THE INDUCTION OF PANCREATIC ACTIVITY BY THE REMOVAL OF THE ADRENALS*

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We reported before the Association of American Physicians in Washington, May, 1909,¹ the results of our work on the relation of certain ductless glands to the pancreas, and we there offered among other conclusions, the following:

1. The inhibition of pancreatic secretion by adrenalin is independent of systemic blood-pressure, as shown by its persistence when the blood-pressure is much below normal and by other evidence.
2. The inhibition by extracts of pituitary and suprarenal bodies also occurs when the pancreas is stimulated by its normal excitant, hydrochloric acid in the duodenum.
3. The evidence now at hand indicates that the suprarenal glands exercise an inhibitory power on the pancreas, and that on the removal of this influence by ablation the pancreas secretes more actively.
4. The agonal period of life (in the sense described) is generally accompanied by an exacerbation of the normal rate of pancreatic flow.

Our report was preliminary, and although our conclusions were strongly suggested by the evidence at our command, they were not supported by that number and variety of experiments which alone could offer substantial proof.

In order to ascertain the truth, and definitely to corroborate or disprove our conclusions, we have devoted the past year to a repetition and amplification of our earlier work, together with certain changes in its terms, on such a scale as would place the results to be obtained by these methods beyond reasonable doubt. The results so obtained we wish now to report.

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1. Pemberton, R. and Sweet, J. E.: Further Studies on the Influence of the Ductless Glands on the Pancreas, Tr. Assn. Am. Phys., 1909, xxiv, 502.

PRIOR WORK

For three years past we have been concerned with the question of pancreatic activity in several of its phases, and have shown that extracts of the adrenal and pituitary glands, when injected into the system, cause a diminution or cessation of the flow of juice from the pancreas, whether this flow be caused by the normal chyme, hydrochloric acid artificially placed in the duodenum, or duodenal secretin intravenously injected. We have obtained this result from no other tissues as yet, though many have been tested; but certain extraneous agents, among them nicotin, are reported to have an analogous action.

The *modus operandi* of this phenomenon is still *sub judice*, though it has been attributed to vasoconstriction. Some evidence supports this, not conclusively as yet, but the observations here to be presented seem to throw further light on the matter.

Other relations between the pancreas and the ductless glands of the body we have elsewhere taken up and need not now consider; but the connection just mentioned between the pancreas, on the one hand, and the adrenals and the pituitary, on the other, concerns us especially.

PRESENT PROBLEM

If the intravenous injections of extracts of the suprarenal and pituitary bodies cause inhibition of the pancreatic flow, after whatever method of excitement, the question is at once presented as to what would be the effect of removing from the pancreas such influence as these glands normally presumably exert. Evidence on this latter point would not only be of interest in enlarging our present conceptions of interglandular action, but would also tend to act as a check on the former observation and possibly help elucidate the mode of action.

As we have elsewhere pointed out, the difficulties to be met in such a problem are very great, and necessitate the utmost care in the interpretation of results as well as in obtaining them. The terms of a biologic experiment are rarely exact, and in this particular instance we have to deal with many factors that are indefinite and poorly understood. In addition to this, the time required for a single experiment in some instances has been so great as to preclude its frequent repetition, such experiments requiring the practically undivided attention of two observers over periods of seventeen or eighteen consecutive hours.

METHOD OF WORK

Our method was as follows: We established in fasting dogs a temporary pancreatic fistula by introducing into the pancreatic duct a can-

nula through which the flow of juice could be observed and measured. This flow was recorded by interruptions of the base line on a kymographion tracing as the juice passed divisions on the cannula. The records are preserved in the form of continuous tracings of each experiment, from the beginning of anesthesia until death.

Coincident tracings were made of the respiratory movements, blood-pressure, and the time in seconds. The details of our work hardly call for explanation here, as they are fully set forth in our previous contributions on this topic.²

Our animals were under complete surgical anesthesia by ether from the beginning of the experiment until the end.

Following the establishment of the above procedures, the adrenals were removed through a large median incision, which also served for the pancreatic manipulations. The adrenals were removed by blunt dissection, the right usually first, since it is the less accessible and operation on it produces a greater disturbance to the general economy than it does in the case of the left gland.

Sometimes the order of procedure varied from that just given, though we usually found the latter the most expedient. Animals which have been subjected to bilateral ablation of the adrenals withstand poorly any further trauma, even that of establishing a connection with the respiratory tambour or blood-pressure manometer, and not infrequently succumb prematurely.

The total number of our experiments was forty-one, exclusive of a number devoted to certain incidental features which will be mentioned later. This does not include those observations on which we made our first tentative report.

Our object was to observe the normal rate of pancreatic secretion under the conditions of a temporary fistula, and then to observe the rate after the removal of the adrenals. In our work of a year ago we had not realized sufficiently the importance of using only fasting dogs, and, as a consequence, the question became complicated by the presence of a flow from the pancreas from digestive causes. We know now that the phenomena to be considered are not essentially altered under these circum-

2. Sweet, J. E. and Pemberton, R.: Experimental Observations on Secretin With Special Reference to Diabetes and Malnutrition, *THE ARCHIVES INT. MED.*, 1908, i, 231; The Inhibition of Pancreatic Activity by Extracts of the Suprarenal and Pituitary Bodies, *ibid.*, 1908, i, 628; 1908, ii, 295; Further Studies on the Influence of the Ductless Glands on the Pancreas, *ibid.*, 1910, v, 466.

stances, and are indeed rendered very graphic and striking; but the interpretation of results is made much more difficult by this complication.

In the experiments now discussed the dogs were, therefore, animals which had been fasted for thirty-six hours, and, except for one or two which had broken loose and had foraged, unknown to us until later, the gastro-intestinal tract was free from food. The experimental and control animals were selected to conform in size as nearly as possible, and were often of the same breed.

FINDINGS IN NORMAL DOGS

In normal dogs under ether there is a slight tendency, even during a fast, for the pancreas to secrete. This may be inconspicuous for hours at a time or even apparently absent, but, sooner or later, it generally shows itself, so that toward the end of a period of observation there is usually a well-marked, though relatively slight, flow. This may, however, be more pronounced throughout, and some dogs, for reasons which we do not understand, may secrete with fair activity. Each dog forms more or less of a law unto itself and, if the flow is sluggish at the start, it never becomes rapid or prolonged later. Within the terminal or agonal moments it often undergoes a distinct exacerbation. The total amount of flow in normal animals may therefore vary between a practically unmeasurable quantity and seven to nine cannulafuls in the course of ten to seventeen hours.

If, as often occurs on introducing a cannula into an organ so vascular as the pancreas, there be a slight hemorrhage and the clear juice become clouded by blood, doubt at once arises as to whether the duct is clear; and, if the flow be sluggish, the condition simulates obstruction so perfectly that only the course of events, or autopsy, after perhaps sixteen or eighteen hours, will show the truth. We know no way of obviating this, as the cannula cannot be removed frequently from such delicate structures. If, however, the duct be clear, the meniscus of juice in the tube moves with the movements of respiration and affords a fairly reliable index of patulency. The evidences of flow when the duct is first opened are also of value as indicating what may probably be expected from the gland. Also, if there be obstruction, and secretion be free, the gland may appear somewhat edematous.

In normal dogs the blood-pressure is but little affected by the operative proceedings described, and it falls only after prolonged etherization or as the strength of the animal fails. This may be after a variable period which sometimes much exceeds seventeen hours, the only condition

to determine death being, apparently, the relation of the amount of ether to the animal. In other words, if the ether is carefully watched, the dog will live for a long period; but, if the ether is carefully pushed, the end can be materially hastened.

In those subjects which have survived so long we have finally given more ether until the blood-pressure slowly fell, since otherwise the observations would have been essentially on normal dogs under conditions which would not serve as controls for the phenomena we wished to examine.

FINDINGS AFTER REMOVAL OF THE ADRENALS

On the other hand, in contrast to the results with normal animals, if the adrenals be removed, the picture becomes very different. The operation of ablation itself produces considerable shock, and when after some oscillation the blood-pressure becomes steady, it is generally found to be significantly lower. This does not seem to be due to the operative disturbance alone.

The right adrenal, as remarked, is difficult to remove, but the left can be taken out with relative ease in a few minutes. Now, if the right alone be removed, the shock of ablation *per se* is very marked, but is not greatly increased if the left be also removed, and animals so treated have lived almost as long as the normal under ether; that is, ten to fifteen hours. When both adrenals are removed the pressure never returns to a height approximating its former level, but suggests the condition seen after many hours in the normal animals. It declines more or less rapidly until the animal dies after a variable period, say six to eight hours. During this period, in every instance encountered so far, the pancreas begins shortly to secrete, and increases in the rapidity of output until in some cases this secretion is so great as to make a record of it difficult, except in terms of five divisions of the cannula as units. The number of cannulas filled is consequently vastly in excess of those seen with normal dogs, and indicates a proportionately greater formation of pancreatic juice.

There is no definite time of the experiment or condition of blood-pressure at which the flow begins, as the factors which regulate the flow seem to depend, for the most part, on the idiosyncrasies of the dog; but, in general, it can be said that it begins in not less than two hours nor more than five.

It can be seen, therefore, that no dependable statistical average can be made of the rate or quantity of flow, or of the other contributory factors under which it takes place; but this much seems definitely sure that,

after removal of the adrenals, there always occurs a flow, and that this flow may reach such proportions that we are unable to duplicate it, save by the injection of powerfully active duodenal secretin.

Indeed, if the animal has not fasted, ablation of the suprarenals induces such activity that even the results sometimes obtained from the last-mentioned stimulus may be exceeded. The contrast between normal control animals and those without their adrenals is, therefore, very marked.

