

STATED MEETING, HELD APRIL 25, 1910

The President, DR. RICHARD H. HARTE, in the Chair.

THE RELATION OF THE DUCTLESS GLANDS TO SURGERY.

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THE relation of any given subject to surgery is primarily and always—in the broad sense—precisely the same as the relation of that subject to the fundamental field of the philosophy of medicine. There are certain things, however, which bear a more particular relationship to some one or other of the various special branches; among those fields in which surgery should be especially interested is the problem of the function and the pathology of the ductless glands.

The problem bears a threefold relation to surgery. In the first place, the surgeon is often specifically concerned with the treatment of the pathological conditions occurring in these glands. A mere enumeration of these structures will suggest many such instances, like acromegaly and exophthalmic goitre; this physiologic group comprises the hypophysis and perhaps the pineal in the brain; the thyroid, parathyroid, and carotid gland in the neck; the thymus in the chest; the spleen and the adrenals in the abdomen; the lymphatic system. There are also certain ganglion-like structures in various parts of the body, belonging to the sympathetic nervous system, and grouped together as the chromaffine system. In addition to the true ductless glands, many, if not all, organs with distinct ducts have also an internal secretion which may be even more important than the external secretion; the internal secretion

of the liver is of far greater importance than its external secretion of bile.

In the second place, the surgeon should have a special interest in all these glands of internal secretion, because it often requires a mastery of surgical technic to make possible an approach to the study of their function. An excellent example of this is the recent work of Cushing on the pituitary gland. Or, again, because of a surgeon's familiarity with the pathological picture, he may have acquired a peculiar position of authority in the study of the etiology of these conditions: an example of this is the work of Bircher on the etiology of goitre.<sup>1</sup>

The last element in this threefold relation of these structures to surgery is the one to which I would especially call attention, a relation which, it seems possible, may exist in the practice of general surgery. I refer to the relation of that group of structures known as the "chromaffine" system to the blood-vascular apparatus, and specifically to blood-pressure. The term "chromaffine" is derived from the presence of certain cells which possess a peculiar affinity for the salts of chromic acid; in the case of the adrenals, it is considered satisfactorily demonstrated that these cells are the ones which contain the pressor substance characteristic of the gland. The chromaffinity of these cells is therefore taken as the index of the functional state of the gland, although a fair doubt of the correctness of this assumption may be entertained.

It is not within the scope of this paper to enter into a discussion of blood-pressure, because it is such a complicated problem that it cannot be handled at all unless exhaustively. For the purpose of the present argument, we will therefore leave out of consideration all the factors concerned in blood-pressure except three, which three, it so happens, are also the factors which must probably be most important in a given space of time, such as a surgical operation. These factors are: first, the vasomotor centres in the brain and cord; second, the paths along which the power generated in the centres is transmitted, the vasomotor nerves; and, third, the mechanism by

which the power generated in the centres, and transmitted by the nerves, accomplishes work.

For our present purpose we may define blood-pressure as the result of an opposing of a resistance to the force of the heart-beat; variations of pressure are brought about by varying this resistance. It is generally held by physiologists that the chief resistance to the blood flow is offered by the arterioles and not by the capillaries: changes in the calibre of the arterioles will greatly vary the resistance, and therefore the blood-pressure. These changes of calibre are made possible by the coat of smooth muscle-fibres which surrounds the arterioles. These muscle-cells are in a condition of semicontraction known as "tone," and they are kept in this state by factors entirely apart from the nerve-centres of the brain or cord.

If I may be pardoned a homely simile in order to make my point of view perfectly clear,—no matter how perfect the construction of the engine, no matter how correct the system for the transmission of power, the engine will probably saw no wood if there be no saw for it to turn; and if a saw be present the total efficiency will depend as much upon the condition of the saw as upon the perfection of the engine. To transfer these terms,—the vasomotor centres may be efficient, and the nerves may be normal, but the musculature of the arterioles may not be able to respond. No theory of shock can be complete unless all these factors are given their due consideration.

The result of the experimental removal of the adrenals as well as the study of cases of pathological destruction of the glands, in Addison's disease, shows that the internal secretion of the adrenals is directly concerned in maintaining the tone of the vascular system. It is for us immaterial whether the adrenalin act directly upon the muscle-fibre or upon the end-plates of the nerves within these fibres.

