to increased permeability of the kidneys, but to a functional disturbance of the glycogen-forming organs. The results indicate that there is a relation between sugar tolerance and blood calcium in these animals.

5. Guanidin injections in a normal dog in amounts large enough to produce violent convulsions did not alter the serum calcium but produced hyperglycemia and lowering of the alkali reserve; phosphates remained normal.

These experiments show that the characteristic feature in the chemistry of parathyroid insufficiency is the drop in blood calcium, which is more marked the more parathyroid tissue is removed. They suggest that the parathyroids control the calcium metabolism and by doing so they influence the function not only of the muscle and nerve tissue, but probably of all organs. When the parathyroids are removed, the threshold for the excretion of calcium in the intestines is lowered. The behavior of the blood calcium indicates that the actual recovery of completely parathyroidectomized dogs in these experiments is not due to compensatory hypertrophy of accessory glands, as the action of these would have been to restore the blood calcium to the normal level; the "adaptation" to a low calcium level, which in the beginning causes tetany, is not explained.

102 (2062)

Experimental diabète gras.

By G. A. FRIEDMAN and J. GOTTESMAN.

[*From the Department of Clinical Pathology, College of Physicians and Surgeons, Columbia University, New York City*]

French authors, especially Lancereaux,[1] have described two types of diabetes mellitus: diabète maigre and diabète gras. Lancereaux believed that the former was due to pancreatic dis-

[1] Lancereaux, quoted by E. L. Opie, Diseases of the Pancreas, 1903, p. 308.

ease; diabetes with obesity, according to him, was not of pancreatic origin. Although most clinicians maintain that it is impossible to recognize the sharp distinction between diabète maigre and diabète gras, yet the fact remains that the physician in the majority of cases sees either lean or stout diabetics.

Diabetic children and young adults are usually lean, from the beginning of the disease until exitus. According to Joslin,[2] obesity is a marked feature of diabètes in the fifth and sixth decade of life. One must admit that while diabète gras may ultimately turn into diabète maigre, the latter condition rarely is transformed to the former.

Clinically three varieties of diabète gras may be distinguished:

1. Obesity associated with excretion of sugar in the urine.
2. Obesity with hyperglycemia in the absence of glycosuria.
3. Obesity with lowered glucose tolerance in the absence of hyperglycemia or glycosuria.

The recognition of the first variety is simple. Diabetics belonging to the first variety may remain obese until coma sets in. In order to diagnose the second variety, one must be sure that the renal filter is intact. Under anti-diabetic treatment patients belonging to the second variety may temporarily lose in weight, the glycemia may become normal, but glucose tolerance is usually lowered.

It is our object to show that obesity and hyperglycemia can be produced in dogs in two ways:

1. By almost complete thyroidectomy in partially depancreatized dogs.
2. By ligation of one pancreatic duct.

It was previously shown that in persistently glycosuric dogs, after pancreatectomy, the glycosuria and hyperglycemia ceased after removal of the thyroid in toto, although the animals were on a liberal diet. The hyperglycemia, however, cannot be checked by slight suppression of thyroid function, as by partial ligation of the thyroid arteries, or by one-sided lobectomy. After these operations depancreatized dogs usually continue to lose weight as without these procedures. But if after removal of one lobe the second lobe of the thyroid is at a later date removed and a

[2] Joslin, E. P., *Jour. Am. Med. Assn.*, 1921, lxxvi, 2, p. 79.

small fragment of thyroid tissue left behind in connection with the superior parathyroid, the animals gain considerably in weight although the hyperglycemia persists. The gain in body weight is also marked in depancreatized hyperglycemic dogs when incomplete thyroidectomy is done in one sitting. Such animals may live indefinitely and if they are disposed of with chloroform in from 82 to 128 days after almost complete removal of the thyroid, the striking finding at autopsies is: the thick layer of adipose tissue on the abdominal walls and in the omentum. The thyroid remnants in these dogs were found to be hypertrophied.

As to the second mode of production of diabète gras, it is well known from the experiments of Ssobolew[3] and especially from the experiments of Banting[4] and Best, that from 8 to 10 weeks after ligation of the pancreatic ducts, the digestive apparatus of the pancreas degenerates and the Langerhans islands remain intact. The blood sugar was never increased after this procedure in the experiments of the latter authors. We found that when one duct of the pancrease was ligated, the animals showed increased bloodsugar content similar to partially depancreatized dogs. These dogs also gained considerably in weight, remained in excellent condition and when they were killed 28 to 42 days after ligation, the findings in the abdominal walls and omentum were similar to those in the obese dogs after incomplete thyroidectomy. Inasmuch as at the former laparatomies no abundance of fat was noted, the adiposity must have been due to the procedure on the thyroid or to partial duct ligation.

Although we admit that our material consists of only eight dogs in whom obesity and hyperglycemia were marked features, we believe we are justified in presenting this work on account of the uniformity of results. The animals during life resembled human beings in the preglycosuric state when they are obese and in the absence of renal disorders show hyperglycemia or lowered glucose tolerance. In concluding it may be said that since Banting and Best have discovered the pancreatic hormone, there hardly remains a doubt as to the pancreatic origin of milder forms of diabetes,—diabète gras of the French.

---

3 Ssobolow, L. W., *Wirch. Arch.*, 1902, clxviii, 91.

4 Banting, F. G., and Best, C. H., *J. Lab. and Clin. Med.*, 1922, vii, 251.