It is important to note that this flow begins earlier, that it lasts very much longer, and that it is greater in volume or rate, or both, than the normal output, despite the fact that death occurs much sooner. Once established, however, the duration of the flow is limited, apparently, only by the life of the animal. The longer the animal lives, the longer secretion takes place.

These facts must be borne in mind in comparing, for example, a dog with adrenals ablated, whose pancreatic flow is sluggish at the start, with a normal dog whose pancreatic flow is active at the start; and especially is this true if the normal dog lives long and secretes a number of canulafuls during, perhaps, sixteen hours, while the ablated dog shows an early exacerbation, perhaps, but also early death, before the total output is very great.

While there is nearly always some little flow from the normal animal, however, it rarely passes a point which we have grown to regard as the usual limit under such circumstances, namely, about six to eight canulafuls in a period of possibly as much as seventeen hours.

More frequently, however, there is almost no flow at all, save at the end, when there supervenes a condition which simulates in some respects that induced earlier by the removal of the adrenals. There seems to be an analogy between these two conditions; and the normal dog may conceivably reach a state in which his system as a whole presents apparently the same need of suprarenal activity as does the animal with adrenals ablated. Whether this is the case, however, is, as yet, purely conjectural.

There is here, however, one point of interest, which seems to us to throw light on the *modus operandi* of the feature under discussion. As has been said, the inhibitory action of epinephrin* has been ascribed³ to its vasoconstrictive power. This may be justifiable, though, as we have elsewhere stated, some evidence opposes it. If the flow from the pancreas

* Adrenalin is the variety of epinephrin used throughout these experiments, except in some early work where the change was noted.

3. Edmunds: *Jour. Pharmacol. and Exper. Therap.*, June, 1909, i. No. 1.

Fig. 1.—Tracing made Feb. 8, 1910, from normal control, with adrenals intact, showing fall of blood-pressure in a lengthy experiment without flow. Ether begun at 9:53.

Fig. 2.—Tracing made Dec. 15, 1909, from dog with adrenals removed; right adrenal removed 11:58 a. m., left adrenal removed 12:02 p. m.

Cannula emptied to
division 1b

Fig. 3.—Tracing from same experiment as Figure 2, showing rate

Cannula emptied to division 22

Cannula full

90

Fig. 4.—Tracing from same experiment as Figures

Cannula emptied

22

31

35

Fig. 6.—Tracings from same experiment as Figure 5, showing

g rate of flow at 5:48 p. m., and covering the filling of one cannula.

figures 2 and 3, showing rate of flow at 7:04 p. m.

flowing flow of juice with a fairly high blood-pressure at 1:38 p. m.

be inhibited by vasoconstriction and a high blood-pressure, it would seem that the opposite condition of affairs would be conducive to a flow. We know that a low blood-pressure alone will not lead to this. If, however, on removing the adrenals we find a marked tendency to secretion, at the same time that the blood-pressure is low or falling, we naturally incline to associate the events, and to regard one as perhaps causative of the other. We have here, however, evidence that this is not the case, because, if a normal dog be watched, as described, the blood-pressure will be found to fall just as low as it does with the dogs whose adrenals have been ablated and remain low just as long, or perhaps longer, but no flow occurs, or at most one which is manifestly inferior.

The problem is not settled by this observation, but the latter strongly suggests that the relation of the adrenals to the pancreas is very close. Taken in connection with the inhibition of pancreatic flow by the intravenous injection of epinephrin, the induction of a flow by the absence or insufficiency of the adrenals presents a potent argument for specificity of control by one gland over the other. This control seems none the less specific, even though possibly caused by the vasomotor properties of epinephrin, but, in the observation just recorded, there is apparently evidence that vasomotor control is not the only factor operating. Even if it is the only factor, the pancreas shows such a degree of susceptibility to the presence or absence of epinephrin as to indicate specificity on this score.

We have tried to establish controls, and have attempted to produce the same results by means of some abdominal injury, on the basis that nervous stimulation or inhibition produced by the removal of the adrenals, induces secretion. Such action would presumably take place much sooner than does the flow in question, but, to investigate the matter we have, in ten instances, removed one adrenal only, especially the right, in order to produce approximately the same amount of disturbance and trauma that occur when both adrenals are removed. This latter injury would be closely simulated, since the removal of the left adrenal, as elsewhere remarked, is relatively easily and quickly accomplished. The left adrenal has also been removed alone, and, again, we have handled and bluntly dissected both adrenals, about as we do in extracting them, without, however, destroying their functioning power, or blood-supply. In all these cases, however, we have been unable to produce the conditions described as occurring when both adrenals are removed. The instances of removal of one adrenal were about equally divided between a moderate flow and no flow at all, and the instance of blunt dissection of both

adrenals without conscious injury to their function, gave absolutely no flow whatever.

It will be noted in the accompanying protocols that in some instances of ablation the dog died before evidence could be obtained one way or the other. Again, others died when a flow had but just begun. These latter distinctly illustrate the point at issue, and yet the accidents and uncertainties of anesthetization make statistical use of them practically impossible.

In a few words, the order of events seems to be that a dog with the adrenals removed gives a marked flow; a dog with one adrenal removed tends to give some flow, though less and often none; and a dog with the adrenals intact gives practically no flow at all, or relatively little.

We have also introduced a cannula into the hepatic duct to determine if the output of bile were increased, but have observed no flow in the instances tried, although the pancreas secreted actively. We expect to try the same thing on the salivary and other glands.

ALLIED PROBLEMS

We feel that, with the methods of procedure hitherto used, the subject is not susceptible of much greater solution, and, because of our desire to approach it by other means, it seems wise to publish what we have done to date before taking up other measures or topics. Some of the studies which we have in mind are:

1. Experiments with duodenal secretin and epinephrin on dogs with adrenals ablated when showing a flow or a beginning tendency to flow.
2. Examination of the pancreatic juice secreted at various periods in all the conditions described above.
3. Transfusion of the blood from a normal dog into one whose pancreas is secreting after ablation.
4. Transfusion of the blood of a secreting dog with adrenals ablated into a normal dog whose pancreas can be watched after the usual method.
5. The production of hemorrhage in a secreting dog with adrenals ablated.
6. Efforts to detect epinephrin in the blood at various periods of the above experiments.
7. Destruction of the adrenals by agents which will not seriously disturb the general economy.
8. Removal of the pituitary body under analogous circumstances, etc.

A number of such problems demands investigation and promises much information of value in regard to our present imperfect conceptions of the adrenals and other ductless glands.

OBSERVATIONS ON DUODENAL SECRETIN

One series of observations, in line with the projected work just outlined, and planned with the idea of throwing light on the main problem, we have taken up. It is not as yet complete, because the methods employed have proved inadequate to a satisfactory definition of the results, but there seems to be indicated a condition which is at once surprising and indicative of interesting possibilities.

On observing the marked flow of pancreatic juice in dogs whose adrenals had been removed, it seemed to us that the pancreas might be conceivably acting as the result of a change in some one of the stimulating factors rather than as a result of the removal of inhibition alone. Or, again, a combination of these might be operative. We therefore turned our attention to the secretin content of the duodenum with a view to ascertaining whether or not it was affected by the absence of the adrenals or their products.

METHOD OF WORK

An examination of this kind proved troublesome because of the difficulty in having the varying terms of the experiment constant. It was necessary to make a preparation of secretin from the intestines of a dog with adrenals ablated, and to compare it with secretin made from a normal dog killed for that purpose. It was then necessary to compare secretin made from a normal dog which had died under similar conditions of anesthesia after a long period, with secretin from a normal dog killed for the purpose.

These comparisons were made by injecting the solutions into a normal dog, the activity of whose pancreas could be observed by means of a cannula in the pancreatic duct. Coincident records were made of the blood-pressure and respiratory movements of the injected dog, as well as the time in seconds. It was desirable to compare directly secretin made from a dog with adrenals ablated, with that from a normal dog which had died after a comparatively long etherization, the flow from whose pancreas had been observed and found to be slight. Because of the physical limitations to our facilities for work, however, this last could not

Fig. 5.--Tracing made Feb. 17, 1910, from experiment on animal with adrenals removed, showing flow of juice, with a high blood-pressure. Right adrenal removed 10 a. m., left adrenal at 10:32 a. m. In this tracing, inadvertently, no record was taken of the flow at the period shown in the segment. The flow appears on the next two tracings.

be accomplished, and we had to compare each of these with a control. Such controls varied among themselves according to the varying amounts of secretin in the intestines of the normal dog, but were, of course, constant for given comparisons.

The secretin solutions were made by taking definite lengths, two to four feet, of intestine from the experimental and control animals and removing the mucosa. Equal weights of these scrapings were then ground up with sand for equal periods in acid of the same strength and treated as described elsewhere, making two solutions, one control and one experimental.

These solutions were decanted and strained. In some of the earlier experiments, when the intestine first worked up gave heavier and more wise normal dogs whose pancreatic activity or inactivity had been like in making the dilutions of the second; but such cases were about equally divided between the control and the other instances, and were later avoided entirely.

Where delay was inevitable between death and the preparation of secretin from an animal which had been operated on, the control dog was killed at the time the former died, and the intestines from both were kept on ice for the same period. In the final tests of these preparations equal amounts were of course used, from 3 c.c. to 10 c.c., generally about 5 c.c., and alternately injected into the femoral vein after the first and usually more active response had subsided.

FINDINGS

For convenience of reference we shall designate the secretin made from dogs whose adrenals had been ablated after many hours of observation and flow, as "terminal adrenal secretin" or T. A. S.; that from otherwise normal dogs whose pancreatic activity or inactivity had been likewise observed over many hours until death, as "terminal normal secretin" or T. N. S.; and that from dogs killed for normal control secretin, as "normal secretin" or N. S. All these dogs had fasted for thirty-six hours.