Within the past few years there have appeared several articles in which the authors have presented the results of studies of the effect of narcosis upon the adrenals, and of studies of the adrenals in cases of death due to narcosis. It is to this relation of the chromaffine system to general surgical practice

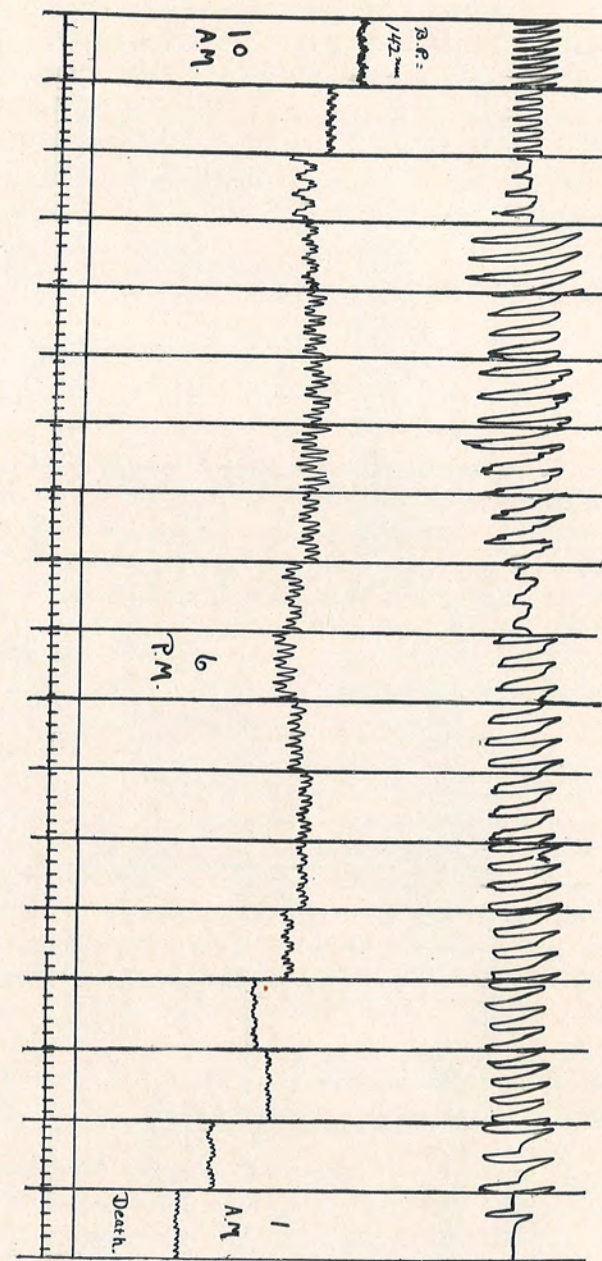
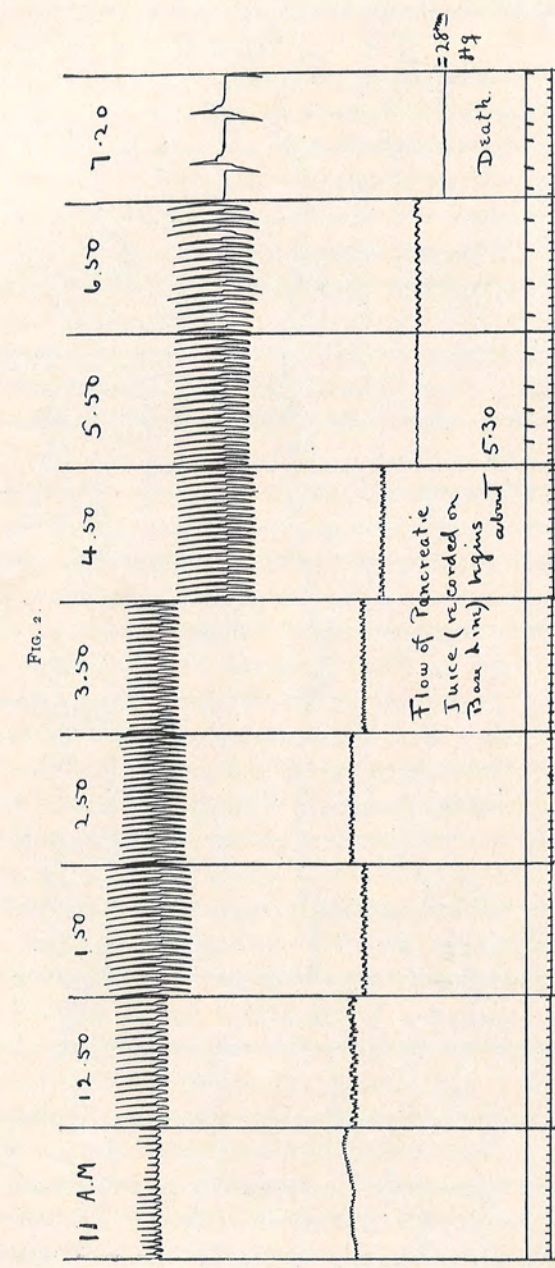


