

Blood Changes Following Bilateral Epinephrectomy in Cats.

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During the last 3 years an intensive study of the functional significance of the suprarenal cortex has been carried on in this laboratory by the writer and his students. The present report is concerned with changes which occur in certain blood constituents following adrenal removal in cats.

It is well known that unilateral epinephrectomy is without demonstrable effect upon cats, hence animals subjected to such an operation were employed as controls. An interval of 5 to 7 days was allowed to lapse before the remaining adrenal was removed. Animals so treated generally survived loss of both adrenals for about 60 hours if untreated.

Phosphorus: The serum phosphorus shows a striking and consistent rise, following bilateral adrenal removal. The increase is considerable, especially when the animal is in the pre-coma or coma stage. Values as high as 15 to 16.5 mgm. per 100 cc. are not uncommon. The accumulation of phosphorus occurs simultaneously with the development of serious symptoms. Animals presenting slight symptoms do not show significant rises in phosphorus. The increase in serum phosphorus is apparently not due to increased blood concentration.

Calcium and Sodium: The results of repeated analyses are not of any significance. In general the calcium rises slightly and the sodium falls to about the same degree as that following bilateral epinephrectomy.

Non-protein nitrogen: The non-protein nitrogen always shows a sharp rise following adrenal removal, and occasionally the increase is very great. The average value for non-protein nitrogen, in unilateral operated cats, is between 42 to 47 mgm. per 100 cc., whereas, the average amount found in the blood of the double operated animals, presenting marked symptoms, is about 91 mgm. The non-protein nitrogen is highest when the animal is in or verging on coma. The increase becomes apparent within the first 24 hours after operation, and slowly increases, until the cat enters the pre-coma stage. Then a sharp rise occurs. Our highest figure for non-protein nitrogen was 170 mgm. per 100 cc.

Urea: The urea increases markedly after double operation, the normal value being 19 to 24 mgm.; whereas values ranging from 40 to 122 mgm. were observed in animals showing marked symptoms.

Protein and total nitrogen: These substances increase after the second operation. However, the increase in serum protein is not so great as we might expect, considering the apparent increase in blood concentration. The blood of animals in the pre-coma stage is concentrated, does not flow readily, clots rapidly, and yields small amounts of serum.

Blood Sugar: The blood sugar of normal cats ranges from 105 to 118 mgm. per 100 cc. Following bilateral operation the sugar drops markedly. The fall begins about 20 hours after the operation and continues slowly until death supervenes some 60 hours later. The blood sugar of cats verging on coma, 60 to 72 hours after operation, ranges from 60 to 40 mgm. per 100 cc. It was observed that the onset of symptoms of weakness and muscular asthenia in double operated cats coincides with the drop in blood sugar. Animals beginning to show muscular weakness and cerebellar symptoms, when walking, had blood sugar ranging from 80 to 75 mgm. As the sugar fell the weakness became more pronounced until finally, when coma developed, the blood sugar had fallen to 40 to 55 mgm. per 100 cc.

The pronounced hypoglycemia, following adrenal removal in cats, is not the cause of adrenal death, since animals injected with glucose eventually die with high blood sugar, although the life span of animals so treated is considerably prolonged. It is interesting in this connection to note that normal cats, injected with insulin, pass into coma and convulsions when the blood sugar reaches the same low level (40 to 55 mgm.) as that of bilaterally epinephrectomized cats in coma or convulsions. Our low figures for blood sugar were obtained from blood taken just before death.

The urine: The quantity of urine passed decreases sharply with the onset of serious symptoms. On the day when death occurs, or on the previous day, the animals void little urine. Some cats show almost complete suppression, others are able to pass small quantities until a few hours before death. Small amounts of albumin appear in the urine of animals showing marked symptoms.

Because of the phosphorus and nitrogen retention and the presence of albumin in the urine, the kidneys of double operated animals were studied histologically for degenerative changes. The results were disappointing in that, aside from hemorrhagic areas and congestion, clean cut pathological changes were absent. Nevertheless,

the data indicate that the kidney is somewhat involved in the syndrome, which results in death following bilateral epinephrectomy. Experiments¹ on the acid-base equilibrium of epinephrectomized cats revealed the fact that one of the train of events leading to death from adrenal insufficiency is an uncompensated, non-volatile acidosis, which appears to be due to an increase of phosphoric and organic acids.

The complete data indicate that one of the causes of death following removal or destruction of the suprarenal cortex is acid intoxication due to accumulation and retention of the acid end products of normal metabolism. In the absence of the cortex the kidneys apparently fail to properly perform their acid eliminating function in relation to the neutrality regulation of the body. For some time, in some of our cases for 5 or 6 days, the respiratory mechanism is adequate to take care of the slowly advancing acid intoxication by throwing off volatile acid and the pH remains within the normal range. Finally there comes a time when the respiratory mechanism proves unequal to the task, and the acidosis becomes uncompensated, with falling pH and marked symptoms. The respiratory mechanism breaks down and death ensues from respiratory failure.

The type of acidosis, which develops following adrenal removal, is of a similar nature to the acidosis characteristic of the terminal stage of certain types of nephritis. It is suggested that the adrenal gland (cortex probably) supplies a hormone which is necessary for the maintenance of normal kidney function.

Complete papers presenting in detail the data summarized in this report will appear shortly in the *American Journal of Physiology*.

¹ Swingle, W. W., and Eisenmann, A. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1926, xxiv, 212.

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The Prevention of Tetany by the Oral Administration of Ammonium Chloride.

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Previous experiments^{1, 2} carried out on parathyroidectomized dogs have demonstrated the effectiveness of the lactates of strontium and magnesium in relieving tetany and in bringing about a cure.