In six experiments in which secretin from a dog whose adrenals had been ablated was tested against normal control secretin, it was weaker twice; twice of about equal strength though possibly stronger; and twice, stronger than the control.

In five experiments in which secretin from an intact animal which had been observed over many hours of relative pancreatic inactivity was tested against a normal control secretin, it was in every instance distinctly weaker.

That the terminal normal secretin should be weaker than the normal secretin was perhaps to be expected *a priori*.

On the other hand, that terminal adrenal secretin, T. A. S., should ever be as strong as the control from a healthy fresh animal, N. S., is surprising, especially in view of the consistently uniform inferiority of the terminal normal secretin (T. N. S.) as compared with the normal secretin (N. S.).

In point of fact, however, the terminal adrenal secretin, T. A. S., was sometimes actually stronger than the secretin from a strong healthy dog. It can hardly be doubted that it would have shown a proportionately greater contrast of strength, if tested against its true analogue, terminal normal secretin (T. N. S.).

The table shows this more graphically:

N.S.	>	T.N.S.							
N.S.	>	T.N.S.							
N.S.	>	T.N.S.							
N.S.	>	T.N.S.							
N.S.	>	T.N.S.							
N.S.	<	T.A.S.		See exp. 44		1	12	10	
N.S.	<	T.A.S.		See exp. 42		1	7	10	
N.S.	>	T.A.S.		See exp. 47		2	18	10	
N.S.	>	T.A.S.		See exp. 43		2	9	10	
N.S.	=	T.A.S.*		See exp. 45		2	13	10	
N.S.	=	T.A.S.*		See exp. 46		2	14	10	

* No definite preponderance in favor of either.

DISCUSSION OF FINDINGS

We must infer from this that our experiments, as far as they go, indicate some peculiarity of the duodenal mucosa in dogs which have had their adrenals removed. By virtue of this it seems to have properties

Fig. 7.--Tracing from same experiment as Figures 5 and 6, showing flow of juice, with a fairly high pressure at 2:05 p. m.

more stimulating to the pancreas, when extracts are made from it, than has the mucosa of normal dogs subjected to the same procedure, or even, sometimes, that of healthy vigorous animals freshly killed.

If these results be corroborated, they may prove to be of further interest. Not only would they further indicate a control over the pancreas by the adrenals, but they would suggest a view of the adrenals as organs related to intestinal digestion. This is by no means proved as yet, and we do not wish to be interpreted as postulating it, but the evidence along this line is not without interest.

It is interesting to note that, if the pancreas secretes more actively in the absence of the usual suprarenal products, vasomotor or of whatever nature, this activity is apparently supplemented and strengthened by the presence in increased amounts of the normal excitors in the intestine. These may be manifestations of one and the same process, hyperstimulation from the intestine, but we are not inclined to this view, as in some instances in which we recorded a very active flow, the activity of the terminal adrenal secretin was not proportionately great, though apparently always greater than the terminal normal secretin. It is conceivable that the terminal adrenal secretin is stronger than the terminal normal secretin, because the terminal adrenal dogs die before it becomes so much reduced as in the others, and yet many of them live so long as to make this difference negligible. This would not explain, in any event, those cases in which the terminal adrenal secretin was equal to, or in two cases stronger than, the normal.

As to the cause of the presence of more than the normal amount of secretin in terminal adrenal dogs, no answer can be given except that, if vascular control be the explanation of this property of the suprarenals, a conceivable determination of more blood to the intestinal mucosa in the ablated animal might afford more of the factors from which the excitor is normally formed. If this be the case, however, it merely affords that concrete explanation of action, which must ultimately exist in any event.

Observations of this general type on the factors which conduce to the formation of secretin may throw light on its nature and the substances that are necessary to its composition.

One or two further points require notice. The first is that, noticing frequently in cases of terminal adrenal flow a congestion of the viscera, we thought it possible that stasis might be the cause of the pancreatic

output, although observations in the past by others⁴ have shown that there occurs no post-mortem flow from the pancreas, due to stasis.

As reference to our protocols will indicate, we studied every animal at autopsy with a view to observing this and other features, but could find no evident relation between the extent and degree of congestion and the flow from the pancreas. In no instance did the pancreas at autopsy show any marked degree of congestion. It never showed the picture of passive congestion such as is caused by interference with the portal outflow, but was often pale.

Occasionally there occurs, after removal of an adrenal gland, a slow oozing from its previous site which is not apparent at first, and is hard to foresee or control. This happened in four instances. In one of these, we had looked for the usual terminal adrenal flow and were surprised at not getting it until the somewhat early fall of blood-pressure and premature death of the dog revealed considerable hemorrhage into the abdominal cavity.

Such observations have inclined us to believe that under circumstances in which a terminal adrenal flow is to be expected, hemorrhage will prevent it, and, indeed, it is possible that it will also prevent the greater activity of secretin made from terminal adrenal mucosa. This may explain the only two instances in which terminal adrenal secretin was weaker than normal secretin as indicated in the table (Experiments of Nov. 7, 1910, and Nov. 8, 1910). There also seems to be in this an argument against the probability that a low blood-pressure *per se* is the determining factor in the flow under discussion, since hemorrhage must contribute to conditions of low blood-pressure but, at the same time, apparently prevents or modifies the flow.

We wish here to call attention again to a certain feature which we emphasized in our first contributions on pancreatic activity.²

Among other conclusions there presented were the following:

1. There would seem to be some factor which makes the preparation of secretin from human intestines more difficult than from the intestines of some animals.
2. This factor may depend on the relatively great abundance of membrane in these animals and consequently greater amount of prosecretin.
3. The abundance of mucosa may be in part a provision of Nature in order that the strongly acid chyme of some animals may meet with a quantity of pancreatic juice sufficient to neutralize it and effect digestion.
5. Dieting and fasting seem to have no appreciable effect on the activity of an extract.
6. Time elapsed between death and the preparation of the extract (within limits) does not seem to be a factor. . . .

4. Bainbridge: Brit. Jour. Physiol., 1906, xxxiv, 275.

It will be noticed that prosecretin is apparently abundant in the duodenum of dogs and that it is more difficult of detection in the duodenum of human beings. In these latter instances, however, the quantity of mucosa obtained is frequently abundant, and gives no *a priori* indication of the difficulty to be met in obtaining an active extract of its prosecretin. Granting that the mucosa is less plentiful in human beings, it would be expected that secretin solutions made therefrom would be inferior to those made from dogs, but there still remains the difficulty of accounting for the apparent entire absence of secretin in the cases of various diseases which we reported.

It appears that our recent observations help to elucidate this point. We have seen that, in every case examined, the terminal normal secretin (T. N. S.) was weaker than the normal secretin, being extracts made respectively from dogs which had died a lingering protracted death over twelve to eighteen hours, on the one hand, and from lively animals killed during health, on the other. In our earlier work, and in the work of the few others who have attempted such observations, comparisons were made between the secretin from human beings who had died "slowly," as is generally the case with hospital subjects, and that from dogs recently killed as recorded.

We seem to have here illustrated, therefore, one of the factors which may be, and doubtless are, operative to prevent or hamper the detection of prosecretin in the diseased human subject. The effect of a lingering death is apparently to make the prosecretin content of the duodenum less easy of extraction and perhaps the mucosa less active, as contrasted with freshly killed animals.

We have made a few observations on the nature of the pancreatic juice which is secreted at various periods during a flow, and tests of its amylolytic power indicate very clearly that, while the juice becomes weaker as it is poured out in larger and larger quantities over long periods, it preserves this one ferment action at least to a very significant degree.

This question, however, is almost one by itself and requires special work devoted to it, but the presumption is all in favor of the view that the other ferments of the juice are also present.

CONCLUSIONS

1. The removal of the suprarenal glands induces in dogs a flow of pancreatic juice. This has been equaled in duration and activity only by the processes, natural or experimental, which depend on activation by duodenal secretin.

2. Taken in connection with the inhibitory action of suprarenal and pituitary extracts on the pancreatic flow, this suggests a control over the pancreas, by the adrenals at least, in the absence of which the gland secretes more actively.

3. This activation of the pancreas may occur with a high systemic blood-pressure, though it generally occurs when the systemic blood-pressure is relatively low. Hemorrhage may modify or prevent it.

4. There is some evidence to indicate that on the death of a dog from removal of the adrenals, there is present in the duodenum more prosecretin than exists in dogs otherwise operated on which have their adrenals intact, and which die after a comparable long period of etherization. This preponderance may be a contributory factor in the production of a flow.

5. One of the factors which seem to make detection of prosecretin in human beings difficult is probably the lingering death of most of those from whom the intestinal extracts are made. In clinical investigations of secretin comparisons should not be made between such preparations and those from freshly killed animals, unless this fact be borne in mind.

PROTOCOLS

The following records are abstracts of our experiments, and are for the most part self-explanatory. The first column indicates the time, either directly or in terms of the intervals between the events recorded. The second column indicates the flow of pancreatic juice, in terms of cannulas or divisions of the cannula.

The same cannula was used practically throughout and contained ninety divisions. Occasionally we failed to record when it was exactly full, the excess being generally estimated on the ungraded distal end.

The last column indicates the blood-pressure in millimeters of mercury. The records of the secretin injections show the pancreatic output in terms of cannulas and fractions of a cannula, the latter giving the actual divisions reached.

The table below indicates the observations on which we based our first report¹ in May, 1909. They were on animals fed at various periods before the operation, in most of whom digestion was taking place more or less rapidly. We were assisted in making these observations by Dr. Stone and Dr. Rulon, then of the fourth-year class in the Medical School of the University of Pennsylvania.