FIG. 1.



that I wish to call your attention. In the course of our study of the interrelation of the internal secretions, Dr. Ralph Pemberton and I have had occasion to keep dogs under ether anaesthesia for long periods, as also to extirpate one or both adrenals in addition to long periods of anaesthesia. We have not been in a position to systematically study all our experiments from the stand-point of the effect of ether narcosis upon the chromaffine system. Our observations have, however, led me to feel that the results obtained by others are, in the main, correct. I have also been able to prepare a few specimens and tracings for demonstration.

Wiesel<sup>2</sup> found in a number of cases of status lymphaticus an extraordinary hypoplasia of the chromaffine tissue. This finding was confirmed on a large material by Hedinger.<sup>3</sup> The fact that the status lymphaticus renders the patient especially susceptible to accidents of narcosis led Schur and Wiesel<sup>4</sup> to an experimental study of the effects of narcosis upon the chromaffine system. They found that the specific cells of the medulla of the adrenals showed a progressive loss of affinity for chromic acid salts, this decreased staining reaction becoming more marked as the time of narcosis lengthened until, after three to five hours of narcosis, no more chromaffine cells were found; synchronous with this loss of chromaffine substance was the disappearance of the mydriatic action of extracts of such adrenals on the enucleated frog's eye, and the disappearance of the iron chloride reaction. If the animals were allowed to recover from the narcosis, the chrom-reaction reappeared, the time of reappearance varying, until from eight to twelve hours later the cells possessed their normal affinity for the chromic acid salts. The extract of an adrenal after five hours' narcosis showed no physiologic effect in one experiment. The result was the same with either ether, chloroform, or Billroth's mixture.

Parkinson<sup>5</sup> states that he found no chromic acid reaction in the medulla of the adrenals from two cases of postoperative shock.

Hornowski<sup>6</sup> found in four cases of postoperative shock a condition similar to that reported by Parkinson. His experimental results are practically the same as those cited from the work of Schur and Wiesel. Hornowski's most interesting conclusions

are the following: "Chloroform increases the need for tonic substance, and at the same time causes an exhaustion of the chromaffine system, which may cause death." "Chloroform does not cause an immediate exhaustion of the tonic substance, but gradually, after several hours." "Chloroform may cause a sudden exhaustion of the chromaffine substance if it be not present in abundance." "The resistance of the organism to surgical shock is expressed in the possibility of satisfying a greater need for tonic substance, and in the ability of the organism to secrete it."

Kostlivy<sup>7</sup> reports two cases, one of death occurring 72 hours after narcosis, in which the chromaffine substance was found intact; this result he explains in the sense of a regeneration, following Schur and Wiesel. A second case in which death occurred 24 hours after narcosis showed no demonstrable chromaffine substance.

Schwarzwald<sup>8</sup> concludes from a study of ten cases of death during and after narcosis, in seven of which the chromic acid reaction of the adrenals was found intact, that the question of the integrity of the chromaffine tissue under the influence of narcosis does not possess decisive importance. It must be added, however, that in three of these cases fatty degeneration of the heart was noted, and a fourth was operated upon while in eclamptic coma.

Kahn<sup>9</sup> endeavors to prove by extensive experiments that the work of Schur and Wiesel is based upon untrustworthy technic, and that therefore their results are incorrect.

