

the normal for these animals. Twenty-eight observations upon 2 animals drained every 6 hours showed an average daily secretion of 78.1 cc. Twenty-four observations on 2 dogs drained every 12 hours showed a daily average secretion of 76.4 cc. Seven observations on 2 dogs drained every 24 hours showed a daily average secretion of 76.2 cc. Thirty-seven observations on 5 dogs drained every 48 hours showed a daily average drainage of 87 cc. In none of the animals except those drained continuously did the gastric acidity rise. The blood chlorides remained within normal limits in all animals. Marked daily variances were observed in the amounts secreted in several of the animals.

Assuming that there was relatively little gastric distention within 6 hours and that gastric distention occurred after 12 hours, the animals were divided into 2 groups. Group I included those animals drained continuously and every 6 hours. The average daily secretion of 22 observations on 6 animals was 115.8 cc. The second group included those drained every 12, 24, and 48 hours, respectively. Thirty-seven observations upon 9 dogs in this group showed a daily average secretion of 83.4 cc.

It thus appears that in the absence of distention there is an increase in the amount of gastro-duodenal secretions.

Although the clinical use of continuous duodenal drainage is justified because it prevents nausea, vomiting, and abdominal distention, these investigations suggest that when it is used there is an increased gastric secretion and a greater loss of electrolytes.

#### 9442 P

### **Failure of Ant. Pituitary Extracts to Maintain Fasting Carbohydrate Levels of Hypophysectomized Rats After Preliminary Treatment.\***

LESLIE L. BENNETT. (Introduced by Herbert M. Evans.)

*From the Institute of Experimental Biology, University of California, Berkeley.*

It has been reported previously that the low muscle glycogen levels of fasted hypophysectomized rats may be maintained at normal or supra-normal levels by the injection of suitable anterior lobe

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\* Aided by the Presnell Fund for the study of the metabolic relations of the anterior hypophysis, contributed by Robert R. Presnell, Frank Tuttle, Arthur Stebbins, and Mrs. Gordon Kahn, of Los Angeles.

extracts during the fasting period.<sup>1, 2</sup> The present investigation is concerned with the effect of two to three weeks' preliminary treatment with the same standard alkaline extract. Hypophysectomies were performed by the parapharyngeal route and completeness checked at autopsy. All animals were fasted for 24 hours over wire, and analyses were carried out as reported previously.<sup>3</sup> In all cases extracts were injected several times during the fasting period, usually at 24, 20, and 4 hours previous to sacrifice. The extract injected was the same as used previously<sup>1</sup> and is rich in growth hormone besides containing at least traces of all the other known anterior lobe hormones.

In Table I are summarized the results of these experiments. Inspection of the data shows that as small an amount of extract as one mg. per 100 mg. body weight produces complete maintenance of muscle glycogen when it is given only during the fasting period. On the other hand, much larger amounts of extracts are without effect if the fasting period has been preceded by 2 to 3 weeks of treatment. During the period of treatment these hypophysectomized rats grew continuously at an average rate of 3 gm. per day.

Since unfasted hypophysectomized rats which have been treated for 3 weeks show normal carbohydrate levels, the low values in these

TABLE I.  
Carbohydrate Levels in 24-hour Fasted Rats.

|  | Muscle<br>Glycogen<br>in mg. % |         | Liver<br>Glycogen<br>in mg. %* |       | Blood<br>Sugar<br>in mg. % |       |
|--|--------------------------------|---------|--------------------------------|-------|----------------------------|-------|
|  | Mean                           | Range   | Mean                           | Range | Mean                       | Range |
| Normal rats (12)†  | 500                            | 480-545 | 22                             | 13-33 | 79                         | 60-89 |
| Untreated hypophysectomized rats (11)†   | 317                            | 251-400 | 16                             | 10-22 | 50                         | 41-63 |
| Hypophysectomized rats receiving 17 mg. of S.A.E.‡ only during fast (9)†                       | 522                            | 421-576 | 16                             | 10-48 | 53                         | 37-61 |
| Hypophysectomized rats receiving 1 mg. of S.A.E. per 100 gm. body weight only during fast (5)† | 506                            | 445-566 | 16                             | 13-21 | 52                         | 44-59 |
| Hypophysectomized rats injected with 10 mg. of S.A.E. per day for 10-11 days§ (5)†             | 388                            | 356-426 | 13                             | 11-17 | 60                         | 53-69 |
| Hypophysectomized rats injected with 14 mg. of S.A.E. per day for 22-24 days§ (5)†             | 342                            | 297-401 | 12                             | 10-13 | 58                         | 45-83 |

\*Fermentable reducing substances only.

†Number of animals in the group.

‡Standard alkaline extract.

§Also injected during fasting period.

<sup>1</sup> Russell, J. A., and Bennett, L. L., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 406.

<sup>2</sup> Fisher, R. E., Russell, J. A., and Cori, C. F., *J. Biol. Chem.*, 1936, **115**, 627.

<sup>3</sup> Russell, J. A., and Bennett, L. L., *Am. J. Physiol.*, 1937, **118**, 196.

fasted animals can only be due to some obscure refractory state against the metabolic effect of the extract, but apparently not against its growth-promoting effect.

Preliminary efforts to detect an inhibitory effect in the serum in chronically treated normal animals have been unsuccessful. However, in confirmation of Black,<sup>4</sup> it has been found that such chronically treated normal rats became resistant to the ketogenic effects of crude anterior lobe extracts. A group of 7 rats during a 72-hour fasting period, while receiving 1.5 cc. per day of extract, excreted an average of 43 mg. of urinary ketone bodies; after one month's daily injection, this fell to 4.6 mg. for the same fasting period while receiving a like amount of extract. An untreated control group of rats excreted 5.3 mg. of ketone bodies during a 72-hour fast.

*Summary.* Crude anterior lobe extracts are able to maintain the fasting muscle glycogen levels of hypophysectomized rats in an acute test, but are unable to do so when injected chronically. Continued treatment of normal rats with such extracts abolishes their ketogenic effect.

#### 9443 P

### Effects of Hypophysectomy and of Anterior Pituitary Extracts on Disposition of Fed Carbohydrate in Rats.\*

JANE A. RUSSELL.† (Introduced by Herbert M. Evans.)

*From the Institute of Experimental Biology, University of California, Berkeley.*

Rapid disappearance of body carbohydrate and correspondingly high rates of carbohydrate oxidation were observed in fasted hypophysectomized rats, and anterior pituitary extracts were found to restore to these animals the ability to maintain their carbohydrate levels.<sup>1, 2, 3</sup> In order to determine whether hypophysectomized rats differed from the normal in their carbohydrate metabolism in the fed state as well as when fasted, and to determine whether anterior lobe

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<sup>4</sup> Black, P. T., *J. Physiol.*, 1935, **84**, 15.

\*Aided by the Presnell Fund for the study of the metabolic relations of the anterior hypophysis, contributed by Robert R. Presnell, Frank Tuttle, Arthur Stebbins, and Mrs. Gordon Kahn, of Los Angeles.

†Porter Fellow, 1937-38.

<sup>1</sup> Russell, J. A., and Bennett, L. L., *Am. J. Physiol.*, 1937, **118**, 196.

<sup>2</sup> Fisher, R. E., Russell, J. A., and Cori, C. F., *J. Biol. Chem.*, 1936, **115**, 627.

<sup>3</sup> Russell, J. A., and Bennett, L. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 406.