

TABLE IV.

No.	Body Weight in Kilos.	Weight of Removed Pancreas in Grams.	Weight of Removed Pancreas per 1 Kilo. of Body Weight in Grams.	Approximate Weight of Removed Gland According to Allen.	Remarks.
106	7.52	18.2	2.4	15.04	No pancreatic remnant at autopsy.
108	8.7	21	2.4	17.4	Complete pancreatectomy.
111	6.56	17	2.4	13.32	Remnant weight at autopsy 4 grams.
120	9.6	21	2.1	19.2	No remnant at autopsy.
121	20	44	2.2	40	Complete removal.
128	13.8	20	1.45	27.6	Almost complete removal. No autopsy.

CONCLUSIONS.

1. The mortality of completely depancreatized dogs after ligation of the thyroid arteries is high.
2. Glycosuria in depancreatized diabetic dogs was checked after complete ligation of the thyroid arteries.
3. Tetany or infection, or both, seem to interfere with the disappearance of the glycosuria.
4. Partial ligation of the thyroid arteries apparently intensifies the diabetes produced by pancreatectomy.

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The relation of the thyroid and parathyroids to pancreatic diabetes in dogs.

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Lorand¹ (1904) and McCallum² (1909) performed complete thyroidectomies in depancreatized diabetic dogs. The former

¹ Lorand, A., *Compt. rend. Soc. Biol.*, 1904, lvi, 488.

² McCallum, William George, *Johns Hopkins Hosp. Bull.*, 1909, Sept.

worked with 3 dogs and the latter with two. In Allen's¹ experiments (1913) with diabetic dogs the thyroidectomies were incomplete. Eppinger,² Falta and Rudinger (1908) removed first the thyroid and later the pancreas in two dogs and they did a simultaneous thyroidectomy and pancreatectomy in one dog. Eppinger³ and his associates (1909) also studied the relation of parathyroid insufficiency to the metabolism in diabetic dogs by removing simultaneously the pancreas with three parathyroids in two animals.

Lorand has asserted that removal of the thyroid sparing the parathyroids is followed by the disappearance of sugar from the urine in two days in depancreatized dogs. In one of McCallum's dogs the glycosuria ceased after removal of the thyroid; in the other one it greatly diminished. In one of the experiments of McCallum two parathyroids were spared; in the other all were left in situ. A marked diminution of sugar after thyroidectomy was also reported by Eppinger. In all these experiments, blood-sugar estimates were not made. The duration of life in the animals of Lorand and McCallum was from one to three days after complete removal of the thyroid even if the parathyroids were left in situ. Three of our diabetic dogs in whom thyroidectomy with partial parathyroidectomy was performed 3 to 4 days after pancreatectomy, died from 1 to 3 days after the operation. From two of these dogs no urine was obtained, and in one dog the glycosuria persisted on the day following the removal of the thyroid.

We may mention here two clinical cases cited by Rohdenburg.⁴ One patient was diabetic and later developed exophthalmic goitre. A portion of his thyroid was removed and he remained permanently sugar-free. The other patient had exophthalmic goitre for which a portion of the thyroid was removed. Several years later he developed glycosuria. The glycosuria in this case disappeared after removal of more of the thyroid gland.

We decided that it would be a better procedure to first partially ligate the thyroid arteries and follow this operation on a later date by partial thyroidectomy, or if possible by thyroidectomy

¹ Allen, Frederick M., 1913, p. 848.

² Eppinger, Falta and Rudinger, *Ztschr. f. Klin. Med.*, 1908, lxvi, 1.

³ Eppinger, Falta and Rudinger, *Ztschr. f. Klin. Med.*, 1909, 380.

⁴ Rohdenburg, G. L., "Endocrinology," 1920, iv, 63.

alone. One may occasionally succeed in sparing all parathyroids while removing the thyroid especially in larger dogs.

In a previous¹ paper we referred to an experiment with dog No. 100, who became diabetic after removal of a little over one half of his pancreas. Such rare results are occasionally reported in the literature. As the external secretory apparatus of the pancreas was not much affected, but continued functioning, we believe that truly by chance, we produced in this animal a condition which came very close to human diabetes. Inasmuch as this experiment is a singular one in literature we shall briefly refer to it.