A fairly extensive series of tests with the enucleated frog's eye, carried out by Dr. Pemberton and myself in connection with another phase of our work, led us to a conclusion in full agreement with Kahn, that results obtained by this method are not dependable; yet the results seem sufficiently accurate to enable one to draw such a general conclusion as the one that narcosis affects the adrenals. At the same time it is also fair to criticize one part of Kahn's own work. He made extracts of the adrenals after narcosis and found that they always gave a positive physiological reaction, but he used no norm for comparison. It is in such experiments a question of the amount of pressor substance as compared with some normal standard, not of its absolute loss. Dr. Pemberton and I have

often observed in the normal animal that the ether must be pushed beyond mere anæsthesia before an effect upon blood-pressure is obtained, so that five hours' narcosis may not have meant the same thing in the experiments of Schur and Wiesel and those of Kahn.

In reviewing the notes of the work with Dr. Pemberton, I find of our last ten experiments, in which special attention to the condition of the adrenals was directed at autopsy, nine are noted as having the gross appearance you will see in the Kaiserling preparations,—the medulla is darker in color than normal, and around the circumference of the medulla are hemorrhages which extend radially a slight distance into the cortex, giving the organ a striated appearance. In one experiment the macroscopic appearance is noted as normal. I have made a few extracts of such adrenals, and in one instance it was evidently much less active than an extract of the adrenal from a normal dog; in another no marked difference could be seen.

Nevertheless, in spite of the fact that part of the technic used by Schur and Wiesel has proved unsatisfactory in our hands, and that the reaction to chromic acid salts may be uncertain or at best may not necessarily show the condition of functional efficiency, I still feel that the facts brought out by Schur and Wiesel and Hornowski are correct. This feeling is based upon the results we have obtained by the use of entirely dissimilar methods.

The most satisfactory proof I have seen that narcosis affects the adrenals is, first, in a comparison of the curve of the blood-pressure of a dog under ether with that of a dog from which the adrenals have been removed. In both there is the same gradual, progressive fall of pressure, occurring sooner in the dog from which the organs were removed; the time of fall in the normal dog can be hastened by increasing the rate at which the ether is administered. And, second, in our study of the interrelation of the glands of internal secretion, Dr. Pemberton and I have found that the pancreas begins to secrete after the removal of the adrenals, and may show an astonishing

secretory activity over a long period until the animal's death. This fact, together with the fact that adrenalin inhibits the flow of pancreatic juice which follows the intravenous injection of secretin, leads us to conclude that the adrenals exercise some sort of control over the pancreas. In the etherized normal dog this flow has never appeared; but there may, and often does, occur in the last minutes of life after prolonged etherization a flow of pancreatic juice, which we are inclined to feel indicates that the adrenals have been so affected by the narcosis that they have lost their control over the pancreas,—in other words, that the adrenals are exhausted.

In all our experiments we have a continuous record from the beginning of the experiment until the end, of the respiration, the blood-pressure, and the time in seconds, as well as the flow from the pancreas whenever it occurred. The only characteristic feature, aside from the flow of pancreatic juice in those cases where it occurs, is the gradual but progressive fall of blood-pressure; in some instances where a valvular heart lesion was found at autopsy, the addition of ether may be seen to cause sudden falls of pressure, which may sometimes be immediately fatal.

It is in regard to this point that the experience and more careful observation of the surgeon is needed to a proper elucidation of the problem. It should be perfectly evident that a change in the adrenals would not be expected in every case of sudden death during or after narcosis. It is astonishing to note that Schwarzwald included three cases of fatty heart, and one of eclamptic coma. I am of the opinion that the term "shock" should be more strictly used, and should only apply to those cases where neither the case history nor an autopsy reveals any other cause of death save the progressive fall of blood-pressure.

At the same time the solution of our problem must await a satisfactory laboratory method for determining the functional efficiency of the adrenals. It does not appear to me that a staining reaction is necessarily indicative of functional efficiency; as we have seen, the mydriatic reaction, as tested

upon the pupil of the enucleated frog's eye, is unreliable for quantitative tests; the iron chloride and the sublimate reactions are of doubtful value; and even the physiologic test of extracts of the organs does not prove the point; for the amount of adrenalin is not the only variable,—the susceptibility of the musculature to the action of the adrenalin may be variable, so that what would be a functional adrenalin content of the gland in one animal would not suffice to maintain the vascular tone of another.

