established, it follows that if a quiet state of the intestine, such as very frequently occurs in its natural condition, were due to a controlling agency on the part of the so-called 'inhibitory system', the complete division of the mesenteric nerves supplying a portion of gut which is at rest, would liberate it from this restraint, and movement would be the result. I performed the operation in one case under such circumstances, but the portion of intestine concerned remained as tranquil as the rest.

[1] Henle and Pfeufer's *Zeitschrift*, 2nd series, vol. viii.

To sum up the above, it appears that the intestines possess an intrinsic ganglionic apparatus which is in all cases essential to the peristaltic movements, and, while capable of independent action, is liable to be stimulated or checked by other parts of the nervous system ; the inhibiting influence being apparently due to the energetic operation of the same nerve-fibres which, when working more mildly, produce increase of function.

After the above conclusions had been arrived at, my attention was directed by Professor Goodsir to a paper by Dr. O. Spiegelberg, published last year, in which he shows that the movement of the intestines is increased by mechanical irritation of the cord. His results are particularly satisfactory, as having been obtained incidentally during an inquiry into the movements of the uterus, and so without any preconceived theory.[1] Spiegelberg also attributes the increased peristaltic action after death to arrest of the circulation, having found that the same thing occurs during life when the aorta or vena cava is compressed above the origin of the mesenteric vessels.

To proceed to the experiments upon the cardiac movements : some of these consisted in irritation of the vagus in rabbits, and this was followed by different results in different instances : thus, on one occasion the pinching of the cardiac end of the left nerve, divided in the neck, was followed by considerable increase in the number of beats as felt through the walls of the chest, but similar treatment of the right nerve afterwards caused great depression of the heart's action. Again, in one animal the evidence obtained from mechanical irritation of the vagus was almost entirely negative. In another case, the left vagus having been exposed, feeble galvanic currents transmitted through the nerve, isolated by a plate of glass placed beneath it, were succeeded by slight increase in the number of contractions. The strength of the battery having been then increased by introducing the rods into the helix, it produced first irregularity, and then complete arrest of the action of the heart, which had been previously exposed. No sign of recurrence of contraction appearing, I filled the jar to the top with acid solution, and sent powerful currents through the vagus, with the instantaneous effect of reviving the action of the heart, which, on their immediate discontinuance, continued to beat, though feebly, for several minutes. During this time I again applied the galvanism very mildly, and the result was great increase in the number of beats on several successive trials. The apparent discordance of these facts is, I believe, partly owing to differences in the state of the nerves in different cases as respects irritability and exhaustion, as will be better understood from the sequel ; and, on the whole, the experiments appear to show that, in a healthy state of the nervous system, very gentle irritation of

[1] Henle and Pfeufer's *Zeitschrift*, 3rd series, vol. ii, part 1.

the vagus increases the heart's action, while a slightly stronger application diminishes the frequency and force of its contractions. This conclusion is in harmony with an observation which I made incidentally upwards of a year ago, that irritation of the posterior part of the brain of a frog with a fine needle was repeatedly followed by improvement in the circulation, whereas it was by the application of a stronger stimulus, that of galvanism, to the same part of the cerebro-spinal axis that Weber first induced an inhibitory action on the heart.

It is said, on apparently good authority,[1] that division of the vagus in mammalia is invariably followed by increase of the action of the heart ; this, if true, would be a strong ground for believing in an inhibiting influence constantly operating upon it through this nerve. But it is also stated that the same thing does not occur in frogs ; and this circumstance appeared to me to throw much doubt upon the evidence regarding mammalia. I therefore made careful experiments on the effects of cutting both vagi, once upon a calf and four times upon rabbits, taking the number of the heart's beats immediately before and immediately after section of each nerve by the momentary stroke of a sharp pair of scissors. In no case was the rate increased at all by the operation, and the very gradual diminution in frequency that commonly took place appeared to depend on general exhaustion from other circumstances attending the experiment. In one rabbit, in which I had removed the skin and pectoralis major from the praecordial region, so as to see the movements of the heart distinctly through the transparent pericardium and intercostal muscles, I noticed particularly that the strength of the contractions, as well as their frequency, remained quite unaffected by the division of the vagi. From these facts I feel warranted in concluding that, whatever may occur under exceptional circumstances, there is certainly no constant control exercised over the heart's action through those nerves.

The influence of the spinal system upon the heart is, however, very apparent after a struggle, which almost invariably increases the frequency and force of the beats ; and I found that this continued to be the case after division of both vagi, implying that those nerves are not the only channels through which this influence is transmitted. A new field of investigation was thus opened. For, supposing the inhibitory agency to be simply the greater action of an ordinary nerve, it would probably not be exercised exclusively by the vagus, but also by the other nerves connecting the cerebro-spinal axis with the cardiac ganglia, viz. the sympathetic branches in the neck ; in which case the action of the heart should be increased or diminished, according to the strength of the stimulus,

[1] Pflüger, op. cit.

by the application of galvanism to the cervical region of the spine after the pneumogastric nerves had been cut.

In an experiment performed with this view, the poles having been fixed to about the fourth cervical and fifth dorsal spinous processes, and both vagi divided in the neck, galvanic currents only just perceptible to the tip of the tongue were first transmitted. This excessively feeble action of the battery, though apparently not very favourably situated for influencing the cord, produced marked effects upon the heart's action, increasing the number of beats, which were about forty in ten seconds, by from three to ten in that period. This effect having been observed for a considerable time, the rods of soft iron, which had been till then only inserted half-way in the helix, were pushed fully in. The battery, thus strengthened, instead of increasing, as before, the rate of the pulsations, diminished it by two in ten seconds on several successive trials. On again half withdrawing the rods, the galvanism, when applied, again increased the number of beats. A little more of the acid solution was afterwards poured into the jar of the battery, when the stronger currents which it produced reduced the number by about five in ten seconds.

Yet distinct as was this inhibiting influence, the shocks were still quite tolerable to the tongue even when the rods were fully in the helix.

These results were of great interest, as proving how slight an increase of the feeble stimulus which promoted the action of the heart sufficed to produce the opposite (inhibiting) effect. But it was by no means clear that the influence had not been exerted through cardiac branches arising from the vagi above the parts where they were divided, or even through the trunks of those nerves, which might possibly have been affected by the galvanism acting through the superjacent spinal column. In order to eliminate the vagi completely, I divided in another rabbit all the soft parts in front of the spine, except the trachea and oesophagus, at the level of the cricoid cartilage, having previously cut each carotid artery between two ligatures. The incisions were carried fairly down to the bodies of the vertebrae, and outwards beyond the tips of the transverse processes, so as to ensure the section not only of the vagi and their branches, but also of the sympathetic cords, with any filaments of those nerves which they might contain. Also the poles of the battery were fixed to the spinous processes of the seventh dorsal and first lumbar vertebrae, so as to avoid all possibility of direct action of the galvanism upon either the vagi or other cardiac nerves. Feeble currents being then transmitted, diminution of the number of beats to the extent of two to four in ten seconds occurred in several successive trials, the results being so constant as to leave no doubt that they were produced by the galvanism.

It may appear almost incredible that such extremely mild galvanic currents, applied through the spinous processes of the posterior dorsal region, should be capable of thus affecting the heart ; but that their effects were really very considerable, was clear from the further progress of this experiment, and from others somewhat similar, which showed that this apparently trivial stimulation gradually exhausted the part of the nervous system through which the heart is acted on by the cord. Thus, in one case, currents only just perceptible to the tongue, transmitted for about thirty seconds at a time through the lower cervical and upper dorsal regions of the spine, at intervals of nine minutes on the average during two hours and twenty minutes, produced at first decided increase of the heart's action, but during the last hour failed to affect it at all. The strongest possible action of the battery which, as proved by other experiments, would, at the outset, have entirely arrested the cardiac movements, was then set on, but with no effect whatever on the organ.

When partial exhaustion has occurred, a much stronger galvanic stimulus is required, to produce the same effect upon the heart, than at the commencement of an experiment ; and thus an action of the battery which, when first applied, causes marked diminution in the number of beats, may after a while come to have the opposite effect, and increase the heart's action as decidedly as it had previously lowered it ; while at an intermediate period it may seem to have no influence at all. This principle gives the clue to understanding what had before appeared incomprehensible in these experiments, showing that facts, which at first seemed utterly inconsistent, were really perfectly harmonious. The case before related, in which revival of the heart's action resulted from powerful stimulation of the vagus, which, had the organ been contracting as usual, would have arrested its movements and probably finally destroyed them, will now be understood. I have seen other analogous cases of revival of action by very powerful galvanism, which under ordinary circumstances would have arrested it, viz. twice in the heart and twice in the intestines. The observation published so long ago as 1839 by Valentin,[1] that mechanical or chemical irritation of the vagus in the neck of an animal recently dead, and with the nerves consequently enfeebled, causes contraction of the ventricles, admits of a similar interpretation, as also does a corresponding fact regarding the splanchnic nerves, given without explanation by Kupfer and Ludwig, in a paper just published,[2] viz. that they lose their inhibitory influence a certain time after death, and acquire a motor power over the intestines.

Two more experiments require mention, as they exclude the possibility of

[1] Valentin, *De Functionibus Nervorum*, p. 62.

[2] Henle and Pfeufer's *Zeitschrift*, 3rd series, vol. ii, part 3.

the agency in them of either the vagi or the part of the brain from which the vagi spring, having been performed upon decapitated rabbits. In one of these cases, the carotids having been tied near the head, the neck was completely severed behind the first vertebra, care being taken to avoid haemorrhage from the vertebral arteries, and artificial respiration, for which provision had been made, was carried on for an hour and a half after decapitation. The results of moderate galvanism, applied to the posterior dorsal region of the spine, to which the poles had previously been attached, were at first not distinct, but afterwards decided increase of action was produced by it when applied at intervals during half an hour, the effect being perfectly apparent in the heart which lay exposed before me. Exhaustion of the nerves concerned having then taken place, the most powerful action of the battery failed to influence the character of the contractions.

In the other case, the poles having been fixed as before, and the head similarly removed, powerful galvanic currents were immediately transmitted. The pulsations of the heart in the opened chest at once fell from thirty-five to sixteen in ten seconds, but rose again to twenty on the removal of the stimulus.

Hence it is clear that the sympathetic branches connecting the cord with the cardiac ganglia have equal claims with the vagi to be called 'inhibitory nerves'. In fact this expression seems to me altogether objectionable, since there is good reason to think that the same fibres which check the movements much more commonly enhance them. The only evidence afforded by my experiments that the inhibiting influence is ever exerted in the natural actions of the animal consisted in the quiescence of the intestines sometimes seen after a struggle, and two doubtful observations of retardation of the heart's beats from the same cause. Indeed it appears very questionable whether the motions of either of these viscera are, under ordinary circumstances, ever checked by the spinal system, except for very brief periods; whereas the increased action of both heart and intestines, familiarly known to result from mental emotion, may last for a very considerable time. The fact that the nerves of these organs are capable of setting them at rest under conditions of extraordinary irritation is nevertheless a matter of great importance, especially in a pathological point of view, and appears to afford an explanation of facts in medicine hitherto little understood—such as failure of the heart's action from violent emotion or pain, and the constipation which attends strangulated omental hernia.

From the observations of Spiegelberg,[1] it would appear that the uterine contractions are promoted by mechanical irritation of the cord, and arrested by transmitting a powerful stream of galvanism through the spine. Also the forcible

[1] Henle and Pfeufer's *Zeitschrift*, 3rd series, vol. ii, part 1.

expulsion of urine very frequently seen in the lower animals in consequence of fear, and the temporary palsy of the detrusor often witnessed in the human subject in surgical practice as the result of severe injury, seem to me to imply that the bladder, too, while sometimes stimulated through the cerebro-spinal axis, is paralysed by its very powerful operation. Hence it seems probable that the movements of all the hollow viscera are liable to similar influence from the spinal system. At the same time it appears to be a mistake to regard this influence in the light of a strict control; for the experiments related in this letter show pretty distinctly that the contractions of the heart and the peristaltic action of the intestines are regulated, under ordinary circumstances, by the independent operation of the intrinsic ganglia.

Professor Schiff has, I understand, observed increase of the heart's action to result from very gentle stimulation of the vagus,[1] and has come to the conclusion, as stated by Spiegelberg in his paper before referred to, that the inhibiting influence depends upon nervous exhaustion. There are some circumstances which make me entertain great doubt as to the correctness of this view. In the first place, the very rapid recovery of the cardiac or intestinal actions when the inhibiting galvanic currents are discontinued, contrasts strongly with the length of time that the impairment of function resulting from a protracted experiment, and certainly due to exhaustion, lasts both in the intrinsic cardiac nerves and in those that connect them with the spinal system. Secondly, although very powerful galvanism not only arrests for the time, but permanently impairs the action of the heart, no such effect is observed to follow the inhibiting influence when it is caused by milder stimulation; indeed, according to my experience, less injurious effects are produced upon the heart by a protracted series of experiments of the latter kind than by a corresponding set with the currents still more feeble, that increase, while acting, the frequency of the contractions. But if the diminished rate of the pulsations were caused by a partial exhaustion of the cardiac ganglia, an opposite result might have been anticipated.

Again, there can be little doubt that dilatation of the blood-vessels, in consequence of a stimulus, is due to an effect produced upon the nervous centres for the arteries, similar to that experienced by the visceral ganglia when subject to the inhibiting influence. Now an inflammatory blush of long continuance may subside rapidly when the source of irritation is withdrawn. Thus I have seen redness which had existed for about three days in the human skin in consequence of tight stitches connecting the lips of a wound, give place at once to pallor on their removal. Had the arterial dilatation in this case been the

[1] Henle and Meissner's *Bericht*, 1857.

result of nervous exhaustion continued during so long a period, such speedy recovery could hardly, one would think, have taken place.

These and other considerations, to which the already excessive length of this letter forbids me to allude, induce me to think it safest in the present state of science to regard as a fundamental truth not yet explained, that one and the same afferent nerve may, according as it is operating mildly or energetically, either exalt or depress the functions of the nervous centre on which it acts. It is, I believe, upon this that all inhibitory influence depends, and I suspect that the principle will be found to admit of a very general application in physiology.

I am, &c.,

JOSEPH LISTER.

SOME OBSERVATIONS ON THE STRUCTURE OF NERVE-FIBRES

Written in Collaboration with William Turner[1], Esq., M.B., Lond.,
Senior Demonstrator of Anatomy in the University of Edinburgh.

[*Quarterly Journal of Microscopical Science*, October 1859.]

Having recently had the opportunity, through the kindness of Mr. Lockhart Clarke, of inspecting some of his beautiful preparations of the spinal cord, we were struck with an appearance which had not yet received a satisfactory interpretation; and, having been induced to investigate the point, we have met with some facts which seem of sufficient interest for publication.

For the sake of clearness it may be well to state briefly the method employed by Mr. Clarke in preparing his specimens.

A portion of perfectly fresh spinal cord having been hardened by steeping in dilute chromic-acid solution, thin sections are made with a razor, and these, after immersion for a while in an ammoniacal solution of carmine, are soaked in spirits of wine to remove the water, and then treated with oil of turpentine. The last-named agent has the effect of rendering the sections transparent, so that the nerve-cells of the grey matter, finely coloured by the carmine, are seen with the utmost distinctness, giving off in various directions long branching processes; while the nerve-fibres, which are similarly tinted, may be traced with equal facility in their course through the cord.

In the preparations which we saw, the cord had been sliced crosswise, and in the columnar regions, where the nerve-fibres have for the most part a longitudinal direction, the transverse section of each fibre showed itself as a carmine-coloured point, surrounded by a perfectly pellucid and colourless ring. This was the appearance which seemed to demand explanation, the question being whether the transparent ring was a mere space, resulting from shrinking of the object during the preparation, or the white substance of Schwann (medullary sheath) rendered transparent by the turpentine, the axial cylinder alone, in that case, having received the carmine colour.

It occurred to us that the point might probably be determined by applying a similar mode of preparation to some nerve the dimensions of whose fibres could be readily ascertained. With this view we steeped in chromic acid portions of the sciatic nerve of a cat just killed, and also parts of the spinal cord of the

[1] Now (1908) Sir William, K.C.B., F.R.S., Principal and Vice-Chancellor of the University of Edinburgh.

same animal; and having allowed them to remain between three and four weeks in the solution, we commenced the investigation in July of the present year, 1859.

A transverse section of the hardened sciatic nerve having been placed for a time in the carmine solution and then dried, we submitted it, without the application of turpentine, to microscopic examination with a power of 130 diameters. Viewed by transmitted light, it appeared as a confused opaque mass; but, by reflected light, it exhibited the structure depicted in Plate IV, Fig. 1,[1] each nerve-fibre presenting in its section a carmine spot, surrounded by a yellowish-white, somewhat granular ring, which, though doubtless corresponding to the pellucid rings in the preparations of the cord before alluded to, was clearly composed of some solid material, in short, of the white substance of Schwann altered by the action of the chromic acid.

