dioxide absorbed during one-hour periods per 100 sq cm of healthy leaf surface exposed to the light varied from less than 1 mg to as high as 25 mg, with 2 to 10 mg the most frequent rate during the morning hours. In a few cases during daylight hours in the forenoon, the leaves actually increased rather than reduced the carbon dioxide content of the air. The respiratory rate is determined during the day by excluding light from leaves whose photosynthetic activity was established during the preceding hour, or by making determinations during the night.

In general, our preliminary results, obtained with the apparatus described, conform with those recorded by the Russian authors previously referred to, and they indicate that wide fluctuations in the activity of a given leaf from hour to hour and from day to day are to be expected, even though the temperature and other environmental factors are the same in successive periods. Nevertheless, a relatively active leaf seems to hold its rank compared to others under many varying conditions. The apparatus described should therefore be useful for many studies involving a knowledge of the leaf efficiency as influenced by a number of conditions or treatments.

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SPECIAL ARTICLES

THE FUNCTION OF THE ADRENAL CORTICAL HORMONE AND THE CAUSE OF DEATH FROM ADRENAL INSUFFICIENCY[1]

THE functional significance of the adrenal cortex is unknown; practically all investigators of the problem agree upon this point. Various tentative hypotheses have been advanced to account for the function of these glands, but none of these hypotheses, or all of them taken together, have materially advanced the problem of cortical function.

We are of the opinion that data now in our possession, merely a brief outline of which will be presented here, explain in large measure the function of the adrenal cortex and the cause of death from adrenal insufficiency. The nature of the data is such that it is highly important to have in mind a clear picture of the type of experimental animal employed.

Bilaterally adrenalectomized dogs are used: they have well-healed wounds, are perfectly normal healthy animals at their peak weight. Any one viewing these dogs would be quite unable to distinguish them by appearance or behavior from control unoperated individuals. From the day of gland removal they are injected daily with adequate maintenance doses of the cortical hormone until ready for use. Some of the animals have been bilaterally adrenalectomized for nearly two years, others for lesser periods. In all cases, however, they were permitted to develop severe symptoms of insufficiency by withdrawal of extract, and then revived and returned to normal health by adequate injections of hormone. This is the routine procedure in the laboratory before any adrenalectomized dog is regarded as a fit subject for experimentation. Several of the older animals have passed through this routine eight to ten times. Our adrenalectomized dogs are, by all anatomical and physiological criteria employed, perfectly normal healthy animals, except that they lack adrenal glands. We reiterate and emphasize this point purposely. When an experiment starts, the cortical hormone is withheld and the animal allowed to become prostrate from insufficiency. Adequate doses of the hormone are then given and the animal returns to normal.

Study of such animals reveals some new and interesting data which, for the sake of brevity and clarity of presentation, will be given as bald statements. The more important points supporting these statements will be discussed more in detail later.

(1) The function of the adrenal cortical hormone is the regulation and maintenance of a normal circulating volume of fluid within the vascular system. In the absence of the hormone, fluid is continually lost from the circulation presumably by transudation through the capillary walls, with the result that the adrenalectomized animal is unable to maintain his normal blood volume, and eventually dies from circulatory collapse due to insufficiency of circulating fluid.

(2) Accompanying the progressive decrease in blood volume is a progressive fall of blood pressure to the death level. The decline in arterial pressure is apparently a direct result of the decreased volume of circulating fluid.

(3) The decrease in blood volume and blood pressure are not terminal phenomena, but first appear within twenty-four to seventy-two hours after discontinuing hormone injections and before active symptoms of insufficiency appear. Both volume and pressure steadily decline to the death point, which may not occur until eight to twelve days later.

[1] The expenses of this investigation, including the cost of enlarging this issue of SCIENCE to make early publication possible, have been defrayed by a grant from the Josiah Macy Foundation of New York.

(4) The manifestations and symptoms of adrenal insufficiency parallel in remarkable fashion the decline in blood pressure.