Two points stand out from the somewhat indefinite condition of the problem of the relation of narcosis to the chromaffine system; first, the necessity for an accurate clinical classification of cases of death due to narcosis; second, the hope that a rational treatment of cases of shock—the prophylactic treatment—may soon be materialized.

## BIBLIOGRAPHY.

- <sup>1</sup> Deutsche Zeitschrift für Chirurgie, 1910, ciii.
- <sup>2</sup> Pflüger's Archiv., Bd. 67.
- <sup>3</sup> Frankfurter Zeitschrift für Pathologie, 1907, Heft 3 u. 4.
- <sup>4</sup> Wien klin. Wochschr., 1908, xxi, 247.
- <sup>5</sup> Transact. of the Path. Soc., London, 1907.
- <sup>6</sup> Virchow's Archiv., 1909, Bd. 198, 93; also, Arch. de med. exp., etc., 1909, xxi, 702.
- <sup>7</sup> Casopis lekuv., 1909, Nr. 2, cited by Schwarzwald, Verhandlungen d. deutschen path. Gesellschaft, 1909, xiii, 268.
- <sup>8</sup> *Loc. cit.*
- <sup>9</sup> Pflüger's Archiv, 1909, cxxviii, 519.

DR. W. M. L. COPLIN (by invitation) said that recently Caccio has published in Italian a paper on cellular lipoids in which he deals with the influence of the chromic acid salts on these bodies and suggests very strongly that there is some relation between chromaffine substance and the lipoids contained within certain tissue cells. Admitting the correctness of views which Dr. Sweet has given, concerning the influence of anæsthetics, then there is a chemical explanation for the observation brought forward in his paper. If these substances are soluble in the agents used in anæsthesia, then, of course, one at once appreciates why they become so readily diffused, and why under such circumstances exhaustion of the lipoid-producing cells would be more

rapidly established under the influence of agents which are in a way solvents of such bodies. One of the most interesting thoughts with regard to these observations is the suggestion that the solubility of some of these constituents of cells appears to be much greater during life than postmortem; the abstraction of these agents by known bodies in which they are soluble would seem to be accomplished less rapidly and less effectively from the excised or dead organ than occurs by circulating through the structures media containing anæsthetics or other substances which are solvents for the lipoids. This might be interpreted as indicating that the change was partly metabolic and not purely chemical. If the stage which is now considered dependent upon excitability after the administration of an anæsthetic is really due to the abstraction of pressor substances from the adrenals or other structures then a new point of view is obtained.

#### ANNUAL ORATION.

DR. ASTLEY P. C. ASHHURST delivered the Annual Oration entitled "The Patience of Surgery."

#### STATED MEETING, HELD OCTOBER 3, 1910

The President, DR. ROBERT G. LE CONTE, in the Chair.

#### OSTEOMYELITIS OF THE SACRO-ILIAC ARTICULATION.

DR. JAMES K. YOUNG reported the history of a youth, aged 17 years, with good family history and without pulmonary or other inherited disease, who was admitted to the service of Dr. David Riesman at the Philadelphia Polyclinic, with the statement that the day after Christmas he fell while playing and injured his hip; two weeks later he had another fall, injuring his left hip, and five days previous to admission he had another fall from a wagon. Upon admission he complained of pain in the region of the left hip, and there were tenderness, heat, and deep fluctuation in this area. The leg could be moved without much difficulty. His condition not improving and a leucocyte count of 14,600 being found, the sacro-iliac joint was exposed, a portion of the ilium was removed, and the hip-joint was exposed, but no pus was found. Within six hours, however, suppuration became profuse and continued for several days. The cultures showed *Staphylococcus aureus*. His recovery was interrupted by an attack of orchitis. The case is reported on account of the rarity of acute suppurative conditions of this articulation and their recovery under treatment.

#### EARLY (TREVES) OPERATION FOR PSOAS ABSCESS.

DR. YOUNG also reported the history of a boy, aged seven years, family history negative for tuberculosis or other inherited disease, who, two days before admission to the Polyclinic Hospital, began to bend forward on the right side and to complain of pain in the right hip, with night-cries. Upon admission the right thigh was flexed, the movements of the right hip-joint were otherwise normal. There was tenderness in the right lumbar region with rigidity of the spine, but without any fulness in the iliac region. The osseous lesion of the spine was revealed by an X-ray, and the diagnosis of psoas abscess was made. The