

In each case a very small bit of ovarian tissue was left *in situ*, together with a greater portion of the capsule. Although these cases were allowed to run for only five weeks, examination revealed a remarkable degree of regeneration; in all five the regenerated mass approximated in size the average normal ovary. In each instance the capsule was markedly thicker than usual, and was very prominently supplied with bloodvessels.

The above evidence leads to the conclusion that, at least in an 8 to 16 week period, no regeneration occurs, provided the ovaries are completely removed. It is the writer's opinion that in mice ovarian tissue regeneration results from incomplete removal, and that such tissue does not arise *de novo* from non-gonadic tissue surrounding the site of the original ovary.

None of the mice examined was killed, and they will be kept alive over a considerable period, in order that the time-element may not be neglected as a possible factor in regeneration.

This is a preliminary report.

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<sup>1</sup> Davenport, C. B., *J. Exp. Zool.*, 1925, xlii, 1.

### 3571

#### Acid Intoxication of Adrenal Insufficiency in Dogs.

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Recent work on the blood chemistry of dogs and cats suffering from adrenal insufficiency suggests the probability that the adrenal cortex secretes a hormone which in some manner controls the normal functioning of the kidney. Several investigators<sup>1</sup> report marked nitrogen retention following adrenal removal. Swingle<sup>2</sup> and Swingle and Eisenmann<sup>3</sup> demonstrated phosphorus retention, and the existence of an uncompensated non-volatile acidosis in severe adrenal insufficiency. The acidosis was considered to be due to retention of the acid end products of normal metabolism.

Owing to the difficulty of bleeding cats repeatedly, and the fact that considerable quantities of blood are necessary for analysis, the writer made a detailed investigation of the acid intoxication following adrenal removal in dogs.

Adult male and non-pregnant dogs were employed, an interval of 5 to 10 days elapsing between operations. Longer intervals were

not found to prolong the survival period, the average survival period to date being 5½ to 6 days. Dogs living less than 4 days were entirely disregarded for this investigation. No greater difficulty was experienced with the right gland than with the left.

All blood for CO<sub>2</sub> capacity and pH was drawn under oil, directly from the heart. Normal blood was drawn at first from unilaterally operated animals since this blood presents no change from normal.<sup>4</sup> Later, however, normal blood was obtained after the second operation. Double-operated animals are always normal for several days following the second operation. They eat, play, and fight with one another just as do unoperated animals. The blood picture of such animals shows no deviations from the normal. Following the onset of the characteristic adrenal insufficiency symptoms, blood was taken at various intervals.

The CO<sub>2</sub> capacity was determined by Van Slyke's method,<sup>5</sup> and the pH by means of Myer's bicolorimeter,<sup>6</sup> using Muntwyler's<sup>7</sup> correction of 0.30 for dog plasma.

*Acidosis.* The blood findings show that with the onset of symptoms of adrenal insufficiency such as refusal of food, muscular weakness and general lassitude the initial fall in the CO<sub>2</sub> capacity occurs, whereas, the pH remains normal. With continued fall in CO<sub>2</sub> capacity the pH remains normal until the capacity has fallen to approximately 30 volumes per cent. At this level the first decline in pH is observed, and when the level of the CO<sub>2</sub> capacity falls below 30 volumes per cent, a rapid decline in pH ensues. The gradual decrease in CO<sub>2</sub> capacity is accompanied by a corresponding increase in depth, and in the later stages, in the number of respirations. There comes a time, however, when respiratory compensation is inadequate and a sharp decline in pH follows, this change occurring between 4 and 12 hours preceding death.

The shifting of compensated acidosis to the uncompensated condition has been commented upon by Swingle<sup>8</sup> and the similarity to the acidosis of chronic interstitial nephritis has been cited.

*Blood Sugar.* With the onset of symptoms the initial fall in CO<sub>2</sub> capacity is accompanied by a marked drop in blood sugar which falls to approximately 75 mg. per 100 cc. The sugar level may fluctuate materially once it has begun to fall and in 2 of the several cases came back to normal. However, it invariably drops in the terminal stages preceding coma, in some cases to as low as 55 to 60 mg. per 100 cc. It seems probable that the early symptoms of adrenal insufficiency such as anorexia and lassitude are due to the initial decline in alkali reserve and blood sugar.

TABLE I. Blood findings following bilateral suprarenalectomy in dogs.