(5) Hemoconcentration, increased blood viscosity and the marked slowing of the circulation which invariably appears, are directly correlated with and chiefly dependent upon the decline in plasma volume and blood pressure.

(6) The heart rate varies inversely as the blood pressure, and the change in rate appears to be due to the progressively diminishing venous return to the right heart, and the effort of the heart to compensate for the greatly decreased quantity of fluid in circulation.

(7) The blood-urea and non-protein nitrogen also vary inversely as the blood pressure. The decreased renal function, so evident during adrenal insufficiency, we attribute to the changes in circulation previously mentioned, *i.e.,* diminished blood volume, decreased pressure, and presumably, therefore, to decreased filtration pressure and blood flow in the kidney.

(8) The increased viscosity of the blood is due to loss of fluid and increase of corpuscles per unit volume, and to the increase in plasma proteins due to hemoconcentration.

(9) Adrenalectomized animals, in the absence of the cortical hormone, are apparently unable to draw fluid back into the blood stream through the capillary walls. The accepted view that the osmotic power of the blood colloids is the chief factor involved in compensation needs further investigation. The blood colloids are proportionately increased in adrenal insufficiency, yet the animal does not dilute or compensate in face of a declining blood volume and arterial pressure.

(10) Following administration of adequate amounts of cortical hormone to prostrate adrenalectomized dogs, the blood volume, blood pressure and blood constituents all return to normal. The animal is able to dilute his blood and build up a normal blood volume, and all symptoms of adrenal insufficiency disappear.

(11) It is our opinion that all the manifestations, symptoms and physiological peculiarities, which have been described as occurring in adrenalectomized animals (see table on insufficiency), are merely results of a progressively failing circulation due to decreasing volume of circulating fluid, in an animal which is unable to compensate (as do normal animals) for its low blood volume and blood pressure by dilution.

(12) The striking similarity between the symptoms of adrenal insufficiency and those of traumatic or secondary shock, as reported in the literature for man, is too obvious to be ignored. The cardinal features of traumatic shock are likewise the cardinal features of adrenal insufficiency—*viz.,* depleted blood and plasma volume, lowered arterial pressure, hemoconcentration and inability to dilute the blood (uncompensated human cases). The really essential point in secondary shock is failure of the blood-diluting mechanism and loss of power to increase the blood volume. This is also the primary cause of the symptoms of adrenal insufficiency.

These statements require supporting evidence of an unequivocal nature. We believe that our data are sufficient to establish these contentions, and the main points will be briefly outlined here.

BLOOD VOLUME

Fig. 1 shows the blood volume, hemoglobin, hematocrit and urea nitrogen changes in one of our experimental animals. The plasma volume of adrenalectomized dogs is invariably low. Losses of 40 to 50 per cent. of the plasma frequently occur. However, it is our opinion that the "vital-red" method of determining blood volume does not really gauge the extent of the plasma loss in an animal coming into insufficiency. The method is as good as any other now in use, but circulatory conditions are so peculiar in adrenal insufficiency that any of the present indirect methods for determining blood volume would be similarly inadequate.

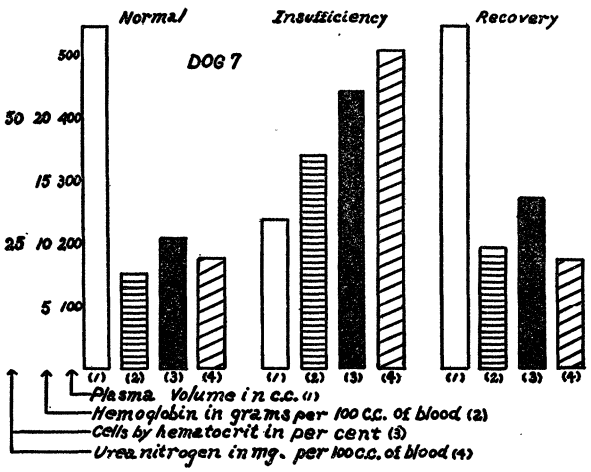

FIG. 1. The changes in plasma volume, hemoglobin, cells by hematocrit, and urea nitrogen in an adrenalectomized dog followed through a cycle of insufficiency. This animal had been adrenalectomized ten months previous and maintained in normal condition by adequate doses of cortical hormone.