Finally, we wish to express our obligation to Dr. Edward T. Reichert for the facilities he has placed at our command which have made possible the observations and studies here recorded. We also desire again to thank Dr. David L. Edsall for the kindly interest and encouragement which have aided us so materially in all our work.

PERSONALLY CONDUCTED OBSERVATIONS

OBSERVATIONS CONDUCTED CHIEFLY BY DR. STONE AND DR. BULON

$\dagger =$ a well-marked flow.

Normal control with flow.....	0
Normal control with no flow.....	6
Adrenals out with flow.....	9
Adrenals out with no flow.....	0
One adrenal out with flow; 1, violent; 1, marked (worms and blood in duodenum); 2, slight; 1, moderate; total.....	5
One adrenal out with no flow.....	4
One adrenal out; failure (clot in cannula).....	3
Abdominal injury with flow (chyme in intestine).....	1
Abdominal injury with no flow.....	1
Adrenals out; early death with flow.....	5
Adrenals out; early death with no flow.....	6
One adrenal out; early death with no flow.....	1
Total	38

9:45 a. m.	Ether.	Flow Active (9 Hours).	Blood-pressure.
	83 min. later	first cannula full	148
1:05 p. m.	1 hr. 49 sec. later	second cannula full	80
	2 hr. 20 min. later	third cannula full	70
4:01 p. m.	1 hr. 24 min. later	fourth cannula full	80
	1 hr. 17 min. later	fifth cannula full	} *75
			*45
6:09 p. m.	27 min. later	flow	40
	6 min. later	sixth cannula full	20
	19 min. later	80 divisions	16
6:34 p. m.	Death.		

Experiment 2, Jan. 3, 1910: Normal, No Flow, 36 hr. Fast

		Blood-pressure.
9:20 a. m.	Ether.	78
	1 hr. 27 min. later	first cannula full 90
	1 hr. 42 min. later	second cannula full 94
	51 min. later	third cannula full 86
	41 min. later	fourth cannula full 80
	35 min. later	fifth cannula full 78
	43 min. later	sixth cannula full 66
4:33 p. m.	36 min. later	seventh cannula full 60
	36 min. later	eighth cannula full 66
	33 min. later	ninth cannula full 64
	30 min. later	tenth cannula full 50
	26 min. later	eleventh cannula full clot
7:34 p. m.	30 min. later	twelfth cannula full 36
7:53 p. m.	19 min. later	64 divisions. death

Blood-pressure was low and early became low for a normal dog, indicating some analogy to the condition after long etherization or removal of adrenals. Intestine very slightly congested. Spleen markedly so in areas. Stomach and intestine alkaline in reaction.

Experiment 3, Jan. 13, 1909: Normal Dog, No Flow

		Blood-pressure.
9:30 a. m.	Ether.	180
	4 hr. 12 min. later	first cannula full 154
3:30 p. m.	2 hr. 16 min. later	second cannula full 160
5:14 p. m.	1 hr. 28 min. later	120
	1 hr. 03 min. later	third cannula full 136
	1 hr. 30 min. later	fourth cannula full 105
	1 hr. 12 min. later	fifth cannula full 58
	1 hr. 20 min. later	sixth cannula three 108
	59 min. later	seventh cannula three 80
	45 min. later	eighth cannula three 70
	18 min. later	69 divisions Death.

Typical nutmeg liver. Apparently respiratory death after 14 hours. Death somewhat sudden.

Experiment 4, Feb. 24, 1910: Normal Dog, No Flow

		Blood-pressure.
9:37 a. m.	Drum starts	136
12:15 p. m.	35½ divisions.	134
	Sucked out as cannula was removed and replaced, thinking the duct possibly blocked. O. K., however.	
4:01 p. m.	28 divisions	130
4:53 p. m.		104
6:39 p. m.	31 divisions	108
7:40 p. m.	Cannula taken out and replaced for the second time. O. K., however; cannula emptied.	
	28 divisions	
9:23 p. m.	43 divisions	94
9:57 p. m.	44 divisions	92

Blood-pressure.

Blood-pressure actually much lower as, owing to an unrecognized clot, it had not fallen and went no lower, even at death.

10:27 p. m. Death 90

Duct clear. Pancreas appeared normal. Intestines congested where handled, otherwise normal. Stomach empty and contracted. Spleen mottled, not bullous. Liver and kidneys show fatty degeneration. Lungs not collapsed. Anthracotic heart greatly hypertrophied. Adrenals very hemorrhagic.

Experiment 5, Feb. 28, 1910: Normal Dog, No Flow

			Blood-pressure.
9:05 a. m.	Ether.		134
10:43 a. m.		first cannula full	136
1:41 p. m.	2 hr. 48 min. later	second cannula full	144
3:55 p. m.		third cannula full	136
	1 hr. 32 min. later	fourth cannula full	110
7:04 p. m.	1 hr. 37 min. later	fifth cannula full	106
8:46 p. m.	1 hr. 53 min. later	sixth cannula full	106
9:40 p. m.	56 min. later	seventh cannula full	82
10:30 p. m.	52 min. later	eighth cannula full	60
11:31 30 sec.	52 min. later	ninth cannula full	60
12:00 p. m.	30 min. later	tenth cannula full	42
12:27 a. m.	29 min. later	eleventh cannula full	42
1:01 a. m.	36 min. later	twelfth cannula full	46
1:42 a. m.	41 min. later	thirteenth cannula full	28
1:48 a. m.	7 min. later	30 divisions.	death

Experiment lasted 17 hours.

Liver shows fatty change and some nutmeg appearance. Duct clear. Intestines empty and not congested. Stomach empty.

Experiment 6, April 8, 1910: Normal Control, No Flow

		Blood-pressure.
9:30 a. m.	Ether.	
9:53 a. m.	Tracing began.	146
1:02 p. m.	No flow	120
3:45 p. m.	No flow	120
5:50 p. m.	No flow	106
7:54 p. m.	No flow	114
9 p. m.	No flow	116
10:49 p. m.	No flow	76
12:13 a. m.	More ether given	108
12:40 a. m.	No flow	58
1 a. m.	No flow	46
1:14 a. m.	Death.	

This dog might have lived many hours yet, as blood-pressure was 108 at midnight; therefore, as the artificial condition of etherization was desired, and no ether had been given for some time except in small amounts, it was added until the blood-pressure fell. Otherwise the observation would have been equivalent to watching a healthy normal dog indefinitely.

Liver not congested. Spleen contracted, normal in color. Duct clear. Stomach empty. Adrenals, distinctly large for a dog of this size (Fox-terrier bitch), show a brown liquid medulla, hemorrhagic junction of medulla and cortex and lighter periphery to cortex. Intestines empty, not congested.

GROUP 2.—BOTH ADRENALS REMOVED*

Experiment 7, Dec. 15, 1909: Adrenals Out and Flow

11:40	Ether		Blood-pressure.
11:58	L.A.O.		96
	1 hr. 26 min. later	first cannula full	100
	38 min. later	second cannula full	96
	47 min. later	third cannula full	108
	1 hr. 50 min. later	fourth cannula full	78
	1 hr. 9 min. later	fifth cannula full	48
	20 min. later	sixth cannula full	†54
	14 min. later	seventh cannula full	42
	4 min. later	eighth cannula full	46
	2 min. 30 sec. later	ninth cannula full	46
	3 min. later	tenth cannula full	46
	4 min. later	eleventh cannula full	42
	6 min. later	twelfth cannula full	44
	11 min. later	thirteenth cannula full	44
	10 min. later	fourteenth cannula full	clot
	6 min. later	fifteenth cannula full	50
	5 min. 30 sec. later	sixteenth cannula full	50
	6 min. later	seventeenth cannula full	50
	5 min. later	eighteenth cannula full	50
	5 min. later	nineteenth cannula full	50
	4 min. 30 sec. later	twentieth cannula full	46
	5 min. later	twenty-first cannula full	42
	4 min. 30 sec. later	twenty-second cannula full	38
	3 min. later	twenty-third cannula full	34
	2 min. later	twenty-fourth cannula full	34
	1 min. 50 sec. later	twenty-fifth cannula full	34
	1 min. 50 sec. later	twenty-sixth cannula full	30
	2 min. 50 sec. later	twenty-seventh cannula full	26

7:23 p. m. Death. Stomach and intestines free from food.

Time of removal of right adrenal inadvertently omitted.

* R.A.O.=Right adrenal out. L.A.O.=Left adrenal out. S.O.=“Sucked out”=cannula emptied and record begins anew.

† 5:35 p. m.

Experiment 8, Dec. 20, 1909: Adrenals Removed; Flow

			Blood-pressure.
10:40 a. m.	Tracing begun; forty-eight-hour fast		110
10:48 a. m.	R.A.O.		
11:08 a. m.	L.A.O.		
11:10 a. m.	Juice at 77		
	12 min. later	first cannula full	90
	1 hr. 41 min. later	second cannula full	96
	1 hr. 16 min. later	third cannula full	90
2:30 p. m.	17 min. later		
	1 hr. 16 min. later	fourth cannula full	80
	1 hr. 19 min. later	fifth cannula full	70
	30 min. later	sixth cannula full; flow began	66
	11 min. later	seventh cannula full	66
	8 min. 30 sec. later	eighth cannula full	70

		Blood-pressure.
	9 min. later	ninth cannula full 74
	9 min. later	tenth cannula full 76
	7 min. 30 sec. later	eleventh cannula full 76
	8 min. 30 sec. later	twelfth cannula full 76
	9 min. 30 sec. later	thirteenth cannula full 80
	12 min. later	fourteenth cannula full 82
	15 min. later	fifteenth cannula full 82
	18 min. later	sixteenth cannula full 82
	21 min. later	seventeenth cannula full 90
	1 hr. 13 min. later *	eighteenth cannula full 50
	56 min. later	15 divisions
10:00 p. m.		death
Cannula probably O. K. Stomach acid, brown fluid; no congestion. Spleen congested; liver not.		
* Then S. O. to 52.		