We next examined sections of the cord treated in the same way, but found that these dry specimens were so incrusted with carmine that they gave no definite results. It happened, however, that one of the sections treated with carmine still remained moist, and, after washing away all superfluous colouring matter, we examined it by transmitted light. A very beautiful appearance now presented itself, carmine points being seen in the columnar regions, as in Mr. Clarke's preparations, surrounded by rings; but the latter, instead of being transparent like mere spaces, were dead white; the carmine points, on the other hand, appearing in the thinnest parts of the section as illuminated spots amid the general opacity. This is represented in Fig. 5.

It will be seen from this sketch, which is drawn on the same scale as Fig. 1, that the nerve-fibres varied very much in their diameter, the largest being of about the same size as those of the sciatic nerve, while others were of extreme minuteness; but in all cases in which they were sufficiently large to be distinguished, they had the same character of a white circle with a central carmine spot from one-fourth to one-third the diameter of the whole fibre. It was obvious that, in the cord, as in the sciatic nerve, the carmine central part of each fibre was the axial cylinder, and the opaque circumferential portion the medullary sheath; and, therefore, that the pellucid rings in preparations treated with turpentine consisted of the white substance rendered transparent by that reagent.

The point at issue was thus satisfactorily decided; but for the sake of confirmation we made some further observations, the results of which seem deserving of mention.

On examining the hardened sciatic nerve, without tinting the preparations

[1] This sketch, like the others illustrating this paper, was drawn by means of the camera lucida.

with carmine, we found that in extremely thin slices the transverse sections of the nerve-fibres, viewed by transmitted light, appeared as brownish rings with central transparent colourless spots (see Fig. 3), whilst by reflected light the central parts appeared black, as shown in Fig. 2. In fact, under a low power the axial cylinders had, in these specimens of the sciatic nerve, as much the appearance of mere spaces as the medullary sheaths had in preparations of the cord treated with turpentine. But on applying a fine glass of high power a granular appearance was disclosed in the pellucid central portion, showing that it was in reality a solid substance, though of a transparency which was very remarkable, considering that it had been so long subjected to the action of chromic acid ; and on afterwards treating similar sections with carmine we found that this part alone became coloured. The higher magnifying power also brought out an appearance of irregular concentric lines in the brown [1] medullary sheath ; and this, together with the granular aspect of the axial cylinder, is represented in Fig. 4.

These facts afford a very striking illustration of the essential difference in chemical composition between the axial cylinder and the medullary sheath, the former being totally unaffected by chromic acid, though the latter is rendered opaque and brown and concentrically striated under its influence, while, on the other hand, the axial cylinder, after being subjected to the action of chromic acid, imbibes the carmine colour with peculiar facility, although the medullary sheath is entirely untinged by it.[2]

We next applied the high magnifying power to extremely thin slices of the spinal cord prepared in the same way. In transverse sections of the columnar regions the white substance of Schwann presented, in the larger fibres, the same concentrically arranged appearance as we had observed in the sciatic nerve, as is illustrated by Figs. 6 and 7, of which Fig. 6 is one of the largest met with, being 1-900th of an inch in diameter, while Fig. 7 is as small as 1-3000th of an inch in transverse measurement. In the very minute fibres no appearance of concentric lines could be detected, yet, wherever the existence of an axial cylinder was indicated by a carmine point, a ring of medullary sheath was always visible, presenting the same proportion to the axial cylinder as in fibres of larger size. This may be gathered from Figs. 8, 9, and 10, of which Fig. 8 measures 1-5000th of an inch across, Fig. 9 1-8000th, and Fig. 10 only 1-14000th.

[1] It must be mentioned that a similar brown colour is seen in the superficial parts of a cord which has been steeped in chromic acid, but the deeper portions of the organ are comparatively only slightly coloured, so that in individual nerve-fibres seen under a high magnifying power the brown tint is not observed.

[2] In a boiled fresh nerve also the medullary sheath remains unaffected by ammoniacal solution of carmine, while the axial cylinder assumes a distinct though very faint pink tint.—J. L.

At the margins of longitudinal sections of the cord, the contrast, both in structure and in tint, between the axial cylinder and the medullary sheath showed itself very beautifully. It often happened that a projecting isolated fibre was, near its extremity, more or less divested of the white substance of Schwann, so that the delicate, carmine-tinted axial cylinder was exposed, though presenting here and there colourless flakes of the medullary sheath adhering to its surface, while in parts where the nerve was still entire, the pink colour of the central fibre could be distinctly discerned through the intervening white substance. Fig. 11 represents a large fibre under such circumstances, and Fig. 12 one of considerably smaller size ; and these sketches also display the remarkable fibroid arrangement which we find the white substance of Schwann invariably assumes under the influence of chromic acid.

In conclusion, we may remark that the successive employment of chromic acid and carmine seems likely to afford valuable aid in discriminating nerve-fibres among other structures, there being, so far as we are aware, no other form of tissue which, after the use of these means, exhibits fibres having a central carmine axis and peripheral uncoloured sheath.

Supplementary Observations by Mr. Lister

The fibroid arrangement of the white substance of Schwann in nerves hardened by chromic acid has been minutely described by Stilling, in his elaborate treatise on the 'Nerve-fibre and Nerve-cell',[1] a work which we had not seen when the foregoing communication was written, but a copy of which was kindly lent me by Professor Goodsir, soon after Mr. Turner had left Edinburgh for the vacation. According to Stilling, the medullary sheath is, even in perfectly fresh nerves, composed of a network of fibres, which are continuous with others in the axial cylinder and in the proper investing membrane ; so that, in his opinion, these three constituents of the nerve-fibre differ from each other only in the manner in which their elements are disposed.[2] This view is not only quite novel anatomically, but is opposed to the generally received physiological opinion, that the axial cylinder is the essential part of the nerve-fibre, and the medullary sheath an insulating investment. Considering the high estimation in which the writings of Stilling on the anatomy of the nervous centres are deservedly held, and the influence which therefore attaches to his opinions, it seems fortunate that we have been able to present so clear a demonstration that the axial cylinder is chemically as well as morphologically totally distinct from the medullary sheath.

[1] *Ueber den Bau der Nerven-Primitivfaser und der Nervenzelle.* Von Dr. B. Stilling. 1856.
[2] Op. cit., p. 6.

With regard to the cause of the fibroid arrangement of the medullary sheath, an observation which I happened to make several years ago, regarding the aggregation of fatty matter, may perhaps tend to throw light upon the subject. I submitted to microscopic examination some of the pultaceous slough of a sore affected with hospital gangrene, thinking it possible that I might discover in it some fungus which might account for the peculiar specific character of that disease; and found in it numerous bodies, each composed of branching fibres radiating from a common centre, and looking, at first sight, like some sort of vegetable growth, so that I made careful sketches of them, one of which is reproduced in Fig. 13. But seeing afterwards, in the same object, some bundles of acicular crystals of margarine having a distant resemblance to the bodies I had drawn, I added ether to the specimen, and found that it dissolved the latter equally with the former. This showed that what first attracted my attention was merely an arborescent form of aggregation of some fat, probably margarine; and it seems not unlikely that the fluid fat which exists in the medullary sheath of a perfectly fresh nerve may tend to a similar arrangement of its particles when passing into the solid form, and so give rise to the appearance in question. It is to be remarked that the fibroid character is not peculiar to specimens treated with chromic acid, but also shows itself, though in a less perfect manner, in nerves which have been subjected to other modes of preparation—for example, after exposure for a few seconds to a temperature of 212° Fahr.

There is another important statement made by Stilling, which the use of the method of examination above described enables me to correct. He speaks of the fibres which connect one nerve-fibre with another as similar in every respect to those seen in the medullary sheath.[1] I find, however, that both in the sciatic nerve and in the spinal cord of the cat, the connective tissue between the nerve-fibres, like the neurilemma and pia mater, with which it is continuous, becomes coloured by the carmine; whereas, the medullary sheath, as before stated, is quite unaffected by it, proving that the two structures are chemically distinct from one another. In both these situations, too, the fibres of the connective tissue are much more delicate than the constituents of the medullary sheath, which are often comparatively coarse, as may be seen from Fig. 11. In the columnar regions of the cord, the former require a high magnifying power to be applied to very thin sections, in order to distinguish them, and are often present in such extremely small quantity that, without very careful examination, the nerve-fibres appear actually in contact with one another. In the sciatic nerve I have observed occasional elongated nuclei in the connective tissue.

[1] Op. cit., p. 7.

I may add that glycerine has proved very useful, not only for permanently preserving the preparations in the moist state, but also as an aid to investigation; for it renders the sections much more transparent, without making the white substance of Schwann invisible, as turpentine does ; and hence the course of the nerve-fibres through the cord can be traced much more easily, and, at the same time, the proportion between the medullary sheath and axial cylinder can be readily ascertained. Thus, by examining transverse sections of the cord in this way, I find that while Kölliker is quite correct in his statement that the fibres of the roots of the nerves diminish in size in passing inwards through the columnar regions,[1] yet the diminution affects only the white substance, the axial cylinder often retaining its full dimensions even in the middle of the grey matter, while the medullary sheath is reduced to a very thin crust, so that the nerve-fibre assumes a character differing but little from that of an offset of a nerve-cell.

[1] Kölliker's *Handbuch der Gewebelehre*, 3rd ed., p. 285.

DESCRIPTION OF PLATE IV

Fig. 1 represents part of a transverse section of the sciatic nerve of a cat hardened by chromic acid, and tinted with carmine, the axial cylinder alone having received the colouring matter. The specimen was dried and viewed as an opaque object.

Fig. 2 shows the appearance of thin transverse sections of some nerve-fibres from the same nerve, simply hardened in chromic acid, and examined moist by reflected light. The axial cylinder has, under this low magnifying power, the aspect of a mere space.

Fig. 3, similar objects to those of Fig. 2, but seen by transmitted light.

Fig. 4, a highly magnified transverse section of a nerve-fibre from the same source, prepared like those of Figs. 2 and 3, and then tinted with carmine. The carmine colour is seen to affect only the axial cylinder and the investing membrane, which, at one part, is torn up from the fibre. This sketch also shows the faintly granular structure of the axial cylinder, and the irregularly concentric striation of the medullary sheath.

Fig. 5, a transverse section of a columnar portion of the spinal cord of a cat, also prepared with chromic acid and carmine, and examined moist by transmitted light. The fibres vary much in size, but all of them resemble those of the sciatic nerve in having the red axial cylinder surrounded by a ring of untinted medullary sheath.

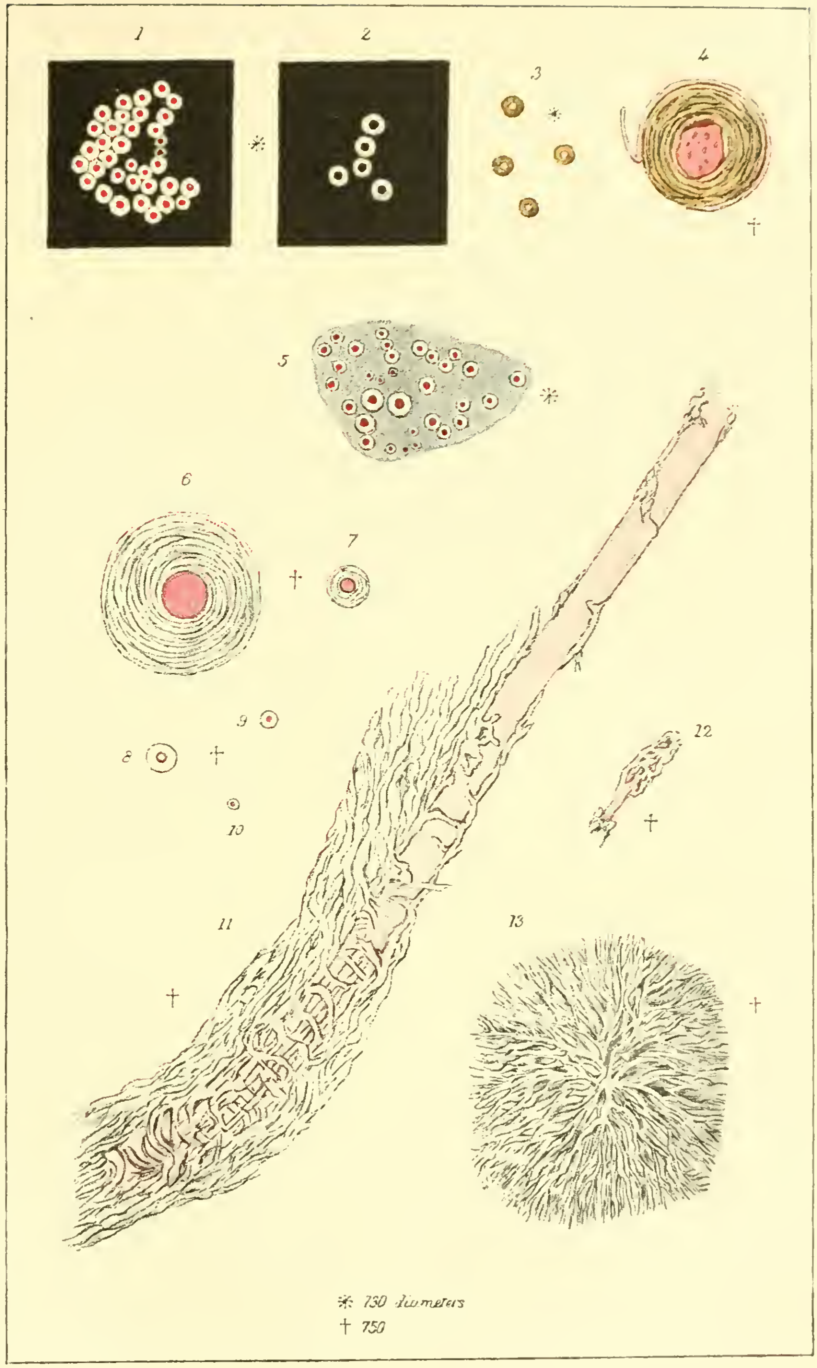
Figs. 6–10 are highly magnified views of some fibres in a section of the cord like that of Fig. 5. They present the same characters as the fibres of the sciatic nerve.

Fig. 11, a fibre from a longitudinal section of a columnar portion of the cord, prepared in the same way The axial cylinder alone is carmine coloured, and is, in some parts, stripped of its investing sheath, the fibroid arrangement of which is also displayed.

Fig. 12, a small fibre under similar circumstances.

Fig. 13, fatty matter in a state of arborescent fibroid aggregation.

Plate IV



NOTICE OF FURTHER RESEARCHES ON THE COAGULATION OF THE BLOOD

Read before the Medico-Chirurgical Society of Edinburgh, November 16, 1859.

[*Edinburgh Medical Journal*, December 1859.]

MR. PRESIDENT.—I take this opportunity of demonstrating what appears to be a point of considerable importance with reference to the coagulation of the blood—a subject to which my attention has been again directed by the recurrence of that period of the Session in which the fundamental principles of pathology are discussed in a course of surgical lectures.

I may remind the Fellows of this Society, that in a paper which I had the honour to read before them the Session before last,[1] I brought forward facts which seemed to prove that the ammonia theory does not apply to blood within the vessels of a living animal. That theory, as my hearers are doubtless aware, asserts that the fluidity of the blood depends upon the presence of a certain amount of free ammonia holding the fibrine in solution, and that coagulation is the necessary result of the escape of the volatile alkali. But it was shown in the paper referred to, that the blood, in man and other mammalia, though coagulating soon after death in the heart and great venous trunks, remains fluid for days in vessels of smaller size, and this under circumstances affording free opportunity for the escape of ammonia; and, on the other hand, that when a portion of a vessel either in an amputated limb or in a living animal is treated in a manner calculated to destroy its vital properties, the blood coagulates in the injured part, but retains its fluidity elsewhere, although there is no greater opportunity for the escape of ammonia in the one case than in the other. A striking instance of the difference between the natural receptacles of the blood and ordinary matter in their relations to the vital fluid happened to come under my notice this morning, in an arm which I amputated last evening at the shoulder-joint, on account of injury inflicted by machinery. On examining the limb, which had lain undisturbed since the operation, I saw that the axillary vein, which was patulous at the part where it had been divided by the knife, contained some blood at a distance of about half an inch from the open orifice; and having squeezed out a few drops, found that it was perfectly fluid, but yielded threads of fibrine when the point of a needle was drawn through it some minutes after emission. The blood had been for upwards of twelve

[1] Vide *Edinburgh Medical Journal*, April 1858 (p. 69 of this volume).

hours freely exposed to the air, but being situated in an uninjured part of a blood-vessel, had remained free from coagulation.