We have strong evidence for the belief that our animals presenting volume readings indicating a plasma loss of 40 to 50 per cent. have really lost greater quantities. Data obtained by employing the "washout" method for blood volume determination reveal that the adrenalectomized dog loses 40–50 per cent. of his total blood volume within the first two or three days after withdrawal of hormone and before

any evident symptoms of insufficiency appear. The animal eats normally, he is active and vigorous and to all appearances normal, yet his blood volume is greatly depleted. Accompanying this early diminution in volume is a small increase in blood urea, and a decline in arterial pressure of approximately 20–25 mm Hg.

The "washout" method of blood volume determination is apparently more reliable than the "vital red" method in so far as adrenal insufficiency is concerned. Unfortunately it necessitates sacrificing the animal. We do not yet know how low the blood volume actually sinks before death occurs. We are now investigating this point. But taking the "vital red" data as it stands, it is clear that the blood volume decreases to a low figure in insufficiency and returns to a normal level following extract administration.

In a normal animal with adrenal glands, a decrease in plasma volume of 40 to 50 per cent. may not be fatal or even necessarily lead to the development of serious symptoms. Such an animal has the ability to compensate or dilute his blood in the face of a falling blood volume or pressure, and thereby can rapidly restore the volume of circulating fluid to a normal level. However, the outstanding feature of the adrenalectomized animal is its loss of the blood compensating and diluting mechanism. Losses of blood, which would be negligible in a normal animal, are fatal to the adrenalectomized dog. Both types of animal are continually losing fluid from the blood stream by transudation through the capillaries. But whereas the normal dog continually dilutes and restores his blood volume, the adrenalectomized dog is unable to do so, and his blood fluids drain into the tissues and are lost from circulation. This point is discussed more in detail in the following section.

Compensation or Dilution Following Hemorrhage, etc.

Further evidence supporting the contention that in adrenalectomized animals the blood volume progressively decreases to a level incompatible with life is furnished by bleeding experiments. Following hemorrhage, the normal animal with intact adrenal glands rapidly dilutes its blood by drawing fluid back into the blood stream to compensate for the decreased plasma volume. This power of compensation is remarkable, as any one will attest who has studied the problem. Normal dogs, weighing 10 to 12 kilograms, can withstand the loss of 40 per cent. of their total blood volume, or as much as 350 to 400 cc at one time, and within a period of a few hours or less, dilute to the extent of regaining their original volume. This compensation is due to withdrawal of water from the tissues. We have repeatedly removed 40 per cent. of the blood volume of normal unanesthetized dogs and cats, and observed that within three or four hours they were perfectly normal. Such observations are, of course, familiar to any student of hemorrhage.

The power of normal animals to compensate by dilution for lowering of blood volume is regarded as due to such reduction of blood pressure in the capillaries that the filtration pressure from within them no longer offsets the greater osmotic pressure of the plasma colloids as compared with the lymph, and consequently fluid passes into the blood stream. This mechanism of compensation, however, is probably not the sole factor involved, for we have evidence that the adrenal cortical hormone is vitally concerned in the phenomenon of blood dilution. In fact, our observations show that in the absence of the cortical hormone the animal lacks the ability to dilute its blood, even after slight or negligible blood loss. Following hormone administration, dilution again occurs.