Seven days after the dog had from 2 to 3 per cent. sugar in his urine, both inferior thyroid arteries were ligated. The glycosuria persisted on daily examinations. Seven days later both lobes of the thyroid were removed and we succeeded in sparing all of his parathyroids. There was not a trace of sugar in his urine on the day following thyroidectomy and the urine remained sugar-free for 108 days, although eleven days after removal of the thyroid, additional pancreatic tissue was removed, and ninety-three days after the second pancreatectomy the last remnant of the gland was taken out. The animal was sugar-free four days after the third pancreatectomy. He died on the fifth day from prolapse of the intestines, which was probably brought about by the three laparotomies.

The dog's condition was excellent; ate well until the day of the accident. He did not show any signs of myxedema during the time of observation and while his original weight was 14 kilos his weight the day before death was 15.9 kilos, or a gain of 1.9 kilos. His blood sugar remained normal and 14 days after removal of the thyroid his sugar tolerance was about 10 grams per kilogram of body weight. Fig. 1 shows a photograph of the dog 93 days after removal of his thyroid.

Conditions become quite different when one does not succeed in imitating human diabetes and when sparing all the parathyroids in doing a parathyroidectomy is impossible. Infection also changes the situation. It is our impression that diabetic dogs

¹ Friedman, G. A., and Gottesman, J., *PROCEED. SOC. EXP. BIOL. AND MED.*, 1921, xviii, 281.

are more susceptible to tetany after thyroidectomy and partial parathyroidectomy than normal dogs. Although in the experiments by one of us¹ in studying the influence of thyroidectomy and partial thyroidectomy on the gastric mucosa, tetany never occurred while leaving in situ 2 or 3 parathyroids; the occurrence

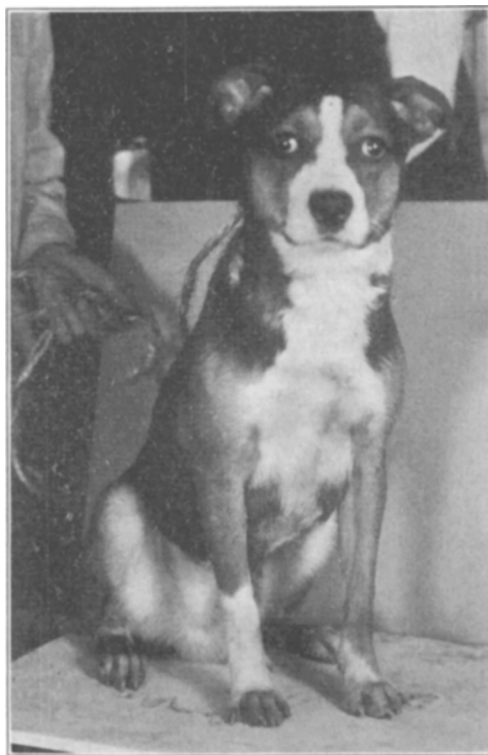


FIG. 1. Dog 100, 93 days after thyroidectomy.

of mild or severe attacks after this procedure was the rule in our diabetic dogs. We were able to observe in one diabetic dog a palliative effect on tetany from calcium lactate injections as proposed by McCallum² and Voegtlin with parathyroidectomy in non-diabetic dogs. The following experiments will show the influence of tetany upon the glycosuria in diabetic dogs and the opposite effect of the thyroid.

¹ Friedman, G. A., *Jour. Med. Research*, 1918, xxxviii, 69.

² McCallum, W. G., and Voegtlin, Carl, *Jour. Exp. Med.*, 1909, xi, 118.

Dog 136.—Male. Weight 13 kilos. Partial pancreatectomy Nov. 9: Glycosuria from Nov. 10 to Nov. 16. Ligation of inferior thyroid arteries Nov. 16. Glycosuria from Nov. 17 to Nov. 30. Thyroidectomy Nov. 30. Superior parathyroids left in situ. Thyroid lobes unusually small. Dec. 1 urine sugar free. Dec. 2 glycosuria. Dog developed a severe attack of tetany early in the morning and died in the afternoon. Autopsy: No demonstrable lesions.