*Experiment 9, Dec. 22, 1909: Adrenals Out, with Flow**

10:30 a. m.	Ether begins	
10:48 a. m.	R.A.O.	
11:08 a. m.	L.A.O.	
11:22 a. m.	Drum starts	
		Blood-pressure.
11:27 a. m.		cannula full 134
	1 hr. 6 sec. later	first cannula full 120
	1 hr. 7 sec. later	second cannula full 102
	1 hr. 39 min. later	third cannula full 92
	53 min. later	fourth cannula full 66
	30 min. later	fifth cannula full 49
	12 min. later	sixth cannula full 46
	11 min. later	seventh cannula full 46
	4 min. later	eighth cannula full 46
	3 min. 30 sec. later	ninth cannula full 44
	3 min. 30 sec. later	tenth cannula full clot
	4 min. later	eleventh cannula full 32
6:06 p. m.		death

* Operative procedures in following order: Adrenals out, cannula in pancreas, respiratory cannula, blood-pressure.

Small amount of ether apparently caused death. Spleen bullous and very congested. Liver moderately congested. Kidneys moderately congested. Intestines greatly congested and almost black in upper part of duodenum. Intestines and stomach empty, and alkaline or neutral.

Experiment 10, Jan. 6, 1910: Adrenals Out with Flow, but Early Death

9:45 a. m.	R.A.O.	
10:00 a. m.	L.A.O.	
10:18 a. m.	Drum starts.	
		Blood-pressure.
10:25 a. m.		88
	2 hr. 9 min. later	first cannula full 40
	24 min. later	second cannula full 20
	17 min. later	third cannula full 20
	8 min. 30 sec. later	fourth cannula full 20
	8 min. 30 sec. later	fifth cannula full 20
Death.	22 min. later	55 divisions

Much bile extruded. Intestines and liver not much congested. Spleen considerably congested. Stomach alkaline. Stomach empty, except for bile and a plum-stone.

Experiment 11, Jan. 10, 1910: Adrenals Removed, Moderate Flow, Early Death

Cannula in bile-duct.		
9:20 a. m.	Ether	
9:40 a. m.	R. A. O.	
9:48 a. m.	L. A. O.	
		Blood-pressure.
10:22 a. m.	Drum starts	124
	31 min. later first cannula full	114
	42 min. later second cannula full	100
	Fall of blood-pressure from manipulation of intestines to replace bile-duct	44
	31 min. later fourth cannula full	28
	18 min. 30 sec. later fifth cannula full	16
	7 min. 30 sec. later sixth cannula full	10
1:06 p. m.	Death	
Spleen greatly congested, though not bullous. Stomach somewhat congested and considerable bile. Liver moderately congested. Intestines locally hemorrhagic where handled and somewhat darkened throughout. Twelve c.c. bile altogether. No flow of bile at end.		

Experiment 12, Jan. 11, 1910: Adrenals Removed, with Flow

		Blood-pressure.
9:38 a. m.	Ether	
10:08 a. m.	R. A. O.	146
10:18 a. m.	L. A. O.	104
	32 min. later first cannula full	
	16 min. later second cannula full	110
	50 min. later third cannula full	120
	25 min. later fourth cannula full	124
	30 min. later fifth cannula full	112
	32 min. later sixth cannula full	102
	25 min. later seventh cannula full	90
	20 min. later eighth cannula full	80
	24 min. later ninth cannula full	80
	22 min. later tenth cannula full	70
	10 min. later eleventh cannula full	clot
	9 min. later twelfth cannula full	60
	8 min. 30 sec. later thirteenth cannula full	60
	6 min. later fourteenth cannula full	50
	2 min. 30 sec. later fifteenth cannula full	44
	2 min. 30 sec. later sixteenth cannula full	44
	4 min. later seventeenth cannula full	44
	5 min. later eighteenth cannula full	44
	4 min. later nineteenth cannula full	44
	3 min. later twentieth cannula full	40
	2 min. 15 sec. later twenty-first cannula full	40
	1 min. 45 sec. later twenty-second cannula full	34
	1 min. 30 sec. later twenty-third cannula full	34
	1 min. 15 sec. later twenty-fourth cannula full	
	1 min. 15 sec. later twenty-fifth cannula full	30
	1 min. later twenty-sixth cannula full	30

Blood-pressure.

50 sec. later twenty-seventh cannula full	30
40 sec. later twenty-eighth cannula full	24
32 sec. later twenty-ninth cannula full	24
36 sec. later thirtieth cannula full	24
30 sec. later thirty-first cannula full	22
30 sec. later thirty-second cannula full	20
1 min. 10 sec. later thirty-third cannula full	20
3 min. later thirty-fourth cannula full	14

4:00 p. m. Death.

Liver not congested. Spleen moderately congested; very dark. Stomach empty; slight amount of chyme. No congestion of intestines anywhere, except at a few spots opposite cannula where handled. No flow of bile to speak of.

Experiment 13, Feb. 3, 1910: Adrenals Removed; Flow

Blood-pressure.

9:45 a. m.	L. A. O.	
9:53 a. m.	R. A. O.	
10:14 a. m.	Drum starts	130
	59 min. later first cannula full (overflow)	132
	41 min. later second cannula full	138
	12 min. later third cannula full	140
	14 min. 30 sec. later fourth cannula full	130
	15 min. later sixth cannula full (overflow)	132
	4 min. later seventh cannula full	126
	5 min. 30 sec. later eighth cannula full	126
	6 min. later ninth cannula full	112
	9 min. later tenth cannula full	110
	4 min. 30 sec. later eleventh cannula full	102
	4 min. 30 sec. later twelfth cannula full	98
	4 min. later thirteenth cannula full	104
	4 min. later fourteenth cannula full	90
	4 min. 30 sec. later fifteenth cannula full	90
	4 min. 30 sec. later sixteenth cannula full	86
	6 min. later seventeenth cannula full	84
	7 min. later eighteenth cannula full	88
	3 min. later nineteenth cannula full	86
	3 min. 55 sec. later twentieth cannula full	80
	5 min. 30 sec. later twenty-first cannula full	76
	7 min. later twenty-second cannula full	70
	5 min. 10 sec. later twenty-third cannula full	72
	22 min. later twenty-fourth cannula full	Death.

Position of blood-pressure above base line somewhat doubtful. Autopsy shows nothing of importance. Spleen shows very small areas of extreme congestion. Intestines show hemorrhagic congestion at edges of folds in that area which was subjected to handling.

Experiment 14, April 4, 1910: Adrenals Removed; Moderate Flow

Blood-pressure.

10:25 a. m.	R. A. O.	
10:35 a. m.	L. A. O.	
10:58 a. m.	Drum starts	
	28 min. later juice flowing O. K.	
	11 min. later first cannula full	130
	6 min. 30 sec. later second cannula full	128

		Blood-pressure.
11 min. later	third cannula full	132
23 min. later	fourth cannula full	104
43 min. later	fifth cannula full	102
13 min. 30 sec. later	sixth cannula full	104
3 min. later	seventh cannula full	112
9 min. 30 sec. later	eighth cannula full	104
7 min. later	ninth cannula full	104
29 min. later	tenth cannula full	98
43 min. later	eleventh cannula full (overfull)	92
11 min. later	twelfth cannula full	82
8 min. 30 sec. later	thirteenth cannula full	78
42 min. later	fourteenth cannula full	62

4:00 p. m. Death.

Autopsy showed no congestion of intestine. A small clot was found in opening of cannula, possibly partially occluding the duct.

Experiment 15, Feb. 8, 1910: Adrenals Removed; Hemorrhage; Flow

		Blood-pressure.
9:50 a. m.	R. A. O.	
10:10 a. m.	L. A. O.	
10:25 a. m.	Drum starts	160
	1 hr. 51 min. later	first cannula full
	1 hr. 8 min. later	second cannula full
	1 hr. 40 min. later	third cannula full
	15 min. later *	fourth cannula full
	3 min. 30 sec. later	fifth cannula full
	3 min. 30 sec. later	sixth cannula full
	3 min. later	seventh cannula full
	3 min. 30 sec. later	eighth cannula full
	3 min. 10 sec. later	ninth cannula full
	3 min. 50 sec. later	tenth cannula full
	4 min. later	eleventh cannula full
	5 min. 10 sec. later	twelfth cannula full
3:54 p. m.	13 min. 30 sec. later	thirteenth cannula full at 70th division

Death.

* Flow begins 3 p. m.

Stomach empty, except for a little bile, as are also the intestines. Pancreas paler than normal. Duct clear and free, extensive hemorrhage in abdomen; few clots; no congestion of intestine and stomach, except for a few spots on the intestines where handled. Blood in abdomen probably 25 per cent. of total blood or more. No supernatant serum. Liver normal in color. No terminal flow. Spleen blue and slightly roughened; rather hard and apparently not swollen. Kidneys not so blue as usual. Apparently no general congestion; little, if any, anywhere.

Experiment 16, Feb. 12, 1910: Adrenals Removed and Flow

		Blood-pressure.
9:50 a. m.		150
10:25 a. m.	R. A. O.	
10:40 a. m.	L. A. O.	76
11:29 a. m.		first cannula full
12:04 p. m.	35 min. later	second cannula full
12:30 p. m.	26 min. later	third cannula full
12:51 p. m.	21 min. later	fourth cannula full

		Blood-pressure.
1:11:30 p. m.	20 min. 30 sec. later fifth cannula full	50
1:30 p. m.	18 min. 30 sec. later sixth cannula full	44
1:43 p. m.	13 min. later seventh cannula full	40
1:48 p. m.	5 min. later eighth cannula full	36
1:49:10 p. m.	1 min. 10 sec. later ninth cannula full	36
1:50:30 p. m.	1 min. 20 sec. later tenth cannula full	36
1:51:18 p. m.	48 sec. later eleventh cannula full	34
1:52:13 p. m.	55 sec. later twelfth cannula full	30
1:55:8 p. m.	55 sec. later thirteenth cannula full	30
1:53 p. m.	at 79th division.	Death.