Further, in the opening meeting of last Session I demonstrated another important principle, viz.—That ordinary solid matter, unlike atmospheric air, induces coagulation of blood in its vicinity when introduced within the living vessels. Having inserted a piece of clean silver wire for a considerable distance into one of the veins of an amputated sheep's foot, I slit up the vessel after a short time had elapsed; when I exhibited a coagulum extending along the whole length of the foreign body, whereas a mere wound of the vein failed to induce a clot except immediately at the spot where the injury had been inflicted. It was obvious that the introduction of the wire could not affect the amount of ammonia in the blood; and from this and many other facts, to which I need not here allude,[1] I was led to the opinion, that as regards what takes place within the living vessels, the ammonia theory might practically be left entirely out of consideration.

What I have to show this evening will, I think, prove that even for blood outside the body, the ammonia theory, whatever degree of truth it may contain, is very far indeed from representing the whole truth.

One of the most remarkable circumstances connected with blood that has been shed from the vessels is, that it refuses to coagulate below a temperature of 40° Fahr. or thereabouts. This is explained by Dr. Richardson on the hypothesis that the low temperature prevents the evolution of ammonia,[2] while the rapidity with which coagulation takes place at high temperatures seems to him satisfactorily accounted for by the increased volatility exhibited by the ammonia under such circumstances. I was myself at first disposed to accept this interpretation, but subsequent reflection led me to think that, to say the least, it required confirmation. It occurred to me that if it were true that the fluidity of blood below 40° was due to free ammonia retained in it, coagulation would take place immediately, in spite of the cold, if the alkali were neutralized by the addition of acid, provided the fibrine were not impaired in its coagulating property by the reagent employed. In order to ascertain whether this result would really follow, I poured blood freshly shed from a sheep into vessels surrounded by ice-cold water, and by this means succeeded in keeping some portions of it fluid for a considerable time, and found that it continued liquid notwithstanding the addition of dilute acetic acid in what I supposed must be

[1] For some of these facts see 'On the Early Stages of Inflammation,' Philosophical Transactions for 1858, pp. 673, et seq.

[2] See Dr. Richardson's *Astley Cooper Prize Essay*, p. 303, where a fact is mentioned, indicating that no ammonia was given off at 34° Fahr. from a specimen of blood which had been artificially ammoniated, and which at 96° afforded distinct evidence of evolution of the alkali.

sufficient quantity to overcome the feeble alkalinity of the blood, while the acidulated specimen retained the property of coagulating very rapidly when raised in temperature. But on attempting to discover whether this blood was really acid in reaction, I found that its red colour entirely vitiated the indications of both litmus and turmeric ; and even the serum obtained after contraction of the clot was too much tinged to admit of the satisfactory application of the test-paper.

Being thus baffled in my experiments with the sheep, I had recourse to the horse, in which the red corpuscles subside with peculiar rapidity in the plasma, giving rise to the buffy coat well known to occur in the blood of that animal in the state of health, so that the opportunity would be presented of obtaining liquor sanguinis free from red corpuscles, to which the tests could be applied without risk of fallacy. Accordingly, yesterday afternoon, a horse having been placed at my disposal by my friend Mr. Gamgee of the New Veterinary College, I tied into the right jugular vein one end of a piece of vulcanized india-rubber tube, four yards in length, the greater part of which was coiled up in a freezing mixture, and some of the blood, having been allowed to remain for a while in the tube, was shed into vessels standing in ice-cold water. Its temperature on first escaping into the air was $39\frac{1}{2}°$ Fahr., and having been since kept in the cold it is still only partially coagulated at the present time (twenty-nine hours after it was shed). At first, however, it appeared as if we were likely to fail, the blood of this horse being a rare exception to the general rule, in exhibiting for a long time no appearance of the 'sizy' layer. But after it had stood for about two hours, I succeeded in removing from the surface, by means of a glass tube, a sufficient amount of liquor sanguinis for the performance of an experiment, taking care that the glass into which it was shed, and the tube, were both near the freezing-point. To half a drachm of this plasma I now added one minim and a half of moderately dilute acetic acid, which had the effect of rendering it distinctly acid, as indicated by its communicating a red tint to litmus and restoring the colour of turmeric paper which had been reddened by dipping it in the portion of the liquor sanguinis which had not been acidulated. I kept the specimen in ice-cold water till this evening. For a long time it remained perfectly fluid, except the formation of little soft coagulum at the surface, just as in the unacidulated blood ; but a few drops placed in a watch-glass and brought into a warmer atmosphere, coagulated in about the same time as the blood that first flowed from the tube, a soft clot forming in about a quarter of an hour. Even at the expiration of twenty-four hours a portion of what remained in the cold was still fluid, though faintly acid, but set into a pretty firm clot on being removed into a warmer situation.

[Mr. Lister now proceeded to perform a similar experiment before the Society. A glass containing some liquor sanguinis of the horse's blood, shed twenty-nine hours before, was taken out of the mixture of ice and water in which it stood, and the contents were seen to be still to a considerable extent fluid, although acidulated with acetic acid two hours previously. A portion of the liquid was poured into a watch-glass, and, having been shown to be acid by litmus paper, was set aside to coagulate, and about a quarter of an hour later was exhibited as a soft clot. Mr. Lister then continued :—]

From these facts it is obvious that the ammonia theory utterly fails to explain the influence of temperature on coagulation. The circumstance that the liquor sanguinis was acid in this experiment is clear proof that it contained no free ammonia whatever, yet the acidulated plasma was affected by cold and heat, just like ordinary blood. It remained fluid near the freezing-point, although the ammonia it originally contained must have entered into combination and lost its reputed power of dissolving the fibrine, and it coagulated when warmed, though the ammonia, fixed by the acid, must have been incapable of evolution. If the author of the ammonia theory were asked to explain why this horse's blood took a quarter of an hour to coagulate, he would no doubt reply that it must have contained a large amount of ammonia, requiring all this time to escape. But we have seen that the acid liquor sanguinis, though possessing no free ammonia at all, took as long to clot. There can therefore I think be little question but that the slowness of coagulation in the horse, compared with the rapidity of the process in the sheep, and the variations met with in the period in the human species, depend not on the amount of ammonia present in the blood, but on differences in its other constituents, and, speaking generally, that the theory which attributes the coagulation of the blood to the escape of ammonia is fallacious.[1]

[1] Since the above communication was made, I have seen for the first time the able essay of Dr. E. Brücke, which competed for the Astley Cooper Prize (see *Med.-Chir. Review*, vol. xix) ; and I find that the principle which he advocates—viz. that the fluidity of the blood within the living body depends upon an action of the walls of the vessels upon it—is supported by many facts which he has observed in the chelonian reptile, very similar to what I have made out in mammalia. Thus, he found that the blood remained fluid in the heart of the turtle for days after death, and for several hours after he had blown air through the veins of the neck, so as to make a foamy mixture in the cavities of the organ. He also found, as had been previously ascertained by Virchow and others, that after the introduction of mercury into the heart the blood coagulated about the globules of the metal, but not elsewhere, and this he regarded as an example of the influence of ordinary matter in inducing coagulation in its vicinity. He also succeeded with the following very striking experiment, which would not have answered with mammalia : he drew blood into a cup from the veins of a living turtle, and injected it into the empty heart of another turtle just killed, and found that the blood remained fluid for several hours in its new situation, instead of coagulating in a few minutes as when retained in a cup.—J. L.

ON THE COAGULATION OF THE BLOOD

THE CROONIAN LECTURE

Delivered before the Royal Society of London, June 11, 1863.

[*Proceedings of the Royal Society of London*, 1863.]

THE subject on which I have the honour to address you this evening is one which lies at the foundation both of Physiology and Pathology, and, on account of its great importance, has engaged the best energies of many very able men, among whom may be mentioned, for example, such distinguished Fellows of this Society as John Hunter and Hewson ; so that it might well seem presumptuous in me to hope to communicate anything new regarding it, were it not that the constant progress of Physiology and the allied sciences is ever opening up fresh paths for inquiry, and ever affording fresh facilities for pursuing them. Indeed, my difficulty, on the present occasion, does not depend so much on the lack of materials as on the complicated relations of the subject, which make me almost despair of being able, in the short time that can be devoted to a lecture, to give, in anything like an intelligible form, even an adequate selection of the facts at my disposal.

It may, in the first place, be worth while, more especially for the sake of any present who may not be physiologists, to mention very briefly some well-known general facts respecting the constitution of the blood. The blood, if examined by the microscope within the vessels of a living animal, is seen to consist of a liquid and numerous small particles suspended in it. The liquid is termed the ' liquor sanguinis ', the particles the ' blood-corpuscles '. Of these corpuscles a few are colourless, and are named the ' colourless ' or ' white corpuscles '. The great majority are coloured and cause the red appearance of the blood, and hence are called the ' red corpuscles '. Soon after blood has been shed from the body, it passes from the fluid into the solid form. This depends upon the development in the blood of a solid material termed ' fibrine ', so called from its fibrous nature, consisting, as examined by the naked eye, of tenacious fibres, and having the same character also under the microscope. These fibres form a complicated network among the blood-corpuscles, and from their tenacity are the cause of the firmness of the clot. Soon after the process of solidification or coagulation is complete, the fibrine exhibits a disposition to shrink, and squeezes out from among the corpuscles entangled in its meshes a straw-coloured fluid termed the serum, very rich in albumen, in fact very similar in chemical composition to the fibrine, which, in its turn, may be said to be identical chemically with the material of muscular fibre.

The question before us, therefore, is, What is the cause of the development of this solid material, the fibrine? The subject may be looked at in two aspects—first, as to the essential nature of the process of coagulation; and secondly, as to the cause of its occurrence when the blood is removed from the body.

With regard to the first point, the essential nature of the process of coagulation, different views have been entertained. John Hunter was of opinion that the coagulation of the blood, the solidification of the fibrine, was an act of life—analogous, in some respects, to the contraction of muscular fibre. This, on the other hand, was made very unlikely by the observation of his contemporary, Mr. Hewson, that blood may be kept in the fluid state by the addition of various neutral salts, but retains the faculty of coagulating when water is added to the mixture. Mr. Gulliver, on one occasion, kept blood fluid, by means of nitre, for upwards of a year, but found that it still coagulated on the addition of water. It seems exceedingly improbable that any part of the human body should retain its vital properties after being thus pickled for more than a year. But here I would wish to make an explanation of the use of this term ' vital properties '. When employing it, I do not wish to commit myself to any particular theory of the nature of life, or even to the belief that the actions of living bodies are not all conducted in obedience to physical and chemical laws. But it appears that every component tissue of the human body has its own life, its own health, just as we ourselves have; and as the actions of living men will ever retain their interest whatever views be entertained of the nature of life, so must the actions of the living tissues ever continue to be essential objects of study to the physiologist and pathologist. When, therefore, I use the term ' vital properties ', I mean simply properties peculiar to the tissues as components of the healthy living body.

Turning now to the other aspect of the subject of coagulation—the cause of the occurrence of that process on the escape of the blood from the living body—we find that here again various theories have been held, which may be divided into mechanical, chemical, and vital. The mechanical theory was, that mere rest of the blood was sufficient to cause coagulation. I say this *was* the theory; but I believe it will be found to be still taught by many that the cause of the coagulation of the blood in an artery which has been tied is its stagnation in the vicinity of the ligature.

As to the chemical theories they have been various. One very natural view was that exposure to the air was the essential cause of coagulation. Mr. Hewson believed that this was, at all events, an important element in the causes of the phenomenon ; and many eminent physiologists and pathologists have held the same view, except that, instead of the air as a whole, the oxygen of the air has been supposed to be the important element.

Sir Charles Scudamore considered that coagulation was greatly promoted by the escape of carbonic acid ; and more recently the evolution of ammonia has been regarded as the essential cause of the change. According to the ammonia theory, due to Dr. Richardson of this city, the fluidity of the blood within the body depends on a certain amount of free ammonia holding the fibrine in solution, and the coagulation of the blood when withdrawn from the vessels is the result of the escape of the volatile alkali.

Then, as to vital theories. These have been held by many physiologists, among whom may be mentioned Sir Astley Cooper and Mr. Thackrah, who, from experiments which they performed, were led to the inference that the living vessels exert an active influence upon the blood, by which coagulation is prevented ; and Mr. Thackrah went so far as to attribute this action of the vessels to nervous influence. The view that the blood is kept fluid by the operation of its natural receptacles has been advocated more recently by Brücke of Vienna, whose essay will be found in the *British and Foreign Medical Review* for 1857. Brücke performed his experiments on turtles and frogs, in which animals the blood remains fluid in the heart for days after death ; and I feel bound to say that some of the facts which he has brought forward seem to me quite sufficient to show that the ammonia theory, whatever amount of truth it may contain, cannot be the whole truth, and cannot explain the fluidity of the blood within the body. For example, Brücke found that, having shed blood from the heart of a living turtle into a basin, and transferred, with a syringe, a portion of that blood into the empty heart of another turtle just killed, the blood thus transferred into the empty heart remained fluid for hours, whereas that which was left in the basin coagulated in a few minutes. He also found that blood continued fluid in the heart of a turtle long after the injection of air into the heart through a vein till the cavities of the organ contained a foamy mixture of blood and air.

Yet it by no means follows that the vital theory and the ammonia theory are necessarily altogether inconsistent. It might be true for anything we could tell, *a priori*, that the coagulation of the blood, when shed from the body, might depend on the evolution of a certain amount of ammonia, previously holding the fibrine in solution, and yet it might, at the same time, be true that the cause of the ammonia remaining in the blood in the healthy vessels might be an action of the living vessels retaining it there. It might be that an action of the living vessels might chain down the ammonia and prevent it from escaping, whereas, when shed from the body, it would be free to escape.

This notion was, I confess, at one time entertained by myself ; and one of my earliest experiments was performed with a view to the corroboration of the ammonia theory as applied to blood outside the body. It seemed to me desirable that further evidence should be afforded of the effect of mere occlusion from air in maintaining the blood fluid. If the ammonia theory were true, then if blood could be shed directly from a living vessel into an air-tight receptacle composed of ordinary matter it ought to remain fluid. For this purpose, I made the following experiment:—I tied into the jugular vein, V (Fig. 1), of a sheep a long vulcanized india-rubber tube, T, adapted by means of short pieces of glass tube at its extremities, both ends being connected with the vessel so that the current of blood might be permitted to flow through the tube, and then continue its natural course. When it had been ascertained that the blood was circulating freely through the tube, which could be readily done by placing the finger on the cardiac aspect of the vein, which was then made to swell if the circulation was proceeding through the tube, pieces of string well waxed were tied at intervals of about two inches round the tube, which was thus converted into a number of air-tight receptacles containing blood, which certainly had no opportunity for the escape of ammonia. The tube was then removed, and I found, in accordance with the view which I was then disposed to entertain, that the blood, instead of coagulating completely in a few minutes as it would have done if shed into a cup, remained partially fluid in these receptacles after the lapse of three hours. But I have since found that if the experiment be repeated in the same way as regards its earlier stages, and if, after a few of the strings have been tied on, the tube be cut across, the blood which is in the part of the tube in the vicinity of the air, just like that which is in the air-tight receptacles, remains fluid in part for two or three hours. In short, that my precautions in ensuring that these receptacles should be air-tight were, in so far as they applied to that object, utterly unnecessary. I mention this partly as an illustration of the deceptions to which one is liable in this inquiry, and partly because the experiment thus modified seems to tell as clearly against

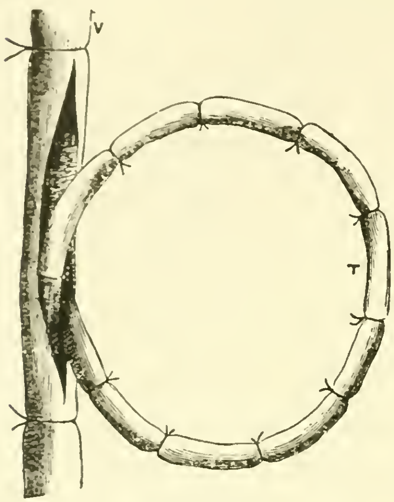


Fig. 1.

the ammonia theory as the original one seemed to tell in favour of it. Those receptacles which had been formed by the application of ligatures before the tube was opened afforded certainly no opportunity for the escape of ammonia, and yet in them the blood coagulated as quickly as in those which had communication with the air—implying that facility for the evolution of ammonia does not in itself affect the process of coagulation at all.