Dog 138.—Male. Weight 17.71 kilos. Partial pancreatectomy Dec. 3. Glycosuria from Dec. 5 to Dec. 7. Ligation of inferior thyroid arteries Dec. 7. Glycosuria persisted from Dec. 8 to Dec. 10. Thyroidectomy preceded by intravenous injection of 10 c.c. of 5 per cent. solution calcium lactate. Three parathyroids left in situ. Dec. 12 and 13 sugar positive. Twitchings of the musculature of the back. 50 c.c. calcium chloride 5 per cent. solution by stomach tube daily. Dog developed a severe attack of tetany early in the morning Dec. 14. At 11 A.M. intravenous injection of 10 c.c. calcium-lactate solution 5 per cent. Recovered from the attack; but twitchings persisted. At 2 P.M. second attack of tetany. Dog very low, in a dying condition. At 3 P.M. another injection of calcium lactate, same dosage. Dog was catheterized twice and sugar found in the urine by adding 2 drops of Benedict's reagent. Dec. 15 and 16, no tetany or twitching. Dog had an excellent appetite. Not a trace of sugar in catheterized or passed specimens with either Benedict's or Nylander's reagents. Dec. 17, 18 and 19 twitchings of the musculature of back. No actual attack of tetany. Sugar in urine strongly positive. Mild attack of tetany though the dog had received subcutaneously 10 c.c. of calcium lactate 5 per cent. solution daily. Dec. 20, attack of tetany. Sugar strongly positive in the urine. Intravenous injection of calcium lactate in the morning and in the afternoon. Dec. 21 and 22, no tetany. Urine sugar-free. Subcutaneous injections of calcium lactate were given for three days. Dec. 23 dog was bitten in the back by another dog. On account of the large open wound he was killed.

Dog 139.—Female. Weight 12 kilos. Pancreatectomy and ligation of inferior thyroid arteries Dec. 17. Glycosuria from Dec. 18 to Dec. 31. Thyroidectomy Dec. 21. Two superior para-

thyroids left in situ. Glycosuria persisted from Dec. 23 to Dec. 25; twitchings of musculature of the back were noted the following day. The twitchings persisted though daily subcutaneous injections of calcium lactate were given. Dog was found dead Dec. 26. Autopsy: No pneumonia. Stomach filled with blood. No food present. Mucosa of the pylorus covered with numerous hemorrhagic erosions.

TABLE V.

MMGR. OF SUGAR IN 100 C.C. BLOOD AND DATES WHEN BLOOD WAS TAKEN FOR ESTIMATION.

No.	After Pancrea- tectomy.	After Partial Ligation.	After Thyroi- dectomy.	Remarks.
100			95 Feb. 15 86 " 9 66 April 13	Sugar-free 108 days after thyroidectomy.
136	250 Nov. 16	285 Nov. 30	145 Dec. 2	Increased bloodsugar after partial ligation. Sugar-free when tetany was absent.
138	290 Dec. 7	310 Dec. 10	238 Dec. 17 100 " 22	Increased bloodsugar after partial ligation. Glycosuria absent on days when tetany free.
139	228 Dec. 21	228 Dec. 21		Pancreatectomy and partial ligation in one sitting. Did not become sugar-free. Mild attacks tetany after removal of thyroid.

Table V.—Note the increase of bloodsugar in dogs 136 and 138 after partial ligation. A similar increase in dog 111, previously reported, after the same procedure. In three dogs the diabetes caused by pancreatectomy was not checked by partial ligation, but became even more intense. Compare these figures for bloodsugar with the normal figures in dog 100 after thyroidectomy with the diminished amounts after thyroidectomy with partial parathyroidectomy in the other dogs. The bloodsugar of dog 138 which amounted to 100 mgr. was found on a day when he was free of urinary sugar and free from tetany. We did not succeed in obtaining blood from dog 139 after thyroidectomy as his veins at the neck collapsed so that it was impossible to introduce a needle.

TABLE VI.

No.	Body Weight in Kilos.	Weight of Removed Pancreas in Grams.	Weight of Removed Pancreas per 1 Kilo of Body Weight.	Approximate Weight of Gland According to Allen.
100	14	? 3.4 10	?	28
136	13	17	1.3	26
138	15.71	26	1.65	31.42
139	12	23	1.91	24

Table VI indicates that it is possible to obtain a persistent glycosuria after removal of 1 to 1.3 grams of pancreas per 1 kilogram of body weight. Allen¹ figures that the pancreas of a dog weighs approximately 2 gm. per kilogram of body weight. This makes us believe that we probably removed 14.6 grams in dog No. 100 at the first operation.

CONCLUSIONS.

1. Diabetic dogs are more susceptible to tetany after partial parathyroidectomy and thyroidectomy than non-diabetic dogs after the same procedure.
2. The removal of the thyroid in diabetic dogs seems to check the glycosuria provided tetany does not occur.
3. If tetany does occur intravenous injections of calcium lactate may act as a palliative in checking temporarily both the tetanic seizures and glycosuria.

¹⁰ Allen, l.c., 716.