Adrenalectomized dogs with well-healed wounds, and kept in perfectly normal condition by maintenance doses of extract, dilute their blood after hemorrhage, just as do normal unoperated animals. If extract is withheld for two or three days until the hormone content of the blood diminishes, the animals remain normal in all respects, except for decreased blood volume and pressure. They are vigorous and eat heartily. However, if small amounts of blood are removed, quantities which would be quite negligible to an animal with intact adrenals, an interesting phenomenon occurs. The blood pressure sinks to a very low level, where it remains unchanged for hours. No dilution occurs, and unless the cortical hormone is given, the pressure starts to decline further, and the animals die presenting all the classical symptoms of adrenal insufficiency. Following injection of the hormone, dilution promptly occurs, the blood pressure rises to normal and the animal returns to a normal condition, as evidenced by the changes in hemoglobin, hematocrit and plasma volume. We will cite one typical example.

An adrenalectomized dog (operated four months previously), weighing 10 kg and maintained in normal health by hormone, was taken off extract for several days. The dog remained normal in every respect; and the day he was bled he had eaten his full ration of 800 grams of kennel ration. His blood pressure had, however, declined from the normal of 106 mm Hg to 85 mm Hg. This decrease did not affect his vigor. A total of 40 cc of blood was withdrawn from the femoral artery over a period of one hour—an amount representing 5 per cent. of his normal blood volume. The animal's blood pressure fell

from 85 mm Hg to 42 mm of Hg and the dog exhibited signs of prostration. He was able to walk back to his cage where he remained in a stuporous condition for 7 hours. At the end of this time his blood pressure remained unchanged at 42 mm of Hg. A few hours later it began to decline and an injection of extract was deemed necessary. Intravenous injection of an adequate amount of the hormone was given. Four hours later the blood pressure had risen to 60 mm and within 12 hours the pressure was 80 mm Hg. The dog was eating, and ran about the laboratory. Twenty-four hours after injection the pressure stood at 100 mm of Hg. Compensation or dilution had occurred, and the animal was again perfectly normal. Dilution never occurs in such animals, and death results, unless the hormone is injected.

In contrast to the type of experiment just mentioned, we can cite numerous experiments on bleeding normal dogs, both from our own experience and that of others, where large quantities of blood, 300 to 350 cc, are drawn at one time. The animals do not exhibit distress, but compensate by dilution extremely rapidly. The evidence seems clear that adrenalectomized animals are unable to dilute their blood, and can do so only when the cortical hormone is supplied.

The experiments upon hemorrhage also lend additional weight to our data on lowered blood volume in the adrenalectomized animal. Normal dogs of 10 to 12 kilograms weight can withstand relatively huge losses of blood without evident symptoms. A similar sized adrenalectomized dog, apparently enjoying equally good health, can not tolerate a loss as trivial as 50 to 75 cc, even when it is withdrawn over a period of an hour or two, without passing into a serious shock-like condition comparable to adrenal insufficiency prostration. The small quantity of blood removed from an adrenalectomized dog is of no significance to a normal animal possessing a diluting mechanism, but the loss of 50 to 75 cc by an animal which by all criteria such as vigor, activity and appetite is normal but which lacks power of compensation, and whose blood volume is already lowered, is fatal.

Another type of experiment showing the relation of the cortical hormone to the diluting mechanism is as follows: When the adrenalectomized dog, in severe insufficiency with a greatly lowered blood volume, a blood pressure of 40 mm Hg and a high blood urea, is injected intraperitoneally with 500 cc of normal saline, nothing happens and the animal dies. The individual is unable to tap the reservoirs of fluid because it can not dilute. However, if to such an injected dog hormone is administered, or fluid given by mouth, he revives in remarkable fashion. The blood pressure may rise 10 mm of Hg per hour for two or three hours until the pressure has risen to 70 to 80 mm Hg and the animal is restored to normal so far as vigor and appetite are concerned. The hormone enables the animal to utilize the injected reservoir of fluid in the body cavity, and dilution occurs very rapidly—more so than when such animals are not given fluids intraperitoneally.