How then, it may be said, is the persistent fluidity of the blood under these circumstances to be explained? That will become more obvious than I can make it at present in the sequel, but in the meantime I may observe that there are probably two explanations: one is, the coolness of the tube, and the other, far more important, that the blood, in slipping through this cylindrical tube, had had little opportunity of being influenced by its walls. The portion of the blood that came first in contact with the walls of the tube had coagulated; and it is to be observed that I never found, in these experiments, the blood altogether fluid, even after a comparatively short time: there has always been a certain amount of coagulation, and only a certain amount of fluidity. A layer of blood having thus coagulated upon the internal surface of the tube, the fresh blood, which continued to flow through it, was not brought into contact with the walls of the tube at all, but with their lining of coagulated blood.

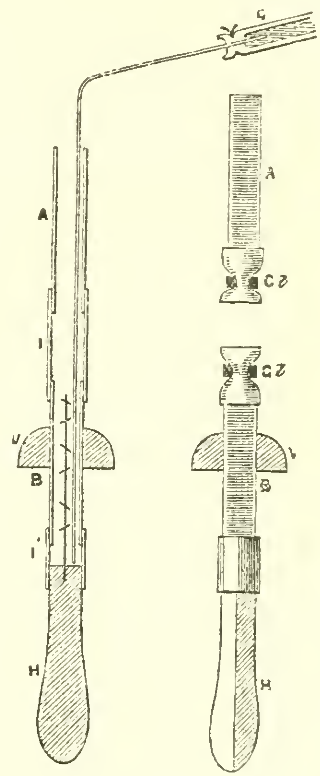


Fig. 2.

It has been long known that if blood is stirred with a rod, the process of coagulation is promoted. It seemed desirable to ascertain distinctly whether the cause of this was the contact of the foreign solid, or the opportunity given for the escape of ammonia; for it is quite true that, in the ordinary process of stirring blood, more or less air is mixed with it. For the purpose of determining this I devised a somewhat complicated experiment, which, however, it may be worth while to mention. I made an apparatus (Fig. 2) of two portions of glass tube, A and B, connected in a vertical position by means of vulcanized india-rubber, I, the lower portion of the glass tube being also connected by india-rubber, I′, with a wooden handle, which handle, H, was provided with an upright piece of wire, from which spokes projected in different directions, so that they would, when moved, act as a churn on any blood contained in the lower portion of tube. When the lower piece of tube was fixed by mean of a vice, V, the flexibility of the india-rubber permitted the churn to be rotated so as to expose the blood to its influence. This having been arranged, I first poured in strong liquor ammoniae, so as to get rid of any slight acidity which the constituents of the apparatus might be conceived to possess, and then, having poured out the ammonia, filled up the apparatus with water, and boiled the whole in a large glass test-tube till all bubbles of air, in any portion of it, were expelled. Having then tied into a branch of the carotid artery, C, of a calf a bent tube of small diameter, as represented, and having permitted the blood to flow till it escaped at the orifice of the tube, I compressed the artery and passed the tube down through the water to the bottom of the apparatus, and then let the blood flow again, which had the effect of displacing all the water ; and when the blood appeared at the top of the apparatus, the tube was withdrawn, when two effectual clamps, Cl, Cl, were placed on the vulcanized india-rubber connecting A and B ; the india-rubber was then divided between the clamps, and we had the state of things represented at the right-hand side of the diagram. The upper portion of the apparatus, the orifice of which was exposed to the air, was set aside and left undisturbed. Having ascertained that the lower portion had been effectually sealed by the clamp, and thus prevented from any opportunity of escape of ammonia, I subjected it to the action of the churn for a certain number of minutes. It so happened that the blood of that calf was very slow in coagulating. I knew this from previous experiments on the animal, and therefore continued the action of the churn for a considerable time, viz. thirty-seven minutes. I then found the wire enveloped in a mass of clot ; and examination of the fluid residue with a needle indicated that the fibrine had been all withdrawn from the blood on which the churn had acted. I did not now examine the other portion of the apparatus, which had been set aside, but at the end of an hour and a quarter, when more than double the time had elapsed, I investigated this, and found the blood in it, for the most part, still fluid and coagulable. Thus the blood in the churn, which, from the time it left the artery, had no opportunity of parting with its ammonia, coagulated much more rapidly than that in an open vessel. The difference between the two was that the lower portion of the blood had been freely exposed to the influence of the foreign solid, whereas the other had only been subjected to the action of the wall of the tube.

The same principle may be illustrated by an exceedingly simple experiment which I performed only this very day. Receiving blood from the throat of a bullock into two similar wide-mouthed bottles, I immediately stirred one of them with a clean ivory rod for ten seconds very gently, so as to avoid the introduction of any air, and then left both undisturbed. At the end of a certain number of minutes I found that, while the blood which had not been disturbed could be poured out as a fluid, with the exception of a thin layer of clot on the surface, and an incrustation on the interior of the vessel, the blood in the other vessel, which had been stirred for so brief a period, was already a solid mass.

I have only lately been aware of the great influence exerted upon the blood by exposure for a very short time to a foreign solid, and I feel that many of my own experiments, and many performed by others, have been vitiated for want of this knowledge. Take, for example, the effect of a vacuum, which was observed by Sir Charles Scudamore to promote coagulation. This has been considered by Dr. Richardson as an illustration of his theory, the vacuum being supposed to act by favouring the escape of ammonia. I have lately inquired into this subject, and I feel no doubt whatever that the greater rapidity of coagulation in a vacuum depends simply on the greater disturbance of the fluid. I made the following experiment :—I filled three bottles, such as these, from the throat of a bullock, placed one of them under the small bell jar of an air-pump in good order and exhausted it, leaving the other two undisturbed. The blood happened to be slow in coagulating, and at the end of about forty minutes, in the vessels where the blood had been undisturbed, there was only a slight film of coagulum on the surface, whereas the blood under the vacuum was found on examination to have a very thick crust of clot upon it. But during the process of exhaustion the blood had bubbled very much. Indeed, any exhaustion of blood recently drawn which is sufficient to cause the evolution of its gases induces great bubbling, so that the pump cannot be used freely for fear of the froth overflowing. To this disturbance, involving the exposure of successive portions of blood in the bubbles to the sides of the vessel, I was inclined to attribute the more rapid coagulation ; but in order to prove the point, I stirred for a few seconds the blood in one of the vessels hitherto undisturbed. After eight minutes I emptied the three vessels. I found that that blood which had not been disturbed at all, either by the vacuum or by the rod, was still almost entirely fluid, only showing a thin crust upon the glass and on the surface exposed to the air. The blood which had been subjected to the vacuum had a thick crust of clot on the surface, and the sides of the glass were also thickly encrusted, but it still contained a considerable quantity of fluid that could be poured out from its interior. But that blood which had been stirred for only a few seconds was a solid mass throughout. In other words, gentle stirring of the blood for a few seconds had much greater effect in producing coagulation than the protracted and efficient exhaustion which was continued for upwards of forty minutes, which was a considerable time after all evolution of gas, as indicated by bubbles, had ceased.

Other experiments precisely similar in their effect were performed. I therefore feel no hesitation in stating that the effects of a vacuum, regarding which, indeed, the statements of different experimenters have hitherto been conflicting, afford no evidence in favour of the ammonia theory.

There is another point of very great interest in the history of the coagulation of the blood, which has been supposed to give support to the ammonia theory; and that is, the effect of temperature. It has been long known that blood coagulates more rapidly at a high than at a low temperature, and, indeed, a little above the freezing-point remains entirely fluid. This seemed beautifully in harmony with the ammonia theory, as heat would naturally promote, and cold retard the evolution of the alkali, and a depression of temperature to near the freezing-point might be reasonably supposed to prevent its escape altogether. Indeed, Dr. Richardson mentions as a fact, that ammonia artificially mixed with blood ceases to be given off under such circumstances.

Though thinking it not unlikely that this was the true explanation of the influence of temperature on coagulation, I thought it worth while to subject the matter to experiment. For that purpose I kept the blood of a horse fluid by means of a freezing mixture, and afterwards by ice-cold water; and when the corpuscles had subsided from the upper part of the blood, I cautiously added to the liquor sanguinis extremely dilute ice-cold acetic acid till it was of distinctly acid reaction, the liquor sanguinis being of a colour that permitted the delicate application of test-paper, which is impossible with red blood. By this means any free ammonia which the fluid might have contained must have been neutralized, yet so long as it was kept in the cold it continued fluid, but when brought into a warm room coagulated just as a specimen which had not been acidulated. Thus, when there could be no free ammonia in the liquor sanguinis at all, it was still affected as usual by temperature.

This experiment may not be satisfactory to all minds, though I confess it appears so to me; and, as this is a point of very great interest, I have sought in another way for evidence regarding it. First, however, I will mention an experiment which will not at once appear to bear on the question of temperature. I drew out a fine glass tube in such a way as to produce a fusiform receptacle continued longitudinally each way into a tube of almost capillary fineness for about two inches, which again expanded at the end, as represented in Fig. 3. Having squeezed out a drop of blood from my finger, I sucked up a portion into the tube till the receptacle A and its capillary extensions were filled. I then broke off the expanded ends, and placed the little tube thus filled, B, in a bath of the strongest liquor ammoniae. Here certainly the blood was in circumstances in which it could not lose ammonia, but where any change in its amount must be by way of increase, and yet I found, on opening the receptacle by snapping it across after a scratch with a file, that instead of remaining longer fluid than in a watch-glass, the blood in it, being more in contact with the glass, was always more quickly coagulated, while coagulation was still more rapid in the capillary tube, where the blood was still more exposed to the influence of the foreign solid—the greater proximity to the liquor ammoniae having no influence upon it.

It may perhaps be argued that the drop of blood employed being a small drop, and this small drop having been drawn up by suction into the tube, it might have parted with its ammonia before it got into the tube ; but then (and now comes the bearing of the experiment on the effect of temperature) I found, if I placed a similar tube filled in the same way in a vessel of snow,

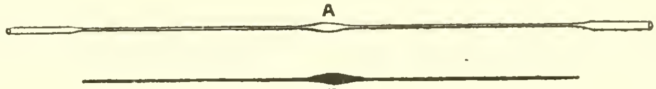


FIG. 3.

so as not to freeze it but to keep it ice-cold, the blood in it remained fluid as long as I chose to keep it there. Now if all the ammonia had left the blood before it was introduced into the tube, cold ought, according to the ammonia theory, to have had no effect in retarding its coagulation ; for, according to that theory, cold operates by retaining the ammonia. On the other hand, if we take the other alternative and suppose that any ammonia which the blood might have contained was still in these tubes, the former experiment proves clearly that the retention of ammonia has no effect in producing fluidity—no effect in preventing coagulation ; and if the retention of ammonia has no effect in preventing coagulation, then cold certainly cannot prevent coagulation by retaining the ammonia, because, even if retained, it would not influence the result. In whatever way we look at them, therefore, these simple experiments prove conclusively that cold maintains the fluidity of the blood in some manner unconnected with any influence it may exert upon ammonia.

Then, again, I varied the experiment in this way. I placed such little tubes of blood in baths of liquor ammoniae at different temperatures. By careful management, guarding against the volatilization of ammonia and consequent reduction of temperature, I succeeded in employing satisfactorily a bath of liquor ammoniae at 100° Fahr., the blood being in the bath within a few seconds of its leaving the vessels of my finger, and I found that the high temperature, though under such circumstances it could not possibly dissipate any ammonia from the blood, yet accelerated its coagulation in precisely the same way as when it was applied to blood in watch-glasses exposed to the air.

It is clear, then, that the promotion of the solidification of fibrine by heat is as independent of the evolution of ammonia as the coagulation of albumen under the same agency. Indeed, it seems probable that the two cases are analogous, except that a higher temperature is required in the one than in the other.

When fine tubes containing blood were placed in liquor ammoniae, the alkali acted only upon those parts which were close to the ends of the tubes; a very small portion was rendered brown by it, and beyond that a little was kept permanently fluid, but the chief length of the blood in the tube was unaffected. Having thus ascertained that ammonia travels so slowly along tubes of this capillary fineness, I thought I might have an opportunity of giving the ammonia theory a fair test by tying such a tube as has been above described into the jugular vein of a rabbit and filling it directly from the vessel, and then ascertaining whether there was any evidence of retardation of coagulation in the blood thus imprisoned. But I could discover no such evidence, although I sought for it in confirmation of a view I then held. To this, however, there is one special exception to be made, viz. in the case of asphyxia. I found that if two such tubes were filled from the same blood-vessel of a creature, one under normal circumstances, and the other after asphyxia had been induced, there was a most remarkable difference between the rates of coagulation of the blood in the two tubes, the asphyxial blood coagulating very much more slowly than the ordinary blood; but when the asphyxial blood was shed into a watch-glass and air was blown through it, it coagulated rapidly, showing that in the state of asphyxia there must be some volatile element in the blood which has an effect in retarding coagulation.

Supposing at first that this volatile element must be ammonia, I hoped to be able by chemical means to find evidence of its accumulation in asphyxia, and thus add a fact of great interest to physiology. Imitating experiments previously made by Dr. Richardson, I passed air successively through blood and through hydrochloric acid, and then estimated the amount of ammonia acquired by the latter by means of bichloride of platinum. In order to prevent the possibility of the loss of any ammonia, I directed blood from the carotid artery of a calf fairly into a Wolfe's bottle by means of a vulcanized india-rubber tube tied into the vessel, and then drew a certain volume of air through it by means of an aspirating jar, the experiment being performed first before, and then during asphyxia. The same procedure was adopted with a second calf, the animal being in each case under chloroform, which does not interfere with the development during asphyxia of the peculiarity in the blood above alluded to, but I could not find satisfactory evidence of accumulation of ammonia ; and without going further into the question at present, I may say that it seems much more probable that the effect is due to carbonic acid, which is known to have a retarding influence on coagulation, and which probably accumulates greatly in asphyxial blood.

But in justice to the author of the ammonia theory, and to myself, too, who at one time expressed a qualified belief in it, it is but fair to say that this theory is extremely plausible. It has been well shown by Dr. Richardson that ammonia is a substance well fitted to keep the blood fluid if it be present in a sufficient quantity. An experiment of my own illustrates very well the same point. I drew out a tube about a quarter of an inch in calibre (Fig. 4), so that

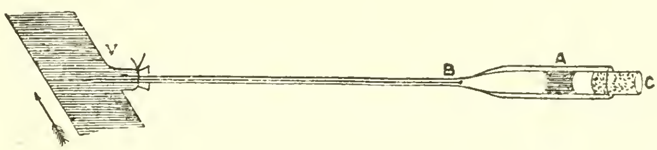


Fig. 4

while for two inches at one end it retained its original width, the rest (some ten inches) was pretty narrow, though far from having the capillary fineness of those before described. Into the thick part I introduced a drop of strong liquor ammoniae, A, and then securely corked that end of the tube, C. The object of this was that there should be a strong ammoniacal atmosphere in the narrow part of the tube. I then opened a branch of a vein, V, in the neck of a sheep, introduced the narrow end of the tube into the vessel, and pushing it in so that its orifice should be in the current of the main trunk of the vein, tied it in securely. I then removed the cork and made pressure on the vein at the cardiac side, causing the vessel to swell and blood to pass into the fine part of the tube, and before the blood had reached the part of the glass moistened by the ammonia I put in the cork again and withdrew the tube. In a short time, on introducing a hook of fine wire into the extremity of the tube, I found the blood already coagulated, but on filing off a small portion of the tube I found the blood there fluid. The portion of blood thus exposed soon coagulated, when, a second small piece of the tube being removed by the file, fluid blood was again disclosed, which again soon coagulated ; and this proceeding was repeated with the same results time after time, till, near the thick part of the tube, the ammonia in the blood was so strong as to prevent coagulation altogether.

This experiment illustrates how fitted the ammonia is to maintain the fluidity of blood, and also how apt it is, when present in the blood, to fly speedily off from it, leaving it unimpaired in its coagulating properties ; and it must be confessed that the end of the tube sealed with a small clot resembled most deceptively the extremity of a divided artery similarly closed. But although the experiment seems in so far to favour the ammonia theory, it will tell differently when I mention the object with which it was performed. It appeared to me that, if the cause of the fluidity of the blood was free ammonia, then, if I provided an ammoniacal atmosphere in the tube, and introduced blood by pressure directly from the vein into this ammoniacal atmosphere, this blood, lying between the strong ammoniacal atmosphere on the one side and the ammonia naturally present in the blood within the vein on the other side, ought to remain fluid ; and if it did remain fluid, this would tend to confirm the ammonia theory by making it appear that the volatile material was the same at both ends of the tube. But, to my disappointment, I invariably found that if I drew away the tube after a few minutes only had elapsed, there was already a clot in its extremity ; in other words, the ammonia had diffused from the end of the tube into the blood within the vein as into a non-ammoniacal atmosphere. This experiment alone, if duly considered, would, I think, suffice to show that the blood does not contain enough ammonia to account for its fluidity.

FIG. 5.