Experiment 17, Feb. 17, 1910: Adrenals Removed; Flow

		Blood-pressure.
9:50 a. m.		136
10:11 a. m.	R. A. O.	
10:32 a. m.	L. A. O.	
10:57 a. m.		86
11:34 a. m.		96
11:46 a. m.	first cannula full	90
1:38 p. m.	second cannula full	84
1:42 p. m.	third cannula full	90
1:44:30 p. m.	fourth cannula full	86
1:51:30 p. m.	fifth cannula full	84
1:55:30 p. m.	sixth cannula full	80
2:02 p. m.	seventh cannula full	78
2:05 p. m.	eighth cannula full	80
2:07:30 p. m.	ninth cannula full	80
2:15:30 p. m.	tenth cannula full	70
2:26 p. m.	eleventh cannula full	70
2:41:30 p. m.	twelfth cannula full	66
2:44:30 p. m.	thirteenth cannula full	64
2:48:30 p. m.	fourteenth cannula full	52
2:57:30 p. m.	fifteenth cannula full	56
2:59 p. m.	sixteenth cannula full	54
3:05 p. m.	seventeenth cannula full	*46
3:18 p. m.	eighteenth cannula full	44
3:47:30 p. m.	nineteenth cannula full	42
4:02:30 p. m.	Death.	

* Ether added and it rises to 100.

Three hundred c.c. blood-stained fluid in peritoneum. Duct clear. Spleen moderately congested. Liver more congested. Intestines hemorrhagic high up.

GROUP 3.—ADRENALS REMOVED; EARLY DEATH

Experiment 18, Dec. 13, 1910: Adrenals Removed and Flow

No mention by accident of time of removal of left adrenal.

		Blood-pressure.
9:30 a. m.	Ether	150
9:47 a. m.	R. A. O.	
	48 min. later first cannula full	86
	48 min. later second cannula full	50
	17 min. later third cannula full	22

Blood-pressure.

* 2 min. 40 sec. later fourth cannula full 18
 5 min. later fifth cannula full

12:10 p. m. Death.
 * Violent flow.

Fasted twenty-four hours, but stomach contained small amount of water and very small amount of food. Duodenum deeply congested. Intestine contained chyme throughout entire length.

Experiment 19, Dec. 17, 1909: Adrenals Removed; Early Death; No Flow

Blood-pressure.

9:58 a. m. R. A. O.
 10:03 a. m. I. A. O.
 10:24 a. m. Drum starts 110
 1 hr. 22 min. later death 98

Slight flow during that time, but no cannula filled.

Experiment 20, Dec. 18, 1910: Adrenals Removed; Hemorrhage; No Flow; Early Death

Blood-pressure.

9:48 a. m. R. A. O. variable 104 to 130
 9:59 a. m. L. A. O. hemorrhage from neck 80
 1 hr. 14 min. later first cannula full, S. O. to 10 32
 Very long cannula, not generally used.
 37 min. later cannula 14 divisions. Death.

Intestine, spleen, liver and kidneys deeply congested. Pancreas not congested. Right adrenal broken in removal.

Experiment 21, Feb. 2, 1910: Adrenals Removed; Early Death, but yet a Flow

Blood-pressure.

9:30 a. m. Ether
 9:45 a. m. R. A. O.
 9:53 a. m. L. A. O.
 10:12 a. m. Drum starts 110
 1 hr. 9 min. later first cannula full 94
 50 min. later second cannula full 20
 3 min. 30 sec. later third cannula full clot
 2 min. 30 sec. later fourth cannula full clot
 12:20 p. m. 6 min. later fifth cannula full Death.

Stomach full of bile and some hair. Spleen blue, but not unduly congested. Intestines empty and not congested. Liver not congested.

Experiment 21, Feb. 7, 1910: Adrenals Removed; No Flow; Early Death.

Blood-pressure.

10:00 a. m. Ether
 10:14 a. m. R. A. O.
 10:21 a. m. L. A. O.
 10:50 a. m. Drum starts 94
 Both adrenals torn in removal.
 35 min. later first cannula full 92
 52 min. later second cannula full 28
 25 min. later third cannula full Death.

Experiment 23, Feb. 7, 1910: Adrenals Removed; Hemorrhage; No Flow
 Blood-pressure.

1:30 p. m.	R. A. O.		
1:37 p. m.	L. A. O.		
2:00 p. m.	Drum started		150
	2 hrs. 14 min. later	first cannula full	130
	1 hr. 25 min. later	second cannula full	40
	1 hr. 5 min. later	80th division	Death.

Much hemorrhage in abdomen. No congestion. No flow.

Experiment 24, Feb. 10, 1910: Adrenals Removed; Slight Flow; Early Death
 Blood-pressure.

9:45 a. m.	Ether		
10:00 a. m.	R. A. O.		
10:06 a. m.	L. A. O.		
10:25 a. m.	Drum starts		130
	7 min. later	hemorrhage from neck, about 4 ounces	110
	3 min. later		126
	45 min. later	dog vomits bile, insufflates and nearly dies; when quiet again blood-pressure	110
	41 min. later	first cannula full	84
	29 min. later	second cannula full	64
	11 min. later	third cannula full	54
	9 min. later	55th division	Death.

Pancreatic cannula free. Lungs do not collapse on opening thorax.

Experiment 25, Feb. 11, 1910: Adrenals Removed; Early Death; No Flow
 Blood-pressure.

9:35 a. m.	R. A. O.		
9:44 a. m.	L. A. O.		
10:14 a. m.	Drum starts		94
	1 hr. 40 min. later	first cannula full	50
	42 min. later	85th division	Death.

Stomach and intestines empty except for bile. Duct clear. Spleen only slightly congested. Intestines much congested everywhere and hemorrhagic in spots throughout. Death too early.

*Experiment 26, Feb. 15, 1910: Adrenals Removed; Hemorrhage; No Flow;
 Early Death*
 Blood-pressure.

9:27 a. m.	Ether		180
9:54 a. m.	R. A. O.		
10:03 a. m.	L. A. O.		136
	1 hr. 9 min. later	40 divisions previously S. O.	100
12:24 p. m.	1 hr. 10 min. later	first cannula full	86
1:30 p. m.	1 hr. 7 min. later	second cannula full	74
2:41 p. m.	1 hr. 5 min. later	third cannula full	34
2:50 p. m.	12 min. later	78th division.	Death.

Five hundred c.c. blood in peritoneal cavity, evidently from the site of right adrenal.

GROUP 4.—LEFT ADRENAL REMOVED

Experiment 27, March 11, 1910: Left Adrenal Removed; Moderate Flow

		Blood-pressure.
9:30 a. m.	Tracing began; adrenal torn in removal	150
9:35 a. m.	L. A. O.	
10:31 a. m.		130
	Juice flowing freely from start.	
11:16 a. m.	first cannula full (100)	120
12:50 p. m.	second cannula full	126
1:59 p. m.	third cannula full	120
2:50 p. m.	fourth cannula full	124
3:09 p. m.	fifth cannula full	80
3:32 p. m.	sixth cannula full	96
3:44 p. m.	seventh cannula full	82
4:01 p. m.	eighth cannula full	92
4:17 p. m.	ninth cannula full	84
4:31 p. m.	tenth cannula full	64
4:43 p. m.	eleventh cannula full	40
4:55:30 p. m.	twelfth cannula full	30
5:12 p. m.	thirteenth cannula full	Death.

Some flow all day. Duct contained a small soft loose clot. Pancreas not congested. Moderate amount of blood-stained fluid in abdomen. Spleen very blue and congested, but smooth. Stomach and intestines full of bile, but no food. Slight congestion where handled. Liver somewhat fatty, but not congested. Left adrenal shows striation and hemorrhage in cortex. Medulla soft and relatively empty.

Experiment 28, March 14, 1910: Left Adrenal Removed; Slight Flow

		Blood-pressure.
9:10 a. m.	Ether	184
9:33 a. m.	L. A. O.	126
11:24 a. m.	first cannula full	158
2:26 p. m.	second cannula full (overflow)	136
3:03 p. m.	B. P. cannula blows out and 50 c.c. blood lost	136
3:26 p. m.	third cannula full	146
4:43 p. m.	fourth cannula full	128
5:52 p. m.	fifth cannula full (overflow)	84
6:37 p. m.	sixth cannula full	64
7:22:30 p. m.	seventh cannula full	52
8:04 p. m.	eighth cannula full	50
8:35 p. m.	ninth cannula full	26
8:43 p. m.	43d division.	Death.

This dog evidently died of heart failure. Intestines extremely congested throughout entire extent. In part the mucosa was hemorrhagic. Spleen dark blue. Pancreatic cannula clear. Pancreas showed no evidence of congestion. Right adrenal was grayish pink, shows hemorrhagic striation on section. Lungs normal. Heart flabby. Liver congested. Stomach and intestines empty, save for bile and possibly some chyme in lower part of small intestine.