Blood Pressure

The importance of close observation of the blood pressure in adrenalectomized animals can not be overemphasized. The great hindrance has been the difficulty of making repeated determinations upon the same animal. The repeated daily arterial cannulation, necessary as a preliminary to the use of the mercury manometer on the unanesthetized adrenalectomized dog, is a technical impossibility. With the exception of Rogoff, who used the carotid loop, no other method has been employed. When consideration is given to the extreme sensitivity of adrenalectomized animals to anesthetics of any kind, to trauma or slight blood loss, it is easy to appreciate the difficulty of any prolonged study of blood pressure in such an individual over a period of several weeks or months.

We are using the direct intra-arterial method of Dameshek and Loman, which is extremely simple, highly accurate, and which makes it possible to determine the arterial pressure of an unanesthetized dog any number of times desired. The device has been repeatedly checked against the arterial cannulation method at high, low and normal pressures, using the two methods simultaneously in the same animal. The readings in mm of Hg are essentially the same in both instruments.

Two further points should be mentioned. Our animals are table trained especially for blood pressure work, and the pressures are determined directly in the femoral artery. The cortical hormone *per se* has no effect upon blood pressures. Slow or rapid intravenous injections of 30 to 40 cc of highly potent hormone does not raise the pressure in either the normal or adrenalectomized dog, except for a slight evanescent rise due to the traces of adrenalin present.

The resting arterial pressure of adrenalectomized dogs on maintenance doses of hormone is perfectly normal. It varies in different individuals from 100 to 115 mm Hg. After cessation of extract injections, the pressure progressively sinks day by day until the death level is reached. Fig. 2 shows the typical changes in arterial pressure in one of our cases. The symptoms of adrenal insufficiency parallel the decline in pressure. When the pressure is at a low level, in many cases as low as 45 to 30 mm of Hg, the animals exhibit severe symptoms and must be injected

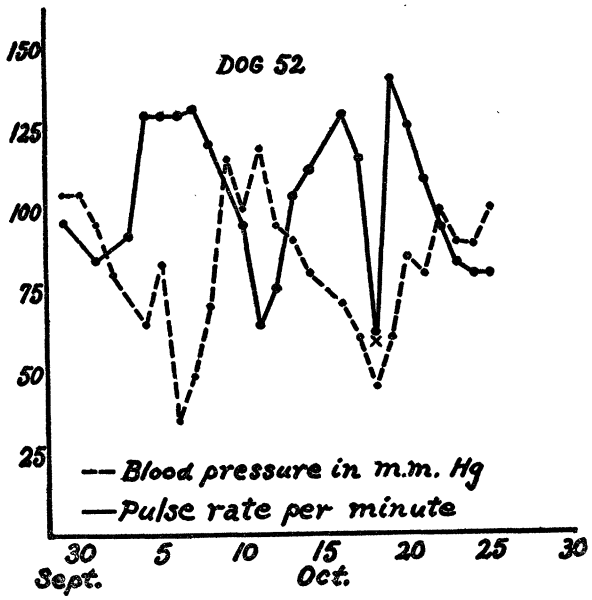

FIG. 2. The changes in blood pressure and pulse rate in an adrenalectomized dog followed through two cycles of insufficiency and recovery on extract. The significance of X is explained in the text.

with cortical hormone in order to prevent the pressure from sinking to the death level. Following injection, the pressure rises steadily and within 72 hours or less has attained the normal level and all symptoms disappear.

The decline in arterial pressure is one of the first departures from normal the animal off extract exhibits. Several days before the animal stops eating the pressure has fallen to 60 to 70 mm Hg. It is remarkable how active and normal such dogs appear with arterial pressures as low as they are. An arterial pressure of 60 to 70 mm of Hg is in general insufficient to produce noticeable symptoms in our dogs. It is only when the pressure sinks to below 60 mm that symptoms appear. We have observed several dogs, with arterial pressures as low as 36 to 39 mm of Hg, which were able to hop off the table and trot back to their cages. They were a bit wobbly on their feet, it is true, but nevertheless they were up and about.