One more experiment, however, may be adduced with the same object. I mounted a short but wide glass tube, open at both ends (T, Fig. 5), upon the end of a piece of strong wire, W, and connected with the latter a coil of fine silver wire, S, so that it hung freely in the tube. I then opened the carotid artery of a horse, and through the wound instantly thrust in the apparatus so far that I was sure the tube lay in the common carotid, which in veterinary language means the enormous trunk common to both sides of the neck of the animal. The tube being open at both ends, and slightly funnel-shaped at that end which was directed towards the heart, had thus a full current of arterial blood streaming through it. Having ascertained how long the arterial blood took to show the first appearance of coagulation in a watch-glass, I very soon after removed the apparatus, and, on taking out the coil of silver wire, found that it was already crusted over with coagulum. Yet here assuredly there had been no opportunity for the escape of ammonia.

From this experiment it is obvious that there is a very great difference between ordinary solid matter and the living vessels in their relation to the blood. But the same conclusion may be drawn much more simply from experiments which I had the opportunity of performing after making an observation which it seems strange should have been left for me to make, and which, I may say, was made by myself purely accidentally; and this is, that the blood of mammalia, although it coagulates soon after death in the heart and the principal arterial and venous trunks, remains fluid for an indefinite period in the small vessels. If, therefore, a ligature be tied round the foot of a living sheep a little below the joint which is divided by the butcher, the foot being removed and taken home with the blood retained in the veins by the ligature, we have a ready opportunity of investigating the subject of coagulation, and of making observations as satisfactory as they are simple. Here are two feet provided in the way I have alluded to. A superficial vein in each foot has been exposed. The veins I see have contracted very much since I reflected the skin from them before our meeting; and I may remark that such contraction, dependent on muscular action, may occur days after amputation, indicating the persistence of vital properties in the veins. Now as I cut across this vein, blood flows out, fluid but coagulable. Into the vein of this other foot has been introduced a piece of fine silver wire, and when I slit up the vein you will see the effect it has produced. Exactly as far as the silver wire extends, so far is there a clot in this vessel. Now this experiment, very simple as it is, is of itself sufficient to prove the vital theory in the sense that the living vessels differ entirely from ordinary solids in their relation to the blood. It is perfectly clear that by introducing a clean piece of silver wire (and platinum or glass or any other substance chemically inert would have had the same effect) I do not add any chemical material or facilitate the escape of any, and yet coagulation occurs round about the foreign solid.

Again, if a blood-vessel be injured at any part, coagulation will occur at the seat of injury. As a good illustration of this, and also as bearing upon the ammonia theory, I may mention the following experiment. Having squeezed the blood out of a limited portion of one of the veins of a sheep's foot, and prevented its return by appropriate means, I treated the empty portion with caustic ammonia, the neighbouring parts of the vein being protected from the irritating vapour by lint steeped in olive oil. After the smell of ammonia had passed off, I let the blood flow back again and left it undisturbed for a while, when I found on examination a cylindrical clot in the part that had been treated with ammonia, while in the adjacent parts of the same vessel the blood remained fluid. I repeated this experiment several times and always with the same result. Where the ammonia had acted there was a clot. The chemical agent used here was one which, so long as any of it remained, would keep the blood fluid, yet its ultimate effect was to induce coagulation, the vital properties of the vein having been destroyed by it.

If a needle or a piece of silver wire is introduced for a short time into one of the veins of the sheep's foot, it is found on withdrawal to be covered over with a very thin crust of fibrine, whereas the wall of the vessel itself is never found to have fibrine or coagulum adhering to it unless it has been injured. Now this seems to imply that the ordinary solid is the active agent with reference to coagulation—that it is not that the blood is maintained fluid by any action of the living vessels, but that it is induced to coagulate by an attractive agency on the part of the foreign solid. We see at any rate that the foreign solid has an attraction for fibrine which the wall of the vessel has not.

And yet I own I was at first inclined to think that the blood-vessels must in some way actively prevent coagulation. There were two considerations that led to this view. One was, that the blood remained fluid in the small vessels after death, but coagulated in the large. Now why should that be ? It seemed only susceptible of explanation from there being some connexion between the size of the vessel and the circumstance of coagulation. It looked as if in the small veins the action of the wall of the vessel was able to control the blood and keep it fluid, but that the large mass in the principal trunks could not be so kept under control. The other circumstance was the rapid coagulation of a large quantity of blood shed into a basin. Why should this occur unless there was some spontaneous tendency in the blood to coagulate ? It seemed scarcely credible that it was the result of contact with the surface of the basin.

Both these notions, however, have since been swept away. In the first place, I have observed recently that it is by no means only in small vessels that the blood remains fluid after death. If blood be retained within the jugular vein of a horse or ox by the application of ligatures, either before or after the animal has been struck with the pole-axe, it will often continue fluid, but coagulable, in that vessel, which is upwards of an inch in diameter, for twenty-four or even forty-eight hours after it has been removed from the body. I say often, but not always. The jugular vein seems to be in that intermediate condition, between the heart and the small vessels, in which it is uncertain whether it will retain its vital properties for many hours, or will lose them in the course of one hour or so. Unfortunately for my present purpose, it happens that in this jugular vein, removed from an ox six hours ago, coagulation has already commenced, as I can ascertain by squeezing the vessels between my fingers. But now that I lay open the vessel, you observe that the chief mass of its contained blood is still fluid, and we shall at all events have an opportunity of seeing that what is now fluid will in a short time be coagulated. It is an interesting circumstance with reference to the question which we are now considering, that the coagulation always begins in contact with the vein, indicating that it is not the wall of the vessel that keeps the blood fluid, but that, on the contrary, the wall of the vessel, when deprived of vital properties, makes the blood coagulate.

The observation of the persistent fluidity of the blood in these large vessels furnished the opportunity of making a very satisfactory experiment, which I hoped to have exhibited before the Society, but as there was some clot in the vein I did not think fit to run the risk of failure. The experiment is performed in the following way. A piece of steel wire is wound spirally round one of the veins in its turgid condition, and with a needle and thread the coats of the vessel are stitched here and there to the wire, care being taken to avoid puncturing the lining membrane, and thus the vessel is converted into a rigid cup. Two such cups being prepared, and the lining membrane of the vein being everted at the orifice of each so as to avoid contact of the blood with any injured tissue, I found that, after pouring blood to and fro through the air in a small stream from one venous receptacle into the other half a dozen times, and closing the orifice of the receptacle to prevent drying, the blood was still more or less completely fluid after the lapse of eight or ten hours. On the other hand, if a fine sewing needle is pushed through the wall of an unopened vessel so that its end may lie in the blood, it is found on examination, after a certain time has elapsed that the needle is surrounded with an encrusting clot. It is scarcely necessary to point out how entirely the ammonia theory and the oxygen theory, as well as that of rest, fail to account for facts like these.

While the blood may remain fluid for forty-eight hours in the jugular vein of a horse or an ox, it coagulates soon after death in the heart of very small animals, such as mice, so that it is obvious that the continuance of fluidity in small vessels is not due to their small size.

It is a very curious question, What is the cause of the blood remaining so much longer fluid in some vessels than in others ? I believe that we must accept it simply as an ultimate fact, that just as the brain loses its vital properties earlier than the ganglia of the heart, so the heart and principal vascular trunks lose theirs sooner than the smaller vessels of the viscera, or than more superficial vessels, be they large or small. We can see a final cause for this, so to speak. So long as the heart is acting, circulation will be sure to go on in the heart and principal trunks ; whereas, on the contrary, the more superficial parts are liable to temporary causes of stagnation, and occasionally to what amounts to practical severance from vascular and nervous connexion with the rest of the body ; and it is, so to speak, of great importance that the blood should not coagulate so speedily in the vessels of a limb thus circumstanced as it does in the heart after it has ceased to beat. Were it not for this provision, the surgeon would be unable to apply a tourniquet without fear of coagulation occurring in the vessels of the limb. As an illustration of the importance of a knowledge of these facts, I may mention a case that once occurred in my own practice. I was asked by a surgeon in a country district to amputate an arm which he despaired of. The brachial artery had been wounded, as well as veins and nerves, and at last, being foiled with the haemorrhage, he wound a long bandage round the limb at the seat of the wound as tightly as he possibly could. It had been in this condition with the bandage thus applied for forty-eight hours when I reached the patient, and the limb had all the appearance of being dead. It was perfectly cold, and any colour which it had was of a livid tint. But having been lately engaged in some of the experiments which I have been describing, and having thus become much impressed with the persistent vitality of the tissues and the concomitant fluidity of the blood, I determined to give the limb a chance by tying the brachial artery. Before I left the patient's house he had already a pulse at the wrist, and I afterwards had the satisfaction of hearing that the arm had proved a useful one.[1]

One of the two arguments in favour of activity on the part of the vessels as a cause of the fluidity of the blood having been completely disposed of, let us now consider the other, viz. the rapid coagulation of blood shed into a basin, appearing at first sight to imply a spontaneous tendency of the blood to coagulate, such as would have to be counteracted by the vessels. This also has proved fallacious.

In the first place it appears that the coagulation, after all, does not go on in a basin so suddenly as one would at first sight suppose, but always commences in contact with the foreign solid. When blood has been shed into a glass jar, if, on the first appearance of a film at the surface, you introduce a mounted needle curved at the end between the blood and the side of the glass and make a slight rotatory movement of the handle, you see through the glass the point of the needle detaching a layer of clot whatever part you may examine. The process of coagulation having thus commenced in contact with the surface of the vessel into which the blood is shed, may, under favourable circumstances, be ascertained to travel inwards, like advancing crystallization, towards the centre of the mass. It appears, however, that this extension of the coagulating

[1] See above, p. 85.

process would not take place had not the blood been prepared for the change by contact, during the process of shedding, with the injured orifice of the blood-vessel and with the surface of the receptacle. I have only very recently become acquainted with the remarkable subtlety of the influence exerted upon blood by ordinary solids. I was long since struck with the fact that if I introduced the point of an ordinary sewing needle through the wall of a vein in a sheep's foot and left it for twelve hours undisturbed, the clot was still confined to a crust round the point of the needle, implying that coagulum has only a very limited power of extension. I thought, therefore, that by proper management it might be possible to keep blood fluid in a vessel of ordinary solid matter lined with clot. But various attempts made with this object failed entirely, till I lately adopted the following expedient. Having opened the distal end of an ox's jugular vein containing blood and held in the vertical position, taking care to avoid contact of any of the blood with the wounded edge of the vessel, I slipped steadily down into it a cylindrical tube of thin glass, somewhat smaller in diameter than the vein, open at both ends, and with the lower edge ground smooth in order that it might pass readily over the lining membrane, and so disturb the blood as little as possible by its introduction, and influence only the circumferential parts of its contents. The tube was then kept pressed down vertically upon the bottom of the vein by a weight, in a room as free as possible from vibration, and I found on examining it at the end of twelve hours that the clot was a tubular one, consisting of a crust about one-eighth of an inch thick next the glass and the part exposed to the air, but containing in its interior fluid and rapidly coagulable blood. In another such experiment, continued for twenty-four hours, though the crust of clot was thicker, the central part still furnished coagulable blood.

But it may perhaps be argued by those who say that the blood-vessels are active in maintaining fluidity that the small portion of the vein covering the end of the tube was acting upon the blood, which certainly was fluid where in contact with it, the clot being in the form of a tube open at the lower end. To guard against such an objection I made the following experiment :—I extended a tube like that above described by means of thin sheet gutta-percha, G (Fig. 6 *a*), contriving that the internal surface of the gutta-percha should be perfectly continuous with that of the glass tube as represented in section in Fig. 6 *b*. The lower part of the gutta-percha tissue was strengthened by a ring of soft flexible wire such as is used by veterinary surgeons for sutures, and the wire, W, was also extended upwards to the top of the glass so as to maintain the rigidity of the gutta-percha portion during its introduction into a vein, but at the same time, from its softness, permit the gutta-percha part to be bent at a right angle after it had been introduced, and so close the orifice of the glass tube with ordinary solid matter. In Fig. 6 *c* the tube is represented pressed down by a weight in a vein, V, with blood, B, in the glass portion, while the gutta-percha part closes it below. At the same time I performed a comparative experiment, to which I would invite particular attention, although I am sorry at this late hour to occupy the attention of the Society so long. I tied a thin piece of gutta-percha tissue over the lower end of a similar glass tube, and simply poured blood into it from the jugular vein of an ox. I wished to compare the condition of blood which had been simply poured into a tube, with blood which had been introduced without any disturbance of its central parts. But in order to make the

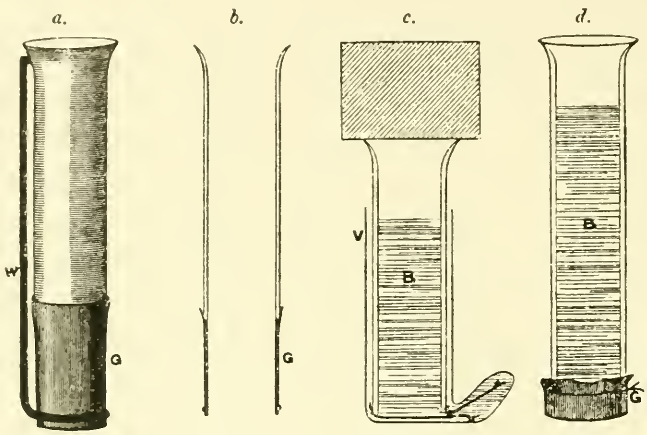


Fig. 6.

experiment a fair one, as it might be said that the blood poured from the vein had been more exposed to the air than that into which the tube was slipped, I proceeded in the following way: I obtained a long vein containing plenty of blood, and having first filled the second tube, with the gutta-percha bottom (Fig. 6 *d*), by simply pouring blood into it from the vein, I cut off a portion of the vein which had been thus emptied, and having tied one end and everted the lining membrane of the other end, and having also everted the lining membrane of the orifice of the remainder of the vessel which was full, I poured the blood from the full portion through the air into the empty part. In doing this I had difficulty in getting blood enough, and it passed through the air in slow drops, and that only when the vein was squeezed by my warm hand. At last, having introduced sufficient for the purpose, I slipped down the compound tube and bent its gutta-percha portion, as represented in Fig. 6 *c*, and left both tubes for a while undisturbed. At the end of three hours and a half I found that the blood which had been simply poured in was a mass of clot, and fluid squeezed from it yielded no threads of fibrine, coagulation being complete. How long it had been so I do not know. I did not examine the other blood until seven hours and three quarters had expired, and then found that, just as in the cases where a simple glass tube was introduced, the clot was tubular, and the chief part of the blood was still fluid in its interior, the only difference being that in this case the clot formed a complete capsule, being continued over the gutta-percha instead of being deficient below, as it was when the vein closed the end of the tube. Now if we consider the two parts of this comparative experiment, we see that the receptacles in which the blood was ultimately contained were precisely similar in the two cases, viz. glass tubes closed below with gutta-percha ; and that the blood which was simply poured into the tube was much less exposed to the air than the other, and also was not subjected, like it, to elevation of temperature, a circumstance which promotes coagulation ; but yet this blood became completely coagulated in a comparatively short time, whereas the other after a much longer time was coagulated only in a layer in contact with the foreign solid. But in the latter case the blood had been so introduced as to avoid direct action of ordinary matter on any but the circumferential parts of it, whereas in the former, though poured quickly, it had run down the side of the glass, and as a consequence of this almost momentary contact with the foreign solid, the central parts, like the circumferential, underwent the process of coagulation.

Mysterious as this subtle agency of ordinary solids must appear, its occurrence is thus matter of experimental demonstration, and by it the coagulation of blood shed into a basin is accounted for ; while it is also shown conclusively from this experiment that the blood, as it exists within the vessels, has no spontaneous tendency to coagulate, and therefore that the notion of any action on the part of the blood-vessels to prevent coagulation is entirely out of the question. The peculiarity of the living vessels consists not in any such action upon the blood, but in the circumstance, remarkable indeed as it is, that their lining membrane, when in a state of health, is entirely negative in its relation to coagulation, and fails to cause that molecular disturbance or, if we may so speak, catalytic action which is produced upon the blood by all ordinary matter.

I afterwards found that the simplest method of maintaining blood fluid in a vessel composed entirely of ordinary matter was to employ a glass tube similar to those above described, except that its upper end was closed by a cork perforated by a narrow tube terminating in a piece of vulcanized india-rubber tubing that could be closed by a clamp. This tube was slipped down into a vein till the blood, having filled it completely, showed itself at the orifice of the india-rubber tubing, to which the clamp was then applied. The whole apparatus was now quickly inverted, and the vein was drawn off from over the mouth of the tube, which was then covered with gutta-percha tissue to prevent evaporation. After the inverted tube had been kept undisturbed in the vertical position for nineteen hours and three-quarters coagulable blood was obtained from the interior of the clot.