Experiment 29, March 16, 1910: Left Adrenal Removed; Some Flow

		Blood-pressure.
9:35 a. m.	Ether	156
10:00 a. m.	L. A. O.	
10:20 a. m.		144
12:30 a. m.		113
	Fluid in cannula at 80 sucked out on account of blood-stain; blood-pressure pen slipped down on piston-rod	138
4:01 p. m.	first cannula full	126
5:19 p. m.	second cannula full	92
6:10 p. m.	third cannula full	78
6:55 p. m.	fourth cannula full	70
7:26 p. m.	fifth cannula full (95)	66
7:58 p. m.	sixth cannula full	68
8:24 p. m.	seventh cannula full	68
8:50 p. m.	eighth cannula full (at 100 overfull)	clot
9:06:30 p. m.	ninth cannula full	40
9:20 p. m.	cannula at 85	Death.

Juice clear for at least three hours and flowing steadily and progressively slightly faster. It was very slow in morning. One hundred c.c. blood in abdomen, including a good-sized clot, evidently the site of the left adrenal. Retroperitoneal fat tissue shows hemorrhage into its substance. Liver shows some fatty and possibly some nutmeg appearance. Small clot in pancreatic duct which does not occlude duct or mouth of cannula. Pancreas normal in color. Intestines intensely hemorrhagic where handled. Stomach contains mucus and hair. Intestines full of a queer gruel-like mass, color of digested blood, which may be the gastric contents in part. Spleen moderately congested and smooth. Right adrenal shows area of hemorrhage on inside edge of cortex all around it.

Experiment 30, March 17, 1910: Left Adrenal Removed; No Flow

		Blood-pressure.
At start		170
10:26 a. m.	L. A. O.	
12:05 p. m.		120
2:26 p. m.		120
5:55 p. m.	first cannula full	106
7:05 p. m.		100
11:20 p. m.	87th division	Death.

Dog's death at 11:20 hastened by ether. Only one cannula in thirteen hours. Bloody all day, however. Liver not congested. Spleen moderately so. Stomach and intestines empty, except for bile. Pancreas pale. Cannula clear below joint. Duct seems clear. Moderate amount of blood-stained fluid in abdomen. Right adrenal in better shape than most. But little injection around the cortex.

This dog was another instance of a practically normal dog which might have lived many hours yet.

Experiment 31, March 28, 1910: Left Adrenal Removed; Big Flow

		Blood-pressure.
9:30 a. m.	Ether	
9:42 a. m.	L. A. O.	174
11:33 a. m.	cannula 25	150
12:37 p. m.		176

		Blood-pressure.
2:53 p. m.		164
3:34 p. m.	first cannula full	170
4:36 p. m.	second cannula full (97)	154
5:09 p. m.	third cannula full	160
5:33 p. m.	fourth cannula full	160
5:57 p. m.	fifth cannula full (overflow)	136
6:10 p. m.	sixth cannula full	134
6:15 p. m.	seventh cannula full	130
6:24 p. m.	eighth cannula full	120
	6 min. 30 sec. later ninth cannula full	clot
	5 min. 30 sec. later tenth cannula full	clot
	5 min. 20 sec. later eleventh cannula full	clot
	5 min. later twelfth cannula full	clot
	Roll changed thirteenth cannula full	clot
	5 min. later fourteenth cannula full	clot
	5 min. 30 sec. later fifteenth cannula full	clot
	7 min. later sixteenth cannula full *	
7:18:30 p. m.	5 min. later seventeenth cannula full	44
	2 min. 20 sec. later eighteenth cannula full	44
	4 min. later nineteenth cannula full	40
7:29 p. m.	4 min. later 79th division	Death.

* Loss of juice as cannula came out; loss of 20 divisions.

Small amount of blood-stained fluid in abdomen. Stomach and intestines not congested. Intestines contain small amount of yellow grumous material, which was possibly chyme. Stomach contains considerable quantity of green, muddy fluid. Spleen not congested, save for a few bullæ. Kidneys congested. Right adrenal very much congested, especially at junction of cortex and medulla. Lungs and heart normal.

Right adrenal, parathyroids and pituitary taken for sections.

Experiment 32, March 29, 1910: Left Adrenal Removed; No Flow

		Blood-pressure.
9:30 a. m.	Ether	130
10:00 a. m.	L. A. O.	
11:23 a. m.	no flow	136
12:50 p. m.	no flow	128
1:55 p. m.	no flow	110
3:22 p. m.	no flow	90
4:30 p. m.	Death no flow	60

Very little fluid in abdomen which pushed intestines into flank. Upper portion of duodenum very hemorrhagic. Intestines, in fact, very deeply congested throughout. Spleen very dark blue and covered with bullæ. No clot in duct. Liver congested; kidneys very much so. Stomach empty, except for air and some bloody, bile-stained mucus. Intestines empty, except for considerable blood. Right adrenal quite congested and blue, especially medulla. Cortex only slightly so. Left adrenal, removed in morning, also shows some cyanosis of the medulla. Heart very dilated and collapsed. Lungs normal.

GROUP 5.—RIGHT ADRENAL REMOVED

Experiment 33, Feb. 26, 1910: Attempt to Cause Abdominal Trauma Analogous to Removal of Both Adrenals; No Flow

		Blood-pressure.
9:05 a. m.	Ether	
9:19 a. m.	R. A. O.	142

			Blood-pressure.
9:25 a. m.		pancreatic cannula in place	
	3 hrs.18 min. later	first cannula full	142
1:43 p. m.	1 hr. 7 min. later	second cannula full	116
	34 min. later	third cannula full	94
	39 min. later	fourth cannula full	82
	About 5 minutes before last entry blood-pressure fell to 42, probably from too much ether.		
	23 min. later	fifth cannula full	58
	21 min. later	sixth cannula full	56
	16 min. later	seventh cannula full	46
4:05 p. m.	12 min. 30 sec. later	81st division	Death.

Duct clear. This dog gave a more than usually active flow at start. Spleen shows a few bullous patches; not especially congested. Liver slightly congested. Intestines very slightly congested and full of hemorrhagic ulcers in the upper part. Stomach contains considerable bile. Right adrenal was considerably torn in removal and was friable.

Experiment 34, March 2, 1910: One Adrenal Out; Early Death; No Flow

			Blood-pressure.
9:10 a. m.	Ether		166
9:30 a. m.	R. A. O.		
9:51 a. m.			120
12:00 m.	2 hrs. 6 min. later	dog dies from sudden respiratory failure.	

*Experiment 35, March 3, 1910: Attempt to Get Flow by Abdominal Injury; No Flow **

			Blood-pressure.
9:49 a. m.			174
10:02 a. m.	R. A. O.		
10:10 a. m.			136
11:44 a. m.		first cannula full	145
12:47 p. m.		second cannula full	145
1:39 p. m.		third cannula full	130
2:47 p. m.		fourth cannula full	120
3:56 p. m.		fifth cannula full	92
5:00 p. m.		sixth cannula full (100)	94
6:04 p. m.		seventh cannula full (105)	78
6:30 p. m.		eighth cannula full (105)	64
7:27 p. m.		ninth cannula full	44
8:39 p. m.		tenth cannula full	40
9:15 p. m.		cannula at 57	Death.

* R. A. O. for control of flow.

Duct free. Stomach contains considerable yellow-green fluid. Intestines empty. From about 2 inches below the pylorus to a point corresponding to the tail of the pancreas, the mucosa is raised in hemorrhagic patches, looking like ulcers (covered with mucus). Spleen not congested, but contains several bullous patches. Kidney and liver show small amount of fatty degeneration. Left adrenal at its larger end markedly hemorrhagic. Pancreas seems slightly congested, showing slight pinkish tinge in contrast to dead white color of fasting pancreas.

Experiment 36, March 9, 1910: Good Flow; Right Adrenal Removed; Worms and Blood in Intestines

		Blood-pressure.
9:30 a. m.		180
9:52 a. m.	R. A. O.	116
10:17 a. m.		106
	Juice running freely, no apparent cause for the fall in blood-pressure.	
1:30 p. m.	first cannula full	114
2:41 p. m.	second cannula overfull	clot
	10 min. later	92
3:25 p. m.	third cannula full	72
4:01 p. m.	fourth cannula full	72
4:32 p. m.	fifth cannula full	60
4:58 p. m.	sixth cannula full	clot
5:25 p. m.	seventh cannula full (100)	42
5:45 p. m.	eighth cannula full	38
6:00 p. m.	ninth cannula full	34
6:14 p. m.	tenth cannula full	30
6:26 p. m.	eleventh cannula full	28
6:36:30 p. m.	twelfth cannula full	24
6:46:45 p. m.	thirteenth cannula full	20
6:56:30 p. m.	fourteenth cannula full	clot
7:06 p. m.	fifteenth cannula full	20
7:12:30 p. m.	sixteenth cannula full	16
7:17 p. m.	seventeenth cannula full	Death.

This dog was very strong constitutionally and lived with blood-pressure very low for several hours—longer in that state than the dogs with both adrenals removed do and almost as long as do the normal.

Small amount of blood-stained fluid in peritoneal cavity. Duct clear. Intestine full of uncinariæ in great numbers, and partially digested blood (this may have increased flow). Mucosa looks somewhat roughened. Liver not congested. In intestines considerable blood-stained fluid and some bile; in lower intestines, much dark grumous blood. Spleen not congested; shows one bullous patch. Stomach distended with gas and contains a considerable amount of mucus and bile. Left adrenal looked normal on section.

Juice flowed fairly freely at the beginning of the experiment.