The heart rate in general varies inversely as the blood pressure. When the pressure is normal, the heart is slow and steady. However, when the pressure starts to decline the heart rate speeds up and maintains a rapid rate so long as the pressure remains low. With a return to normal pressure, the heart rate decreases to normal. Fig. 2 illustrates these points. Some of our dogs show a precipitous fall in heart rate a few hours before death occurs. This is shown at X in Fig. 2. Following extract injection, the heart rate of such animals increases to a high figure and then declines to normal as the pressure returns to normal level.

Since the fall in blood pressure in the adrenalectomized dog is dependent upon the decline in plasma volume, the rise in pressure after extract administration depends upon the rapidity with which fluid is drawn back into the circulation and the blood volume increased. We have observed rises in arterial pressure of 10 mm of Hg per hour for the first two or three hours after injection, though generally the rise is around 5 mm of Hg per hour. When rapid dilution has occurred and the pressure stands at 65 to 70 mm of Hg, the rate of increase slows up. In all cases the pressure attains its normal level along with a normal blood volume by the end of 72 to 80 hours. The effect of the cortical hormone upon blood pressure is indirect, it raises the pressure by increasing the plasma volume, *i.e.*, the amount of fluid in circulation, and in no other way, so far as we have been able to determine.

BLOOD VISCOSITY

The blood of adrenalectomized animals becomes increasingly viscous. Data obtained from two experimental dogs are shown in Fig. 3. The increased viscosity is attributable in large part to (1) the increase of corpuscles per unit volume due to decreasing plasma volume, and (2) increase in plasma proteins due to hemoconcentration.

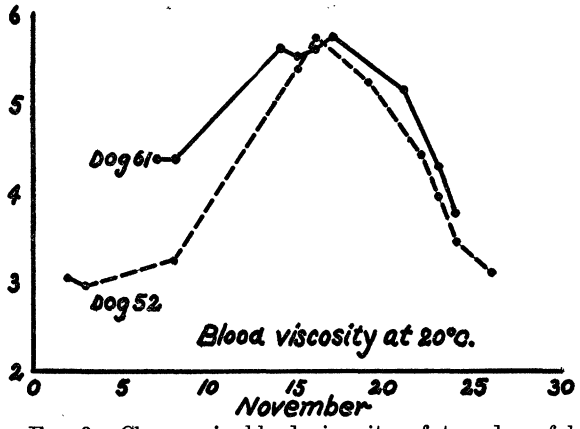

FIG. 3. Changes in blood viscosity of two dogs followed through a cycle of adrenal insufficiency and recovery after extract administration. The peak of the curve coincides with the point where extract was injected and when symptoms were most severe.

BLOOD UREA AND NON-PROTEIN NITROGEN

One of the earliest changes from normality in the adrenalectomized dog deprived of extract is a rise in blood urea and non-protein nitrogen. This rise occurs

simultaneously with the fall in arterial pressure, and an inverse ratio exists between the two, as a glance at Fig. 4 will show. When the blood pressure is normal,

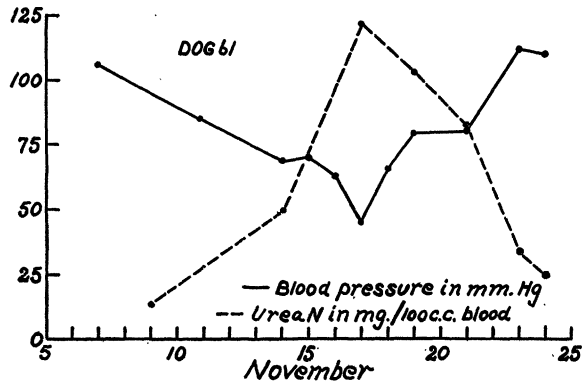

FIG. 4. Blood pressure and urea nitrogen changes in an adrenalectomized dog followed through a cycle of insufficiency and recovery on extract treatment.

the blood urea is low and at the normal level. When the pressure falls the urea rises and attains its peak when the arterial pressure is at a low level. Following extract injections the blood pressure slowly rises along with the blood volume, and the urea and non-protein nitrogen slowly falls.