We have seen that a clot has but very slight tendency to induce coagulation in its vicinity unless the blood has been acted on by an ordinary solid, and it is probable that with perfectly healthy blood it would be unable to produce such an effect at all. This appears to me to be very interesting physiologically, but especially so with reference to pathology. I must not go now fully into the circumstances that lead me to it, but I may express the opinion I have formed, that clot must be regarded as living tissue in its relation to the blood. It is no doubt a very peculiar form of tissue, in this respect—that it is soft, easily lacerable, and easily impaired in its vital properties. If disturbed, as in an aneurysm, it will readily be brought into that condition which leads to the deposition of more clot ; but if undisturbed, it not only fails to induce further coagulation, but seems to undergo spontaneous organization. I have seen a clot in the right side of the heart, and extending into the pulmonary artery and its branches, unconnected with the lining membrane of auricle or ventricle or with the pulmonary artery except at one small spot where it had a slight adhesion, developed into perfect fibrous tissue by virtue, it would appear, of its own inherent properties. Another observation which I once made, and which then completely puzzled me, now seems capable of explanation. In laying open the blood-vessels of a dead body I observed in many of the veins a delicate white lace-like tissue which evidently must have been formed from a clot. This I now believe to have had the same relation to the coagulum as the flimsy cellular tissue of old adhesions has to lymph.

It may not be altogether superfluous to mention some other facts illustrative of the active influence of ordinary matter in promoting coagulation, and the negative character of the lining membrane of the vessels. I find that a needle introduced into one of the veins of the foot of a sheep for a much shorter time than is necessary to produce the first appearance of the actual deposit of fibrine upon it, leads after a while to coagulation where the needle had lain ; in other words, that a foreign solid, by a short period of action on the blood, brings about a change that results in coagulation, though the blood still lies in the living vessels. I have also ascertained that after blood has been made to coagulate in a particular vessel by introducing a needle into it, if the coagulum as well as needle is removed, and more fluid blood is allowed to pass in, this blood remains fluid for an indefinite period, showing that the needle had not impaired the properties of the vessel by its presence ; so that the previous coagulation must be attributed not to any loss of power in the vein but simply to the action of the foreign solid.

In seeking for an analogy to this remarkable effect of ordinary solids upon the blood, we are naturally led to the beautiful observations of Professor Graham, lately published in the *Philosophical Transactions.* He has there shown what insignificant causes are often sufficient to induce a change from the fluid or soluble to the ' pectous ' or insoluble condition of ' colloidal ' forms of matter. Indeed, Mr. Graham has himself alluded to the coagulation of fibrine as being probably an example of such a transition.

There is, however, another remarkable circumstance that must be taken into consideration, of which I myself have been only recently aware, and which may be new to several Fellows of the Society ; and that is, that in spite of the influence of an ordinary solid the liquor sanguinis is not capable of coagulating *per se.* It was observed many years ago by my colleague, Professor Andrew Buchanan, of Glasgow, that the fluid of a hydrocele, generally regarded as mere serum, coagulated firmly if a little coagulum of blood diffused in water was added to it—an effect which he was disposed to attribute to the agency of the white corpuscles.[1] I repeated Dr. Andrew Buchanan's observations last year, and satisfied myself first that the diffused clot did not act simply by providing solid particles to serve as starting-points for the coagulating process. I tried various different materials in a finely divided state, and found that none of them, except blood, produced the slightest effect. But I found that if a mixture of serum and red corpuscles from a clot was added to some of this hydrocele-fluid, it was soon converted into a firm solid mass. If a small quantity of the serum and corpuscles was dropped into the fluid and allowed to subside without stirring, coagulation rapidly took place in those parts where the red corpuscles lay, while other parts of the fluid remained for a long time uncoagulated. This seemed to indicate that the red corpuscles had a special virtue in inducing the change. I confess, however, that till very lately I was inclined to suppose that in the hydrocele-fluid the fibrine must be in some peculiar spurious form. We know that the buffy coat of the horse's blood coagulates in a glass without addition of clot, and we know that lymph coagulates, so that I did not doubt that liquor sanguinis would always undergo the change when influenced by ordinary matter. But an observation which I made not many days ago shows that this was a mistake. I obtained the jugular vein of a horse, and having kept it for a while in a vertical position till I could see through its transparent coats that the red corpuscles had fallen from the upper part, I removed all

[1] *Proceedings of the Glasgow Philosophical Society*, February 19, 1845.

bloody tissue from that part of the vein, and punctured it so as to let out the liquor sanguinis into a glass. Finding after eighteen minutes that the liquid had not begun to coagulate, I added a drop of serum and corpuscles to a portion of it, and within seven minutes there was a clot wherever the corpuscles lay, whereas the rest of the fluid was still very imperfectly coagulated after another half-hour had elapsed. That the liquor sanguinis to which no addition had been made coagulated at all was sufficiently explained by microscopic investigation, which showed not only abundant white corpuscles, but also several isolated red ones that had not subsided. This observation was made three hours after the death of the horse, but I obtained essentially similar results on repeating the experiment in another horse an hour after death ; so that there can be no doubt whatever that the fibrine was in the same condition as it is in the blood-vessels of a living animal. The observation appears also particularly satisfactory on this account, that the liquor sanguinis was not separated from the corpuscles by any process of transudation through the walls of the blood-vessels, which might be conceived to involve retention of some constituent of the liquid, which, though in solution, might be unable to pass through their pores, but simply by the subsidence of the corpuscles, which must have left all the materials of the liquor sanguinis behind them. Hence it is proved beyond question that if the liquor sanguinis could be separated completely from the blood-corpuscles it would resemble the fluid of hydrocele in being incapable of coagulation when shed into a cup.

Now this struck me as a very satisfactory and beautiful truth, inasmuch as it clears away all the old mystery of the distinction between inflammatory exudations and dropsical effusions. Dropsical effusions, exhibiting little disposition to coagulate, have been supposed to consist almost exclusively of serum, and the exudation of the entire liquor sanguinis has been regarded as the special characteristic of inflammation ; and very unsatisfactory theories have been put forward by ingenious pathologists to account for this difference. But it now appears that a dropsical effusion, like that of hydrocele, is undistinguishable from pure liquor sanguinis.

Various dropsical effusions have been lately investigated with reference to their coagulability on the addition of blood-corpuscles by Dr. Schmidt of Dorpat, who finds that while they differ from one another in the amount of water they contain (just as is the case with serum filtered artificially through animal membranes under different degrees of pressure), yet they are all but universally coagulable. Schmidt has also carried the investigation further. He has found that by chemical means he can extract from the red corpuscles a soluble material which, when added to these exudations, leads to coagulation.

In other words, he shows that the corpuscles do not act as living cells, but by virtue of a chemical material which they contain, which can be used in the state of solution, free from any solid particles whatever. He found also that the aqueous humour made a dropsical effusion coagulate, and that the same effect was produced by a material extracted from the non-vascular part of the cornea. Hence he regards the blood-corpuscles as only resembling other forms of tissue in possessing this property. These observations are extremely interesting, if trustworthy; and that they are so I do not at all doubt, but having only read Schmidt's papers within the last day or two I have not yet had opportunity of verifying his statements.[1]

It remains to be ascertained what share the material derived from the corpuscles has in the composition of the fibrine. Schmidt inclines to the opinion that the fibrine is probably composed, in about equal proportions, of a substance furnished by them and one present in the liquor sanguinis. If this be true, the action of an ordinary solid in determining the union of the components of the fibrine may be compared to the operation of spongy platinum in promoting the combination of oxygen and hydrogen.

It may be asked, How comes it that when the blood of a horse is shed into a cup, the buffy layer coagulates as rapidly, or nearly so, as the lower parts rich in corpuscles?

This is indeed a question well worthy of careful study. We know that the liquor sanguinis left by the subsidence of the red corpuscles within a healthy vein is incapable of coagulating when shed, except in a slow manner, which is accounted for by the corpuscles that remain behind in it. Hence it appears that when the blood as a whole is shed into a glass, the agency of the ordinary solid leads the corpuscles to communicate to the liquor sanguinis, before they subside, a material or at least an influence which confers upon it a disposition to coagulate, though it still remains fluid for some time after they have left it. Just as we have seen that a very short time of action of the ordinary solid upon the blood as a whole is sufficient to give rise to coagulation, so we now see that, provided an ordinary solid be in operation, the presence of the corpuscles for but a little while is enough to make the liquor sanguinis spontaneously coagulable, though not immediately solidified. We shall see, before concluding, an illustration of the importance of this fact to pathology.

[1] Since this lecture was delivered I have verified an important observation made by Schmidt, viz. that a given amount of corpuscles causes complete coagulation of only a limited quantity of hydrocele-fluid. From this he draws the inference that the action of the corpuscles cannot be of the nature of fermentation—the coagulative efficacy of the corpuscles being not continued indefinitely, but becoming exhausted in the process of coagulation. For Schmidt's papers, see *Archiv für Anat. Phys.*, &c., 1861 and 1862.

It remains to be added that serous membranes resemble the lining membrane of the blood-vessels in their relations to the blood, as is implied by John Hunter's observation that blood which had lain for several days in a hydrocele coagulated when let out. The same thing is well illustrated in a frog prepared like this which I now exhibit. About four hours ago, a knife having been passed between the brain and cord to deprive the creature of voluntary motion in the limbs and trunk, the peritoneal cavity was laid open in the middle line, and its edges being kept raised and drawn aside by pins, I seized the apex of the ventricle of the heart with forceps and removed it with scissors. In a short time the whole of the animal's blood was in the peritoneum, and it may be seen that it is still fluid in spite of this long-continued exposure. When I first performed the experiment three years and a half ago, the weather being cool (about 45° Fahr.) and a piece of damp lint being kept suspended above the frog to prevent evaporation and access of dust, I found that the blood remained fluid in the peritoneal cavity for four days, except a thin film on the surface and a crust of clot on the wounded part of the heart ; but a piece of clean glass placed in the blood in the peritoneum became speedily coated with coagulum. Here, it will be observed, not merely the liquor sanguinis, but the corpuscles also were present in the serous cavity, yet no coagulation took place in contact with its walls.

I think it probable, though not yet proved, that all living tissues have these properties with reference to the blood. We know that the interstices of the cellular tissue contain coagulable fluid, and I have seen anasarcous liquid coagulate after emission, but this indeed may possibly have been merely liquor sanguinis coagulating in consequence of slight admixture of blood-corpuscles from the wounds made in obtaining it.

Looking now at the principal results which we have arrived at, it must, in the first place, be admitted that the ammonia theory is to be discarded as entirely fallacious. The fact that this theory is exceedingly plausible, and has been supported by many ingenious arguments and experiments, is of course no reason why we should retain it if unsound. On the contrary, the more specious it is the more necessary is it that it should be effectually cleared away, for it mystifies the subject of coagulation most seriously ; and I may say, for my own part, that it has cost me an amount of experimental labour of which the illustrations brought forward this evening convey but little idea. Still these have been, I trust, sufficient to show that the coagulation of the blood is in no degree connected with the evolution of ammonia, any more than with the influence of oxygen or of rest. The real cause of the coagulation of the blood, when shed from the body, is the influence exerted upon it by ordinary matter, the contact of which for a very brief period effects a change in the blood, inducing a mutual reaction between its solid and fluid constituents, in which the corpuscles impart to the liquor sanguinis a disposition to coagulate. This reaction is probably simply chemical in its nature, yet its product, the fibrine, when mixed with blood-corpuscles in the form of an undisturbed coagulum, resembles healthy living tissues in being incapable of that catalytic action upon the blood which is effected by all ordinary solids, and also by the tissues themselves when deprived of their vital properties.

These principles have, of course, very extensive applications to the study of disease, but I must content myself with alluding very briefly to inflammation, the most important of all pathological conditions.

If we inquire what is the great peculiarity of inflamed parts in relation to the blood as examined by the naked eye, we see that it consists in a tendency to induce coagulation in their vicinity—implying, according to the conclusions just stated, that the affected tissues have lost for the time being their vital properties, and comport themselves like ordinary solids. Thus, when an artery or vein is inflamed, coagulation occurs upon its interior, in spite of the current of blood, precisely as would take place if it had been artificially deprived of its vital properties. On one occasion I simulated the characteristic adherent clot of phlebitis by treating the jugular vein of a living sheep with caustic ammonia, and then allowing the circulation to go on through the vessel for a while, when, on slitting it up, I found its lining membrane studded with grains of pink fibrine which could be detached only by scraping firmly with the edge of a knife. Again, comparing an inflammatory exudation into the pericardium or into the interstices of the cellular tissue with dropsical effusions into the same situations, we are struck with the fact that, while the liquor sanguinis effused in dropsy remains fluid, the inflammatory product coagulates. Now we know that in intense inflammation the capillaries are choked more or less with accumulated blood-corpuscles, which must cause great increase in the pressure of the blood upon their walls; and from what we know of the effect of venous obstruction in causing dropsical effusion of liquor sanguinis through increased pressure, we are sure that we have in the inflammatory state the physical conditions for a similar transudation of fluid through the walls of the capillaries. And the natural interpretation of the difference in the two cases as regards coagulation seems to be, that whereas in dropsy the fluid is forced through the pores of healthy vessels, in inflammation the capillary parietes have lost their healthy condition, and act like ordinary matter; so that the liquor sanguinis, having been subjected, immediately before effusion, to the combined influence of the injured tissue and the blood-corpuscles, has acquired a disposition to coagulate, just like the buffy coat of horses' blood shed into a glass, or like the frog's liquor sanguinis filtered by Müller from its corpuscles, the injured vessels acting upon the blood like the filter.

This view of the condition of intensely inflamed parts is exactly that to which I was led some years ago by a microscopic investigation, the results of which were detailed in a paper that received the honour of a place in the *Philosophical Transactions*.[1] It was there shown, as I think I may venture to say, that the tissues generally are capable of being reduced under the action of irritants to a state quite distinct from death, but in which they are nevertheless temporarily deprived of all vital power, and that inflammatory congestion is due to the blood-corpuscles acquiring adhesiveness such as they have outside the body, in consequence of the irritated tissues acting towards them like ordinary solids.

I cannot avoid expressing my satisfaction that this inquiry into the coagulation of the blood has furnished independent confirmation of my previous conclusions regarding the nature of inflammation.

[1] 'On the Early Stages of Inflammation,' *Phil. Trans.*, 1858 (p. 209 of this volume).

ON ANAESTHETICS

[*Holmes's System of Surgery*, vol. iii, third edition. London, 1883.]

PART I. WRITTEN 1861

To prevent or diminish pain in surgical operations is an object so desirable, that many in various ages in the history of Medicine have sought to attain it, either by means of narcotic drugs designed to act on the body generally, or by compressing or otherwise locally affecting the nerves of the part concerned.[1]

The first really valuable suggestion, however, was made in the year 1800 by Sir Humphrey Davy, who, having himself experienced relief from pain when breathing nitrous oxide gas, threw out the hint that it might probably be employed with advantage to produce a similar effect in surgical practice.[2]

The same idea occurred, after the lapse of nearly half a century, to Dr. Horace Wells, a dentist in Hartford, Connecticut, who, in 1844, underwent the extraction of a tooth without pain after inhaling the gas, and gave it with satisfactory results to several of his patients ; but he soon after found the practice so uncertain that he abandoned it entirely.[3]

About the same period Dr. W. T. G. Morton, of Boston, in America, who had previously been a partner with Wells, but did not, as he informs us, receive any suggestion from him, became possessed with the desire of discovering an efficient anaesthetic, and commenced a series of experiments upon himself and the lower animals, which at last resulted in his extracting a tooth painlessly from a patient to whom he had administered the vapour of sulphuric ether by inhalation. This was on September 30, 1846.[4] Soon afterwards he publicly exhibited his method at the Massachusetts General Hospital ; and thenceforward anaesthesia in surgery was an established blessing to mankind.

Sulphuric ether is still extensively used as an anaesthetic in America, but in Europe chloroform is generally preferred to it. Disguised under the name 'chloric ether', in which it exists diluted with spirit of wine, this agent was the subject of Dr. Morton's first experiment upon himself ; [5] and it was

[1] For much curious information regarding the history of this subject the reader is referred to the work of the late Dr. Snow on *Anaesthetics*.

[2] *Chemical Researches*, p. 556.

[3] *Statements of William T. G. Morton, M.D., on his Claim to the Discovery of the Anaesthetic Properties of Ether*, &c. Washington, 1853, pp. 42 et seq.

[4] Dr. Morton's *Statements*, &c., pp. 45 et seq. [5] Op. cit., pp. 45, 46.

used in the same form at St. Bartholomew's Hospital, in preference to sulphuric ether, by Mr. Lawrence in the summer of 1847.[1] In the autumn of that year Dr. (afterwards Sir James Y.) Simpson, who was engaged in a series of experiments with various narcotic vapours, employed for the first time the active principle of chloric ether, at the suggestion of Mr. Waldie, of the Apothecaries' Hall of Liverpool;[2] and finding that the pure chloroform was more potent than sulphuric ether, yet caused less bronchial irritation, while its odour was more agreeable, and its inferior volatility rendered its exhibition more easy,[3] he zealously recommended it to the profession, and it has since been generally employed throughout Europe.