GROUP 6.—ABDOMINAL INJURY

Experiment 37, April 4, 1910: Abdomen Injured; Adrenals Intact; Chyme in Intestines

		Blood-pressure.
9:05 a. m.	Ether	
	Abdomen disturbed for control. Adrenals bluntly dissected, but left intact	142
	Dog quite susceptible to ether	
10:27 a. m.	first cannula full	148
	Juice flowing freely when cannula put in place at onset.	
10:56 a. m.	second cannula full	130
11:28 a. m.	third cannula full	148
12:00 m.	fourth cannula full	156
12:33 p. m.	fifth cannula full	142

		Blood-pressure.
1:00 p. m.	sixth cannula full	138
1:26 p. m.	seventh cannula full	136
1:49 p. m.	eighth cannula full	136
2:15 p. m.	ninth cannula overfull	142
2:31 p. m.	tenth cannula full	142
2:48 p. m.	eleventh cannula full	104
3:12 p. m.	twelfth cannula full	clot
3:29 p. m.	thirteenth cannula full	115
3:46 p. m.	fourteenth cannula overfull	80 *
4:00 p. m.	fifteenth cannula overfull	70 *
4:12 p. m.	sixteenth cannula overfull	54 *
4:22 p. m.	seventeenth cannula full	54 *
4:32 p. m.	eighteenth cannula full	46*
4:41 p. m.	nineteenth cannula full	44*
4:49 p. m.	twentieth cannula full	42
4:57 p. m.	twenty-first cannula full	74
5:06 p. m.	twenty-second cannula full †	72
5:12 p. m.	twenty-third cannula full	52
5:18:30 p. m.	twenty-fourth cannula full	50
	7 min. 30 sec. later twenty-fifth cannula full	40
	5 min. later twenty-sixth cannula full	26
	1 min. 30 sec. later 10 divisions	Death.

* Blood-pressure-recording pen probably slipped down.

† 105.

Intestines contained chyme within a few inches of pylorus. It will be noticed that a flow existed in this dog from the start. Spleen mottled with dark blue areas. Liver not congested, yellowish. Intestines not congested. Stomach empty. Adrenals both congested and hemorrhages at junction of cortex and medulla.

Experiment 38, April 6, 1910: Abdominal Injury; Adrenals Bluntly Dissected; No Flow

		Blood-pressure.
9:32 a. m.	Ether	
9:50 a. m.		dissection finished 134
12:09 p. m.		no cannula filled 108
5:07 p. m.		no cannula filled 110
7:02 p. m.	Death	no cannula filled 34

Duct clear. Pancreas and intestines pale rather than congested. Juice moved 11 divisions all day. Spleen contracted, hard, with a few dark blue patches. Liver not congested. Adrenals hemorrhagic between cortex and medulla. Stomach and intestines empty, save for bile. Heart and lungs normal, save that heart is somewhat flaccid.

GROUP 7.—RECORDS OF THE TESTS OF THE VARIOUS SECRETIN PREPARATIONS AGAINST EACH OTHER

Experiment 39: Normal Secretin Versus Terminal Normal Secretin

Dec. 30, 1909: T. N. S. made from experiment of Dec. 29, 1909 (See Experiment 1).

	N. S.*	caused the filling of 4 cannulas and 45 divisions.†
T. N. S.	" " " "	1 " " 28 "
N. S.	" " " "	4 " " 32 "
T. N. S.	" " " "	1 " " "

N. S. caused the filling of 4 cannulas and 39 divisions.†
 T. N. S. " " " " 1 "
 N. S. " " " " 3 "

T. N. S. much weaker than N. S.

* Where the quantity of secretin injected is not specified, inadvertently no record was taken of the amount at the time of the experiment, but it was always either 5 or 10 c.c., and was constant for any given comparison.

† It will be remembered that the cannulas used were marked off into 90 divisions each.

Experiment 40: Normal Secretin Versus Terminal Normal Secretin

Jan. 4, 1910: T. N. S. made from experiment of Jan. 3, 1910 (See Experiment 2).

5 c.c. N. S. caused the filling of 1 cannula and 38 divisions.
 5 c.c. T. N. S. " " " " 0 " " 45 "
 10 c.c. N. S. " " " " 2 " " 44 "

Dog died.

N. S. stronger than T. N. S.

Experiment 41: Normal Secretin Versus Terminal Normal Secretin

Jan. 5, 1910: T. N. S. made from experiment of Jan. 3, 1910 (See Experiment 2); repetition of tests of Jan. 4, 1910.

N. S. Cannula stuck.
 T. N. S. Accident to apparatus.
 10 c.c. N. S. caused the filling of 3 cannulas.
 10 c.c. T. N. S. " " " " 1 " and 69 divisions.
 10 c.c. N. S. " " " " 2 " " 44 "
 10 c.c. T. N. S. " " " " 1 " " 48 "

N. S. stronger than T. N. S.

Experiment 42: Normal Secretin Versus Terminal Adrenal Secretin

Jan. 7, 1910: T. A. S. made from experiment of Jan. 6, 1910 (See Experiment 10).

7 c.c. N. S. caused the filling of 2 cannulas and 48 divisions.
 5 c.c. T. A. S. " " " " 3 " " 70 "
 5 c.c. N. S. " " " " 0 " " 72 "
 5 c.c. T. A. S. " " " " 1 " " 83 "

T. A. S. stronger than N. S.

Experiment 43: Normal Secretin Versus Terminal Adrenal Secretin

Feb. 9, 1910: T. A. S. made from experiment of Feb. 8, 1910 (See Experiment 15).

5 c.c. N. S. caused the filling of 12 cannulas and 30 divisions.
 5 c.c. T. A. S. " " " " 10 " " 78 "
 5 c.c. N. S. " " " " 6 " " 65 "
 5 c.c. T. A. S. " " " " 4 " " 40 "
 5 c.c. N. S. " " " " 4 " " 70 "

N. S. stronger than T. A. S.

There was hemorrhage from the dog which gave T. A. S. This may have modified the activity.

Experiment 44: Normal Secretin Versus Terminal Adrenal Secretin

Jan. 12, 1910: T. A. S. made from experiment of Jan. 11, 1910 (See Experiment 12).

N. S. caused the filling of 3 cannulas and 25 divisions.

T. A. S.	"	"	"	"	6			
N. S.	"	"	"	"	4	"	"	57 "
T. A. S.	"	"	"	"	5	"	"	37 "
N. S.	"	"	"	"	3	"	"	59 "
T. A. S.	"	"	"	"	5	"	"	83 "
N. S.	"	"	"	"	2	"	"	49 "

T. A. S. more active than N. S.

Experiment 45: Normal Secretin Versus Terminal Adrenal Secretin

Feb. 13, 1910: T. A. S. made from experiment of Feb. 12, 1910 (See Experiment 16).

5 c.c. N. S. caused the filling of 6 cannulas and 73 divisions.

5 c.c. T. A. S.	"	"	"	"	3	"	"	32 "
5 c.c. N. S.	"	"	"	"	3	"	"	54 "
5 c.c. T. A. S.	"	"	"	"	3	"	"	41 "
5 c.c. N. S.	"	"	"	"	2	"	"	40 "
5 c.c. T. A. S.	"	"	"	"	2	"	"	82 "
5 c.c. N. S.	"	"	"	"	2	"	"	52 "
5 c.c. T. A. S.	"	"	"	"	4	"	"	59 "
5 c.c. N. S.	"	"	"	"	1	"	"	62 "
5 c.c. T. A. S.	"	"	"	"	2	"	"	30 "

N. S. grows weaker; T. A. S. grows stronger.

Action eventually reversed.

Experiment 46: Normal Secretin Versus Terminal Adrenal Secretin

Feb. 14, 1910: T. A. S. made from experiment of Feb. 12, 1910 (See Experiment 16).

N. S. caused the filling of 1 cannula. (Clot.)

T. A. S.	"	"	"	"	3	"	and 70 divisions.
N. S.	"	"	"	"	1	"	" 75 "
T. A. S.	"	"	"	"	2	"	" 36 "
N. S.	"	"	"	"	1	"	" 79 "
T. A. S.	"	"	"	"	3	"	"
N. S.	"	"	"	"	3	"	" 59 "
T. A. S.	"	"	"	"	2	"	" 48 "

T. A. S. stronger than N. S. in all but last pair of tests.

Experiment 47: Normal Secretin Versus Terminal Adrenal Secretin

Feb. 18, 1910: T. A. S. made from experiment of Feb. 17, 1910 (See Experiment 17).

5 c.c. N. S. caused the filling of 8 cannulas and 60 divisions.

5 c.c. T. A. S.	"	"	"	"	7	"	"	62 "
5 c.c. N. S.	"	"	"	"	8	"	"	68 "
5 c.c. T. A. S.	"	"	"	"	3	"	"	56 "
5 c.c. N. S.	"	"	"	"	6	"	"	74 "
5 c.c. T. A. S.	"	"	"	"	1	"	"	75 "

N. S. stronger than T. A. S. There was hemorrhage from the dog, which gave the T. A. S. This may have modified the activity. Compare with Experiment 43.

Experiment 48: Normal Secretin Versus Terminal Normal Secretin

Feb. 26, 1910: T. N. S. made Feb. 25, 1910, from experiment of Feb. 24, 1910 (See Experiment 4).

5 c.c.	N. S.	caused the filling of 1 cannula and 40 divisions.
5 c.c.	T. N. S.	" " " " 0 " " 49 "
5 c.c.	N. S.	" " " " 1 " " 49 "
5 c.c.	T. N. S.	" " " " 0 " " 20 "
10 c.c.	N. S.	" " " " 3 " " 31 "
10 c.c.	T. N. S.	" " " " 1 " " 45 "

N. S. stronger than T. N. S.

Experiment 49: Normal Secretin Versus Terminal Normal Secretin

Jan. 27, 1910: T. N. S. made from experiment of Jan. 13, 1910 (See Experiment 3).

	N. S.	caused the filling of $4 \frac{1}{5}$ cannulas.
T. N. S.	" " " "	2 "
N. S.	" " " "	$5 \frac{1}{3}$ "
T. N. S.	" " " "	$1 \frac{1}{5}$ "
N. S.	" " " "	$5 \frac{1}{6}$ "
T. N. S.	" " " "	1 + "

N. S. shows decidedly greater activity than T. N. S.

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