Daily observation of blood urea and blood pressure reveals that, in general, the pressure starts to decline at approximately the same time as a detectable elevation of urea occurs, thus indicating that the rise in urea and non-protein nitrogen depends upon the falling pressure. However, we have observed several animals which showed a slight elevation of blood urea before the blood pressure had changed significantly. In such cases it seems likely that the blood flow through the kidneys is lessening as a result of a decreasing volume of circulating fluid.

When the animal exhibiting marked symptoms of adrenal insufficiency, with a very low arterial pressure, and a high blood urea, is given adequate injections of cortical hormone, the blood pressure invariably rises to the normal level before the blood urea sinks to its normal level. There is a lag of 24 to 48 hours after the normal pressure has been attained before the urea reaches the normal level. This lag is to be expected when we consider that the rise in blood pressure means that the animal is building up a normal volume of circulating fluid. The fall in urea occurs when the kidney function is resumed with consequent outpouring of urea.

The fact that the elevation of blood urea and non-protein nitrogen turns out to be dependent upon diminished blood flow through the kidney does not detract from the importance of the urea as a means of biological assay of the adrenal cortical hormone. The writers have long recognized that this method of assay is based upon a secondary phenomenon of adrenal insufficiency, namely, lowered renal activity. However, since the changes in blood urea are so easy to follow and so simple to quantitate, this method of assay retains its value.

ADRENAL INSUFFICIENCY AND TRAUMATIC SHOCK

It is obvious that the conditions existing in adrenal insufficiency in animals are strikingly similar to those reported as occurring in traumatic or secondary shock in man. During the war detailed studies of traumatic shock were made on large numbers of individuals. In the following table we have listed the chief findings in adrenal insufficiency and traumatic shock and have arranged them for comparison. The signs and symptoms of the two conditions are very similar.

TABLE 1

CONDITIONS EXISTING IN ADRENAL INSUFFICIENCY (ANIMALS) AND TRAUMATIC SHOCK (MAN)

1. Blood volume	Decreased
2. Blood pressure	Decreased
3. Hemoglobin	Increased
4. Hematocrit	Increased
5. Red cell count	Increased
6. Venous pressure	Decreased
7. Rate blood flow	Decreased
8. Blood viscosity	Increased
9. Hemoconcentration	Increased
10. Cardiac output	Decreased
11. Venous return to R. heart	Decreased
12. Heart rate	Increased
13. Heart condition	Normal apparently
14. Weak, fast pulse	Present
15. Vaso constriction	Present
16. Ability to dilute	Lacking
17. Blood non-protein nitrogen and urea	Increased
18. Alkali reserve	Decreased
19. Basal metabolism	Decreased
20. Blood sugar	Decreased in adrenal insufficiency Normal or slightly above in traumatic shock
21. Body temperature	Decreased
22. Use vaso constrictor drugs	Ineffective
23. Effect forcing fluids	Beneficial
24. Vaso motor center	Normal apparently
25. Sensitivity to painful stimuli	Decreased
26. Sensitivity to cold	Increased
27. Sensitivity to anesthetics	Increased
28. Sensitivity to histamine	Increased in adrenal insufficiency, action unknown in shock
29. Sensitivity to infections and toxins	Increased
30. Urine volume	Decreased
31. Sensitivity to hemorrhage	Increased
32. Sensitivity to trauma and operation	Increased

Blood sugar in insufficiency is generally lowered, whereas in traumatic shock it is either at the normal

level or else slightly above. However, there is generally considerable laceration and tearing of tissue, together with blood loss in traumatic shock. These conditions may tend to raise blood sugar, for Aub has reported high blood sugars in shocked cats whose thigh muscles had been crushed. The cause of the low blood sugar in adrenal insufficiency will be discussed in a later paper.