The effects produced by chloroform are such as to fit it remarkably for the purposes of the surgeon. Like most narcotics, it tends to cause, after temporary excitement, suspension of the functions of the nervous centres, but affects them not simultaneously, but in a certain order; and the brain is the first to show loss of power in failure of sensation and voluntary motion. If this were all, anaesthesia would be a questionable boon, as the work of the surgeon would be interrupted and often marred by involuntary struggles on the part of the patient. But very soon the spinal cord also is subdued, and the reflex functions of the cerebro-spinal axis are abolished so far as concerns the voluntary muscles, which consequently lie perfectly relaxed and passive, better suited for operative purposes than the most resolute will could render them. To this, however, there is one remarkable exception, viz. that the parts concerned in the respiratory movements remain active; and the same is the case with the sympathetic ganglia of the heart. In other words, when the administration of chloroform is carried to a certain point, the nervous system is deprived of such powers as would cause pain to the patient or inconvenience to the surgeon, but retains intact the faculties essential to life.

There are, however, yet other advantages derived from the inactivity of the cerebro-spinal centre. It seems now clearly established that the cessation of the contractions of the heart in the shock of injury depends upon an action of the brain and cord upon the cardiac ganglia through the medium of the vagus and sympathetic nerves; and chloroform, rendering this action impossible, protects the heart from the indirect effect of external violence. In this way it has greatly diminished the risk of death upon the operating table, and also

[1] Snow on *Anaesthetics*, p. 20. That chloric ether was employed at St. Bartholomew's Hospital has been further confirmed by information kindly communicated to me by Mr. (now Sir James) Paget.

[2] Snow on *Anaesthetics*, pp. 21, 22; also Dr. Simpson's original pamphlet, *Account of a New Anaesthetic Agent*, &c., p. 6.

[3] For operations performed by artificial light, chloroform has another advantage over ether, in the fact that its vapour is not inflammable.

has overthrown the old rule of deferring amputation in cases of injury till the patient has recovered from the state of collapse, thus shortening the period of mischief to the system from the presence of the mangled limb, and in extreme cases sometimes saving life where it would be hopeless to wait for returning consciousness. Indeed, an amputation performed under chloroform has often the effect of improving instead of lowering the pulse.

The most striking instance of this that has fallen under my notice occurred in a labourer, whose right arm and thigh had been destroyed by a railway accident, just enough sound tissue being left to admit of amputation through the hip and shoulder joints, which was accordingly performed as a forlorn hope by the surgeon in charge of the case. The vital powers being in a state of extreme depression, it is probable that without chloroform this severe measure would have killed him outright, but by help of the anaesthetic it was followed by marked improvement of the pulse, which continued for some hours, so as to lead us to entertain hopes of his recovery.

Faintness during the operation, a species of shock, is also got rid of by chloroform ; and this, besides its obvious convenience, has the advantage of lessening the chance of secondary haemorrhage ; for the vessels which require ligature declare themselves as such by bleeding, instead of deceptively eluding observation in consequence of the feebleness of the heart and the general arterial contraction which coexist in the state of syncope.

The welfare of the patient is besides greatly promoted by the mental tranquillity arising from the prospect of immunity from suffering, which also induces persons to submit much more readily to the necessary operations, and often to undergo without hesitation treatment which was formerly impracticable because intolerable.

Such being the great benefits conferred by this agent, it is melancholy to reflect that in many parts of Europe, and even of the United Kingdom, it is either withheld altogether or given so scantily as to be nearly useless. This arises from fear, inspired by several fatal cases that have occurred. But when I state that Mr. Syme has given chloroform about five thousand times without ever meeting with a death, and that Sir J. Simpson's experience, also very extensive, has, so far as I am aware, been equally satisfactory, it is clear that it may be used so as to be practically free from any risk whatever.

How then are the fatal cases to be accounted for ? Heart disease has been supposed to be a common cause of them ; and it is a prevalent opinion that it is highly dangerous to administer chloroform to persons affected with cardiac disorder.

It happens that the only death I ever witnessed under chloroform occurred in a person whose heart proved, on examination, to be extensively affected with fatty degeneration, such as would be regarded as sufficient explanation of sudden death under any circumstances. The particulars of this case, however, presented peculiar features, which lead me to take a different view of the part played by the chloroform from what might at first be assumed. The patient was a man above the middle period of life, affected with cancer of the penis, for which amputation of the organ was to be performed. The gentleman in charge of the chloroform, considering the momentary nature of the operation, purposely abstained from giving it as fully as usual, and had removed the cloth containing it from the face before the operation was commenced. The surgeon now placed his finger on the patient's wrist, and having ascertained that the pulse was good, at once effected the amputation almost instantaneously. I observed that the passage of the knife through the member was accompanied by a start of the patient's body; the bandage used to control the bleeding was then removed, but no blood flowed from the arteries; he was found to have no pulse at the wrist; in short, he was dead. From these facts we can hardly doubt that death was a consequence of the shock of the operation acting on a diseased heart; and the only question is whether the circumstance that he had taken chloroform promoted that result. From the foregoing considerations such a thing seems altogether improbable, as we have seen that chloroform protects the heart from the effect of shock. The fact that the patient started proved that reflex action was not abolished in the voluntary muscles, and confirmed the statement of the administrator that the chloroform was imperfectly given. My own impression is, that if it had been pushed to the usual degree the fatal occurrence would have been averted.

I have given this case in detail because I believe it may be regarded as typical of a considerable class in which death has taken place suddenly at the commencement of an operation with imperfect administration of chloroform, which stands to the fatal event in the relation of an accidental concomitant, or rather a preventive insufficiently used[1].

A death essentially similar, though more obviously unconnected with chloroform, took place on the occasion when it was intended to have administered it for the first time in the Edinburgh Infirmary; but Dr. Simpson being prevented from attending, the operation was commenced without the anaesthetic, and the patient died suddenly immediately after the first incision. It has been often remarked that if the original intention had been carried out, chloroform would never have been heard of again in Edinburgh, but it is very likely that the man might then have lived to testify to its benefits.

There is another class of fatal cases in which the use of chloroform seems

[1] An observation made several years ago by Mr. Bickersteth, of Liverpool, has an interesting bearing upon this class of cases. He noticed on three occasions in amputation of the thigh that the pulse stopped suddenly at the moment the knife entered the limb, but recovered itself in a few seconds. The patients were under the influence of chloroform; but as Mr. Bickersteth never observed the same thing again, though he watched the pulse carefully at the same period in a great number of capital operations under chloroform, it seems probable that the anaesthetic was not administered to its full degree in those instances. (See *Monthly Journal of Medical Science*, September 1853.)

to have been simply a coincidence, the real cause of death being mental emotion, acting usually upon a disordered heart.

Dr. Snow mentions a distinct example of this, where a mere profession of administering chloroform was made, and the patient died of fright;[1] and I am able to give, from Edinburgh experience, an instance in which chloroform was still more remotely concerned. The late Dr. Richard Mackenzie, being called to see a gentleman who had fractured his radius, had some thought of employing chloroform in examining the arm, but, changing his mind, made the necessary manipulations without it. He then proceeded to leave the house, but had not got down the steps leading from the door when he was called back with the announcement that his patient had suddenly expired.

Had chloroform been held near the face a few seconds before this occurrence, it would certainly have been blamed, though with manifest unfairness; and a similar injustice seems to have been committed with regard to several cases in which fatal syncope has taken place early in the administration of the anaesthetic, when the brief period of inhalation concurred with the symptoms in showing that the patient was little, if at all, under its influence. A fear of the chloroform itself seems to have been the exciting cause in some of these cases; and one reason why no such instance has occurred in the Edinburgh Infirmary is probably the unlimited confidence reposed in this agent by the inmates of that institution.

It might, perhaps, have been expected *a priori* that chloroform, in the early or exciting stage of its operation, would act upon a diseased heart like mental emotion, and cause irregularity or cessation of its contractions. This, however, does not seem to be the case; and, judging from my own experience, I should say that it tends rather to remove intermission or irregularity of the pulse. On the whole I believe that chloroform, by preventing shock and mental effort during the operation as well as anxiety before it, is in reality a great source of safety in heart disease; and that if a person with known cardiac affection decides to place himself in the hands of the surgeon, so far from being unsuited for the anaesthetic, he is before all others the man who stands most in need of its protecting influence.

Nevertheless, even when the heart is perfectly healthy, it is quite possible to administer chloroform so as to produce a directly sedative and deadly influence upon the cardiac ganglia. This truth was deeply impressed upon me eight years ago by the following occurrence.

An eminent London physician, desirous of making some experiments upon the heart, selected a young donkey for the purpose, and requested me to maintain artificial respiration, which was done by means of a large pair of bellows con-

[1] Snow on *Anaesthetics*, p. 201.

nected with a tube tied into the trachea, the animal having been previously put under the influence of chloroform. The chest having been opened, the investigation was continued for a while, when the creature began to exhibit signs of returning consciousness. To avert this I removed the bellows, and poured into them a considerable quantity of chloroform, and resumed the artificial respiration with energy for a short time, the natural respiratory movements meanwhile continuing ; when suddenly the heart, which lay exposed before us, ceased to beat, and refused to contract again even when its muscular substance was pinched, which showed that its nervous apparatus was paralysed.

This was no doubt caused by the air becoming highly charged with chloroform in passing over the extensive evaporating surface presented by the interior of the bellows. For it had been before shown by Dr. Snow, from experiments upon the lower animals, that an atmosphere containing more than a certain percentage of the narcotic vapour stops the heart before breathing ceases, whereas the reverse occurs when the chloroform is more diluted with air.[1] Hence, with the view of preventing fatal syncope, Dr. Snow contrived an inhaler for regulating the amount of chloroform vapour in the inspired air, and used it in upwards of four thousand cases, of which only one was fatal, and even that seemed to be so independently of the chloroform. Finding his ingenious efforts crowned with such success, and charitably supposing that all were as careful as himself, he concluded that fatal cases in the hands of others could result only from a faulty method of administration ; and assuming that when chloroform is given from a folded cloth it is apt to be in too concentrated a form, he attributed most of the deaths that have occurred to paralysis of the heart from this cause.

But the cloth being the means which has been used from the first in Edinburgh, with success even superior to Dr. Snow's, I have been long satisfied that his argument was fallacious ; yet as his special devotion to the subject, and the valuable facts which he has communicated regarding it, render his opinion influential, I have thought it worth while to subject a matter of such great practical importance to experimental inquiry ; and, about the usual quantity of the liquid being employed, I find that, so far from the amount of chloroform given off from the cloth being in dangerous proportion to the air inhaled, the whole quantity which evaporates from the under surface, even when the rate is most rapid, viz. just after the liquid has been poured upon it, is below Dr. Snow's limit of perfect security against primary failure of the heart.[2]

[1] I have noticed, however, that different animals differ in their susceptibility to chloroform. Thus frogs or mice may be kept for any length of time under its influence ; but bats are very apt to die when treated in exactly the same way.

[2] The experiments were performed in the following manner : A cloth, similar in all respects to what would be used in practice, was supported upon a light wire framework, and suspended at a little distance

But, considering the great diffusibility of the vapour, and the large amount blown away in expiration, it is evident that only a small proportion of that which comes from the lower surface of the cloth really enters the lungs. Were it otherwise, it would be extremely dangerous to give chloroform with the cloth to infants, for as they inhale but a small amount of air, they would then breathe the vapour in a very concentrated state ; yet all are agreed that infants are peculiarly favourable subjects for chloroform. In truth, the quantity dissipated into the surrounding air when the cloth is used involves considerable wastefulness in this means of administration, which is its only disadvantage as compared with an inhaler, but this is abundantly compensated by its greater simplicity, and consequent greater safety. For any apparatus which has the effect of preventing the free access of the atmosphere must be liable to operate in the same deadly manner as the bellows in the case above related, and even when constructed upon the best principles, it will require most careful management, as is admitted by Dr. Snow with regard to his own inhaler.[1] On the other hand,

from the floor by a thread, connected with one end of the beam of a balance, projecting over the edge of the table on which it stood. The weight of the cloth having been ascertained, a weighed quantity of chloroform, corresponding to fl. ℥jss., which is about the amount commonly used, was poured upon the middle of the lower surface of the cloth, which was then allowed to hang close above my face, so that I might breathe fully upon it, while inspiration was performed through a long india-rubber tube to avoid inhaling the chloroform vapour. The amount lost by the cloth was indicated by the weights in the scale at the other end of the beam. At the commencement of an experiment the weight was made a few grains less than the sum of the weights of the cloth and chloroform together, and an assistant noted the second when the scale with the weights in it came to preponderate ; then removed ten grains so as to allow the scale to rise, and again watched the time of its descent ; and repeated this process several times, thus obtaining a very accurate record of the rate of alteration in the weight. The lower surface of the cloth, which was made slightly concave, was circumstanced just as in the early period of the administration of chloroform, except that the inspired air was drawn from a distance. Inspiration does not, however, materially affect the rate of evaporation, as was found by experimenting with a cloth arranged above the mouth of a tube into which air was drawn by an appropriate apparatus. Allowance being made for the slight gain in weight that the cloth would obtain from absorbing moisture from the breath, the amount of chloroform lost from both surfaces together was thus easily determined. In order to ascertain how much escaped from the upper surface, experiments were made with the same cloth, having first the upper and then the under side securely covered with oil-silk, the arrangements being as above described, except that my face was not below the cloth. The quantity given off from the upper surface in a normal atmosphere was thus determined ; and this being subtracted from the whole loss from both surfaces under the circumstances of inhalation, gave the amount that evaporated from the lower surface only. At the temperature of 70° Fahr. this proved to be, from the average of several experiments, at about the rate of 24 grains per minute during the first half-minute ; and allowing, with Dr. Snow, that 20 grains of chloroform correspond to 15·3 cubic inches of the vapour, and that 400 cubic inches of air are inhaled in a minute, we get 4·5 per cent. as the proportion of the chloroform to the inspired air, on the hypothesis that all that evaporates from the lower surface enters the lungs ; 5 per cent. being what Dr. Snow was led by his experiments to regard as the proportion at which the respiration was quite sure to fail before the circulation, and that at which he aimed with his inhaler (op. cit., p. 34). On the other hand, Dr. Snow assumed that, when the cloth is used at a temperature of 70° Fahr., 9·5 per cent. of chloroform is really inhaled (op. cit., p. 34) ; whereas, in truth, of the 4·5 per cent. a large amount is dissipated into the surrounding air.

[1] Op. cit., pp. 181, 188.

there can be no mistake about the manner of using the cloth, which is also always at hand under all circumstances.

The theory of syncope from too great strength of the anaesthetic vapour when the cloth is employed being erroneous, the greater number of the deaths still remain unaccounted for ; and, if we except a very few instances for which we seem to have nothing to fall back upon but an idiosyncrasy so rare that it may practically be left out of consideration altogether, their explanation will, I believe, be found in an overdose of this potent narcotic from too long continued administration.

This is what might be expected from a general view of the statistics. Were we to ask ourselves in what sort of operations we should have anticipated most frequent deaths during the employment of chloroform, we should say in those which are likely to inspire great dread on account of their magnitude and severity, and to cause great shock and great haemorrhage. More especially should these preponderate among fatal cases in general hospitals, where serious operations constitute the majority of those performed. The reverse of this, however, is what we actually find. Of the whole number of cases recorded by Dr. Snow in 1858, as due to the use of chloroform throughout the world during ten years, nine only occurred in any considerable surgical procedure at a general hospital ; remarkably few, considering the enormous number of important operations that must have been performed during so long a period, and the variety in the qualifications of those who administered the chloroform. On the other hand, fourteen took place at similar institutions in connexion with the most trivial matters, such as the removal of a toe-nail, the amputation of a finger, the passing of a catheter, or the cauterizing of a wart. The only rational explanation of this seems to be, that when some great operation is to be performed, like the amputation of a thigh or the removal of a stone from the bladder, plenty of well-qualified assistants are present, and each of them, including the giver of the chloroform, is duly impressed with the importance of his office, and bestows the requisite pains upon it. But when some trifle is to be done, the whole affair is apt to be regarded too lightly, and the administration of the anaesthetic is perhaps confided to some unsuitable person, who also allows his attention to be distracted by other matters. This conclusion is entirely in accordance with my own experience, which, while it has convinced me more and more of the safety of chloroform if properly given, has impressed me deeply with the necessity for more vigilant care in its employment than is sometimes apt to be bestowed.