Animal	Date	Time	CO <sub>2</sub> capacity	pH	Sugar mg./100 cc.	Phosphorus mg./100 cc.	Remarks
Dog 1. Female Terrier	Feb. 4-27	8:30 p. m.					Right suprarenal removed.
	" 11	10:00 a. m.	44.40	7.36	95	4.25	Left suprarenal removed.
	" 13	10:00 a. m.	41.40	7.37	77		Normal. Ate well.
	" 15	2:00 p. m.	33.10	7.32			Venous.* Refused food. Vomited. Moody.
	" 15	9:30 p. m.	28.60	7.27	83	6.75	Respiration—24/min. Deeper.
	" 16	5:00 a. m.	24.40	7.19	62	13.00	Resp.—24/min. Deep with sighs. Prostrate. Died at 8 a. m.
Dog 2. Female Collie	Feb. 12-27	2:00 p. m.					Right suprarenal removed.
	" 17	10:00 p. m.	46	7.43	109	5.3	Left suprarenal removed.
	" 19	10:00 p. m.	38	7.42	67		Normal. Ate meat. Drank milk.
	" 22	10:00 a. m.			78		Refused food. Moody and weak.
	" 22	10:00 p. m.	37	7.40			Resp.—20/min. Vomiting.
	" 23	3:30 a. m.	31(29)*	7.17	64	10.00	Weaker. Resp.—24/min. Deep. Venous. Restless. "Flat." Died at 4 a. m.
Dog 3. Female Spitz	Mar. 2-27	4:00 p. m.					Right suprarenal removed.
	" 12	9:30 p. m.	40.3	7.38	111.1	4.72	Left suprarenal removed.
	" 14	9:30 p. m.			100		Normal. Eating and drinking.
	" 15	4:00 a. m.	37.4	7.32	80		Muscle twitchings.
	" 16	9:00 a. m.			93		No food. Hind legs weak.
	" 16	2:15 p. m.	37	7.34	94		Cerebellar symptoms. Swaying.
	" 17	10:00 a. m.	35	7.33	108		Ate meat. Muscle twitchings.
	" 18	9:30 a. m.	27	7.27	76.8		Ate. Yelling fits. Resp.—shallow.
	" 18	7:15 p. m.	22	7.10	66	11.12	No food. Legs very weak. Resp.—14/min. Deep.
	" 18						Venous.* Resp. deep and full—26/min. Died at 8:15 p. m.
Dog 4. Male Mongrel	Apr. 9-27	3:00 p. m.					Right suprarenal removed.
	" 14	10:00 a. m.	45	7.41	91	3.1	Left suprarenal removed.
	" 16	2:30 p. m.	34	7.42	78	5	Normal dog.
	" 18	8:00 p. m.			77		No food. Resp.—16/min. Deep. Lying around. Moody.
	" 18	10:30 a. m.	32		77	6.25	Vomiting. Resp.—still 16/min.
	" 20	4:00 p. m.	28	7.16	62	7.5	Deep respiration. Very moody. Prostrate. Died at 5:30 p. m.

\* Venous blood is two vol. per cent higher than arterial.

*Phosphorus.* The inorganic phosphorus of the serum shows a gradual rise with the onset of symptoms but the rise is most rapid in the later stages. This increase in phosphoric acid is not sufficient, however, to account for the degree of acidosis. Other non-volatile acids undoubtedly play an important rôle. The data obtained from an extensive series of dogs clearly indicate that the cause of death following adrenal removal is acid intoxication, which appears to be due, in part at least, to failure of the kidney to eliminate certain of the acid end products of normal metabolism.

Table I shows data on four typical cases and is an attempt to correlate the corresponding deviations of the CO<sub>2</sub> capacity, pH, blood sugar and phosphorus with the visible characteristic symptoms.

This is a preliminary report.

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<sup>1</sup> Swingle, W. W., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiv, 208; Stewart, G. M., and Rogoff, J. M., *Am. J. Physiol.*, 1926, lxxviii, 3,711; Lucas, G. H. W., *Am. J. Physiol.*, 1926, lxxvii, 1, 114.

<sup>2</sup> Swingle, W. W., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiv, 208.

<sup>3</sup> Swingle, W. W., and Eisenmann, A. J., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiv, 212.

<sup>4</sup> Swingle, W. W., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiv, 208; Lucas, G. H. W., *Am. J. Physiol.*, 1926, lxxvii, 1, 114.

<sup>5</sup> Van Slyke, D. D., and Cullen, G. E., *J. Biol. Chem.*, 1917, xxx, 289.

<sup>6</sup> Myers, V. C., *J. Biol. Chem.*, 1922, liv, 675.

<sup>7</sup> Myers, V. C., and Muntwyler, E., PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, this issue.

<sup>8</sup> Swingle, W. W., *Am. Naturalist*, 1927, lxi, 132.

## 3572

### Colorimetric Estimation of Hydrogen Ion Concentration of Blood.

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Recently Myers, Schmitz and Booher<sup>1</sup> described a simple micro-colorimetric technique of estimating the hydrogen ion concentration of the blood plasma, based upon an adaptation of the colorimetric method of Cullen<sup>2</sup> to the Myers bicolorimeter.<sup>3</sup> The pH readings are obtained on diluted plasma at room temperature and must be corrected to the actual pH of the plasma at body temperature by a constant. This constant includes corrections for dilution, temperature