It is the opinion of the writers that, since the essentials of adrenal insufficiency in experimental animals are very similar with those of traumatic shock in man, the two syndromes may possibly have a common origin —namely, some derangement of the adrenal cortex and deficiency of its hormone. In the adrenalectomized animal the glands have been extirpated, while in the shocked man they are still present, but the question arises—are the glands fully functional? If one may judge from the symptoms of traumatic shock the cortex would appear to be non-functional. In traumatic shock the individual is either unable to dilute his blood and increase his depleted blood volume (uncompensated cases) or else is able to partially do so, but only slowly (partially compensated cases) and must be aided by injecting fluids to increase the volume of fluid in circulation. The same condition exists in adrenal insufficiency in experimental animals. The animal lacks ability to dilute its blood in the face of a falling plasma volume and arterial pressure, and, in the absence of the cortical hormone, invariably dies. For some time the writers have been tempted on theoretical grounds alone to suggest that the secret of traumatic shock may possibly lie in the adrenal cortex, and that the cortical hormone may be found to be of benefit in controlling this syndrome in man.

Recently we have performed a set of experiments to test the relation between failure of the cortex and traumatic shock. The results are highly suggestive. Adrenalectomized dogs on maintenance doses of extract were used. The extract injections were discontinued for two days to permit the concentration of hormone in the animals to diminish. The dogs were still in perfectly normal condition and indistinguishable from normal dogs. They were lightly anesthetized with ether, the blood pressure determined and the testicles crushed in a vise by gradually increasing pressure. The recovery from ether was rapid and the animals were up and about within thirty minutes. The blood pressure was followed closely. One typical case will be cited. The arterial pressure dropped from 112 mm of Hg to 79 mm of Hg immediately after injury. One hour later the pressure stood at 54 mm of Hg. Two hours later it had risen to 67 mm of Hg. From this time on, however, the pressure slowly declined until at the end of eight hours it was 46 mm of Hg and the animal was prostrate and in profound shock. No dilution or compensation had occurred, except the evanescent rise during the first two hours. The dog was in such desperate straits that it was injected intravenously with adequate doses of extract. Two hours after injection the blood pressure rose from 46 mm Hg to 68 mm, and at the end of four hours from time of injection, the pressure was 74 mm of Hg. The dog was running about, was bright, energetic and ate his food in normal fashion. At the end of 48 hours the dog's pressure was 112 mm of Hg.

Control experiments where normal dogs with intact adrenal glands were similarly treated gave results as follows: Blood pressure before injury 135 mm Hg. (Animal under ether). Immediately after injury pressure 112 mm Hg, one hour later pressure 92 mm Hg. Animal ate meat eagerly. Two hours later pressure 92 mm, animal normal. Three hours after injury pressure 109 mm of Hg. The animal appeared perfectly normal at all times during the experiment.

A second set of somewhat similar experiments has been performed, in which profound surgical shock was induced in normal dogs by double adrenalectomy at one sitting. Immediately following completion of the operation, the blood pressure was normal. After twelve hours, the degree of shock was such that the animals appeared moribund. Blood pressure 35 to 39 mm of Hg, heart rate 200, femoral pulse so feeble it could barely be felt. The animals were conscious, but apathetic and quite insensitive to pain. The blood-diluting mechanism had completely broken down and compensation was lacking. Intravenous injections of adequate doses of the cortical hormone restored these profoundly shocked animals to normal life and vigor within 48 to 72 hours. These animals are alive and well at the present time, some three weeks after operation. Dogs similarly "shocked" and not injected with hormone invariably die within 48 hours.

These experiments lend considerable weight to our suggestion that the signs and symptoms of adrenal insufficiency, and of traumatic or secondary shock, are possibly due to one and the same thing, *i.e.*, failure of the blood volume and blood-diluting regulator mechanism, the adrenal cortex. The idea that the adrenal cortical hormone might prove of benefit in the treatment of human traumatic shock is advanced merely as a suggestion. Adequate proof can only come through clinical trial.

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