But an overdose of chloroform may be caused by attention misapplied, as well as by want of attention. The requisites for safety in using it will be best introduced by a short account of what ordinarily occurs in the mode of administration with which I am most familiar. A common towel being arranged so as to form a square cloth of six folds, enough chloroform is poured upon it to moisten a surface in the middle about as large as the palm of the hand, the precise quantity used being a matter of no consequence whatever. The patient having been directed to loosen any tight band round the neck, and to shut his eyes to protect them from the irritating vapour, the cloth is held as near the face as can be comfortably borne, more chloroform being added occasionally as may be necessary. After a time, varying considerably in different individuals, but generally longest in adults who have been accustomed to the free use of narcotics, and shortest in young children,[1] signs of excitement begin to manifest themselves in various ejaculations and muscular efforts, which soon give place to a state of complete repose. The struggles of the patient are sometimes so violent as to require considerable force to restrain them, and, for this reason, at least one efficient assistant should always be in attendance. On the other hand, I have seen chloroform induce nothing but a tranquil slumber ; and it is important to bear in mind that the stage of excitement cannot be reckoned on as invariably declaring itself at all.

The most convenient test of the patient being prepared for undergoing the operation is presented by the eye ; not in the size of the pupil, which is inconstant in its indications, but in what is commonly spoken of as insensibility of the conjunctiva, though in truth it has no relation to sensation, which is abolished considerably earlier ; but when unconscious winking no longer occurs on the eyeball being touched with the tip of the finger, we have a good criterion of the suspension of reflex action in the body generally. At this period the pulse is in about a normal condition, and the respiration is usually either natural or very slightly stertorous, though persons with a strong tendency to snore may do so almost from the commencement of inhalation. But if the administration of the chloroform be further persisted in, strongly stertorous breathing will soon be induced, and will become aggravated till it passes into complete obstruction to the entrance of air into the chest, though the respiratory movements of the thoracic walls still continue. Occasionally, however, the premonitory stertor is deficient, and the breathing becomes more or less suddenly obstructed. This is a point of great importance, for without close attention

[1] I once met with an instance in which chloroform seemed incapable of affecting a patient. It occurred in the private practice of Mr. Syme, who was about to perform an operation, for which we proceeded to administer the anaesthetic ; but after we had used the cloth till we were tired without any apparent effect, Mr. Syme went on with the operation while the patient was conscious. Such a case is, no doubt, excessively rare, but it is interesting as giving some colour to the hypothesis that idiosyncrasy in the opposite direction has existed in some very few fatal cases, which seem to admit of no other explanation, as alluded to in the text.

it may escape notice, when the patient will be placed in imminent peril. For though the respiration may be resumed spontaneously, this cannot be relied on, and it would seem that when chloroform is given in an overdose, the cardiac ganglia are apt to become enfeebled ; and on this account asphyxia produces more rapidly fatal effects under its influence than in ordinary circumstances. But if the obstructed state of the breathing is noticed as soon as it occurs, and the cloth is immediately removed from the face, and the tip of the tongue seized with a pair of artery forceps[1] and drawn firmly forwards, the respiration at once proceeds with perfect freedom, the incipient lividity of the face is dispelled, and all is well.

I am anxious to direct particular attention to the drawing out of the tongue, because I am satisfied that several lives have been sacrificed for want of it. In order that it may be effectual, firm traction is essential. I have, more than once, seen a person holding the end of the organ considerably beyond the lips without any good effect, and, placing my hand on his, have given an additional pull that has re-established the respiration.

A simple experiment, which any one may perform upon himself, is illustrative of this point. Stertorous breathing, such as occurs under chloroform, may be produced at will, and may be carried on even while the tongue is protruded to the extreme degree. But if the tongue is laid hold of with a handkerchief and pulled so as to cause decided uneasiness, stertorous breathing of any kind becomes impossible. That further traction, when extension already exists to the utmost, should produce such an effect is an apparent anomaly which it seemed important to explain. On investigating the subject, I noticed in the first place that stertorous breathing is of two essentially different kinds, of which one, that may be called *palatine*, consists in vibrations of the velum, and has either a buccal or nasal character, according as the air passes through the mouth or the nose ; while the other, which is the profound stertor essentially concerned with chloroform, depends on a cause seated further down the throat, and, for reasons to be given immediately, may be termed *laryngeal*. By digital examination of my own throat I found that the latter variety, and the complete obstruction into which it passes, could still be produced when the tongue was separated by a considerable interval from the back of the pharynx, while a free passage for the air existed onwards to the lips, which showed that the general belief, that the obstruction depends on a 'falling back of the tongue', is erroneous. Also the epiglottis, instead of being folded back during the

[1] The artery forceps are the most convenient means of drawing the tongue forwards. The puncture which they inflict is of no consequence ; the patient, if he notices it at all, supposes that he has bitten his tongue when under the chloroform.

obstruction, as some have supposed, had its anterior edge directed forwards; and though it was thrown into vibrations when the stertor was strongest, it was evident that the cause of the sound was more deeply placed. I also found that, although firm traction upon the tongue abolished the obstruction and the stertor, it did not appear to produce the slightest change in the position of the base of the tongue; nor did it move the os hyoides upon the thyroid cartilage, as examined from without. Hence I was led to conclude that the beneficial effect of this procedure could not be explained mechanically, but must be developed in a reflex manner through the medium of the nervous system. The fact that, when sensation is perfect, some degree of pain is caused in the process, implying an irritation of the nerves, was in favour of this view; while the general abolition of reflex action by chloroform did not seem strongly opposed to it, considering that the reflex respiratory movements, including those of the glottis, go on in a person under the influence of chloroform.

For further elucidation of the matter I had recourse to the laryngoscope; and, after a little patience, found no difficulty in inspecting my own vocal apparatus without employing any depressor of the tongue, using simply the small oblique long-handled speculum and a common mirror in bright sunlight. I then ascertained that the true laryngeal stertor results from the vibration of the portions of mucous membrane surmounting the apices of the arytaenoid cartilages, i.e. the posterior parts of the arytaeno-epiglottidean folds (thick and pulpy in the dead body, but much more so when their vessels are full of blood), which are carried forwards to touch the base of the epiglottis during the stertorous breathing, and are placed in still closer apposition with it when the obstruction becomes complete. Having one hand at liberty, I was able to observe the effect of drawing forward the tongue under these circumstances, and I saw that firm traction induced the obstructing portions of mucous membrane in contact with the epiglottis to retire from it for about an eighth of an inch, so as to allow free passage for the air, while the epiglottis itself was not moved forwards in the slightest degree.[1]

[1] While the true laryngeal stertor was thus produced and thus removed, a sort of spurious snoring might be made by approximation of the vocal cords; but this spurious stertor was, like the voice, quite unaffected by drawing out the tongue. These observations were made on September 21 of the present year (1861). I find that there are four ways in which the passage through the larynx may be closed. First, the folding back of the epiglottis over the opening into the pharynx, as is generally believed to take place in swallowing, and may be demonstrated by arresting an act of deglutition in its progress, and insinuating the finger between the tongue and the roof of the mouth to the epiglottis, which is then felt to be turned backwards, and to return to its usual position as the act of deglutition is finished. Secondly, an approximation of the *sides* of the superior orifice of the larynx, in which the epiglottis is directed forwards, but folded longitudinally, so that its edges are in contact with one another while the arytaeno-epiglottidean folds are also in lateral apposition. [Note written in April 1908: This fact was observed in the retching caused by the application of a solution of nitrate of silver

Whether pulling the tongue operates by inducing or relaxing muscular contraction in the larynx may be matter for discussion, but the main conclusion, that it does not act merely mechanically, but through the nervous system, appears satisfactorily established. I have not hesitated to give the evidence on which it rests in full, as it appears to me to be of the highest practical moment. For it shows at once how grievous a mistake is committed by those who content themselves with gently drawing the apex of the tongue a little beyond the teeth, or pushing forward its base with the finger, or perhaps ascertaining that the epiglottis is not folded back. Such proceedings are instances of attention misapplied, and waste the golden opportunity for rescuing the patient from death. The proper treatment, like many other good things in medical practice, owes its origin to a false theory, but though the erroneous notion of obstruction by the tongue did good service in the first instance by suggesting the original method, it now tends to encourage supposed improvements upon it, which rob it entirely of its efficacy.

If the above description is correct, if it is true that when the administration of chloroform with the cloth is carried too far, the first serious symptom is an obstructed state of the respiration, which without watchful care may occur unnoticed, and, if allowed to continue, will endanger the life of the patient, but, if promptly treated, will harmlessly disappear—it follows that the attention of the administrator ought to be concentrated on the breathing, instead of being, as it too often is, diverted by the pulse, the pupil, or other matters still less relevant.

As an example of the risk that is run by want of close attention to the respiration I may mention the following case. A surgeon of considerable experience was giving chloroform to a patient on whom an operation was being performed, of which I was a mere spectator, but I noticed that stertorous breathing came on, and gradually passed into complete obstruction, at a time when the administrator was gazing with interest upon the proceedings of the operator. Seeing that the patient was in danger, I suggested to the giver of the chloroform the propriety of pulling forward the tongue. He replied that this was uncalled for, and pointed to the heavings of the chest as evidence that

to the larynx of a patient. I find that it is not universally recognized.] This occurs in retching, and doubtless also in vomiting, when a folding back of the epiglottis, instead of protecting the larynx, would tend to direct into it the material passing from below upwards. Thirdly, an *antero-posterior* coaptation of the structures of the laryngeal aperture at a somewhat deeper level, without any change in the position or form of the epiglottis, towards which the folds of mucous membrane above the apices of the arytaenoid cartilages are carried forwards, till they are in contact with its base. This is seen in coughing, and also in laryngeal stertor ; and it is probable that during sleep, when the respiration is so apt to become stertorous, there is but a very narrow chink between the epiglottis and these folds of mucous membrane, which would thus serve to protect the deeper parts of the air-passages from the introduction of foreign matters in the state of unconsciousness. Fourthly, the closure of the *rima glottidis* in the production of voice. The white *chordae vocales* form a beautiful contrast with the highly vascular structures in their vicinity.

breathing was proceeding freely. Knowing from what had gone before that those efforts were doing nothing for the respiratory function, and feeling that there was no time for discussion, I stepped out of my province so far as to seize the tongue myself and draw it forward, when a long and loudly stertorous inspiration demonstrated the necessity for the interference. Had the delusive movements of the chest been trusted, it is probable that they might have continued till the heart had become so enfeebled by the asphyxial state as to cause no perceptible pulse at the wrist; and had death occurred under these circumstances, the case would have been set down as one in which the circulation failed before the respiration. The administrator would thus have been absolved from all blame, and the fatal event would have been attributed to idiosyncrasy, or to any heart disease which might have been discovered on post mortem inspection.

The very prevalent opinion that the pulse is the most important symptom in the administration of chloroform is certainly a most serious mistake. As a general rule, the safety of the patient will be most promoted by disregarding it altogether, so that the attention may be devoted exclusively to the breathing. The chance of the existence of heart disease may seem to make this practice dangerous, but having followed it myself with increasing confidence for the last eight years, and knowing that it has been pursued all along by Mr. Syme, who has also acted on the maxim that every case for operation is a case for chloroform, and must, therefore, have given it to very many patients in whom cardiac disorder existed unknown to him, besides some in whom its presence had been ascertained, I feel no hesitation in recommending it. Even when serious disease of the heart is known to exist, it must be remembered that there is much less risk of syncope than of obstruction to the respiration; and while the latter will demand and repay immediate attention, the former, should it by any chance occur, being in all probability independent of any excess of chloroform, would not imperatively demand its discontinuance; nor would it be much influenced by treatment, supposing the patient to be already in the horizontal posture, which is generally considered safest in all cases when chloroform is given.[1]

From these considerations it appears that preliminary examination of the chest, often considered indispensable, is quite unnecessary, and more likely to induce the dreaded syncope, by alarming the patient, than to avert it.

[1] From the views expressed in the text regarding the relation of syncope to the administration of chloroform, it might be inferred that no great danger would be incurred by giving it in the sitting posture when circumstances particularly require it; and accordingly Dr. Snow informs us that he has done this on several occasions without any bad result. But considering the possibility of an overdose, and the feebleness of the heart which that seems to entail, it is no doubt wisest, as a general rule, to have the patient reclining. Dentists, it is true, give chloroform in the sitting posture; but, so far as I have seen, they do not carry the administration beyond a slight degree, sufficient to deaden sensation without affecting reflex action, dexterously managing to open the mouth and operate upon it while the muscles of the jaws are rigid.

The obstructed state of the breathing, if allowed to continue long, would lead to a far more serious affection—paralysis of the nervous centre concerned in the respiratory movements. Pulling out the tongue would then of course have no good effect of itself, but it should be done to clear the way for artificial respiration, which is the means to be essentially trusted to under such circumstances; and if the air still fail to enter freely into the chest, an opening ought to be made without delay through the crico-thyroid membrane. Cold water should also be occasionally dashed upon the face and chest; and if a galvanic battery happen to be in readiness, one of its poles may be applied over the spinous processes of the upper cervical vertebrae, and the other to the praecordial region, with the object of rousing the respiratory and cardiac ganglia. This, however, is a means not very likely to prove beneficial, and if used in too intense a form it may do harm instead of good.

Preparatory to taking chloroform the patient should be directed to omit the last meal which would naturally precede it, as any food in the stomach is almost sure to give rise to troublesome vomiting during the inhalation. The only after-treatment necessary is to allow the effects of the chloroform to pass off in a quiet sleep; and the only bad consequence likely to arise is a tendency to sickness, which sometimes causes annoyance during the first twenty-four hours or so.[1]

Chloroform is universally applicable in the various departments of surgery, except in some few cases in which the assistance of the patient is required, and in operations involving copious haemorrhage into the mouth. Blood may trickle in small amount into the pharynx without risk of choking, deglutition being carried on unconsciously during anaesthesia; and even in some instances when the bleeding is more serious, as in removing portions of the jaws, pain may be avoided to a great extent by giving the chloroform during the more superficial parts of the operation, and allowing the patient to recover partially before undertaking its deeper stages.

The main conclusions arrived at in this article may be expressed in a few words. It appears that chloroform, though resembling many other valuable means of treatment in being deadly when mismanaged, is free from danger

[1] It has been supposed by some that the use of chloroform increases the risk of pyaemia after capital operations; but experience has now abundantly proved the groundlessness of this apprehension. To take a single instance, the veins of the pelvic viscera being perhaps, next to those of the bones, more liable than any others to originate phlebitis after surgical interference, lithotomy would be much more fatal now than formerly were there any foundation in fact for the notion. The reverse, however, appears to be really the case. Thus, Mr. Cadge, one of the surgeons of the Norfolk and Norwich Hospital, an institution long celebrated for the successful treatment of stone, in a district abounding in calculous disease, informs me that the mortality after lithotomy has been still further reduced there since the introduction of chloroform.

if properly used, the following being the rules for its safe administration. A drachm or two of the liquid having been sprinkled upon the middle of a folded towel, hold it near the face, taking care that free space is afforded for the access of air beneath its edges, till the eyelids cease to move when the conjunctiva is touched with the finger. Meanwhile watch the breathing carefully; and if at any time it should become obstructed or strongly stertorous, suspend the administration and draw the tip of the tongue firmly forwards till the tendency to obstruction has disappeared.

These simple instructions may be acted on without difficulty by any intelligent medical man. The notion that extensive experience is required for the administration of chloroform is quite erroneous, and does great harm by weakening the confidence of the profession in this valuable agent, and limiting the diffusion of its benefits.

Part II. Written 1870

The nine years which have passed since the above article was written have tended to confirm its main doctrines.

The safety of chloroform when administered according to the rules laid down in the preceding pages has hitherto been verified without exception in my own personal experience; and I may add that Mr. Syme, though he continued to within the last two years in the full activity of his career as an operator, never lost a patient through its use, either in public or private practice. Further, I believe I am correct in stating that no case of death from chloroform has occurred during these nine years in the operating theatre of either the Edinburgh or the Glasgow Infirmary, two of the largest surgical hospitals in Great Britain. Yet in both these institutions a folded towel on which the anaesthetic liquid is poured, unmeasured and unstinted, is still the only apparatus employed in the administration; preliminary examination of the heart is never thought of, and during the inhalation the pulse is entirely disregarded; but vigilant attention is kept upon the respiration, and, in case of its obstruction, firm traction upon the tongue is promptly resorted to. And it is worthy of special notice, as showing that success is due to soundness of the principles acted on, rather than any particular skill, that the giving of the chloroform, instead of being restricted to a medical man appointed for the function, as is elsewhere often thought essential, is entrusted to the junior officers of the hospital. In Edinburgh each of the five surgeons has two ‘clerks’, intermediate in position between the house surgeon and the dressers. They, besides other duties, take it in turn to administer the anaesthetic; and if I had to be placed under its