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STUDIORUM PROGRESSUS

Uncoupling of the Disorder of Carbohydrate Metabolism from Fat Metabolism in Experimentally-produced Diabetes in Baboons (*Papio ursinus*)

By J. GILLMAN, CHRISTINE GILBERT, E. EPSTEIN¹, and J. C. ALLAN²

The object of this communication is to report the preliminary results of various endocrine ablations and endocrine substitution therapy on the fat and carbohydrate metabolism of the baboon, as measured by the blood glucose and serum lipids. The experimental procedures and the number of baboons used for each experiment are shown in the Table.

Complete pancreatectomy in the baboon produces the classical picture of diabetes including hyperglycaemia, glycosuria, elevation of all the lipid fractions and ketosis. These disturbances of fat and carbohydrate metabolism can be efficiently corrected by the administration of insulin (Experiments 1, 2, 3 in the Table).

The administration of thyroxin to insulin-treated, depancreatized baboons is accompanied by a reduction in the total cholesterol while the total lipids remain unaffected (Experiment 4 in the Table). If insulin treatment is suspended for 4 days but thyroxin continued, all the lipid fractions rise and particularly the lipid phosphorus which shows a 2 to 2½ fold elevation over and above that occurring in depancreatized baboons not treated with thyroxin and not receiving insulin for a comparable period (compare Experiment 5 with Experiment 3 in the Table). Moreover, the blood ketones are 2-4 times as high in the thyroxin-treated, insulin-deprived depancreatized baboons as in depancreatized baboons not receiving thyroxin. The administration of insulin to the thyroxinized, depancreatized baboons results in a return to normal of all the lipid fractions as well as the ketones within 3 to 5 days.

Removal of the hypophysis from depancreatized baboons (D-H baboons) markedly increases the sensitivity to insulin, as reported in other animals, and improves the physical condition of the baboons. However, the disorder in carbohydrate metabolism persists and, in the absence of insulin, the resting blood sugar, at the end of a 16-h fast, ranges from 500 to 600 mg%. The D-H baboon thus behaves like the D-H dog and cat described by LONG and LUKENS³.

During a 7-10 day period of insulin deprivation, the D-H baboons remain in good physical condition in con-

trast to the depancreatized baboons which become ill and lose their appetite within 4-6 days after the last injection of insulin. Furthermore, in D-H baboons not receiving insulin, the total serum lipids rise slightly due to a 1½ fold increase in total cholesterol and lipid phosphorus but there is no ketonaemia or ketonuria (Experiments 6, 7 in the Table).

After a three-week course of cortisone (1 mg/kg body weight/day) in conjunction with insulin (Experiment 8) followed by a 4 to 5 day period of withdrawal of insulin, a D-H baboon showed a rapid rise in blood sugar, total lipids, total cholesterol and lipid phosphorus to levels similar to those occurring in a depancreatized baboon with an intact pituitary but not receiving insulin for a comparable period (compare Experiment 9 with Experiment 3 in the Table). Unlike the depancreatized, insulin-deprived baboons, the ketones in the blood of the cortisone-treated, D-H baboon not receiving insulin did not exceed 2.8 mg% despite the fact that the total lipids reached a level of 1588 mg% (Experiment 9 in the Table). Cortisone significantly increased the insulin requirements of the D-H baboon but the baboon does not become insulin resistant.

The administration of thyroxin (0.2 mg/second day for 3 weeks) to one D-H insulin-treated baboon (Experiment 10) followed by a 4-day period of insulin withdrawal is unaccompanied by any change in the serum lipids or ketones although the blood sugar is greatly elevated (Experiment 11 in the Table). One insulin-treated D-H baboon received a 3-week course of cortisone (1 mg/kg body weight/day) followed by a 2-week course of cortisone and thyroxin (0.2 mg/second day) (Experiment 12). Thereafter, insulin was withdrawn but cortisone and thyroxin continued. At the end of the sixth day of insulin withdrawal, the total serum lipids rose to 2003 mg% and the blood ketones to 9.8 mg% (Experiment 13 in the Table).

Although the numbers of baboons used in some experiments are still too few to draw firm conclusions, nevertheless, if the experiments are examined as a whole, it is apparent that (1) removal of the hypophysis from depancreatized baboons fails to correct the disorder of carbohydrate metabolism but markedly alleviates the disturbance in fat metabolism. (2) The reappearance of the lipaemia in depancreatized-hypophysectomized baboons not receiving insulin following a course of treatment with cortisone indicates that an actively functioning adrenal cortex at least is essential for the lipaemia of the depancreatized, insulin-deprived baboon. (3) Thyroxin intensifies the lipaemia of the depancreatized-hypophysectomized baboon receiving cortisone thus emphasizing the role of the thyroid as well as the adrenal in the regulation of the serum lipid levels. (4) The ketonaemia of depancreatized baboons not receiving insulin disappears after hypophysectomy and cannot be restored to prehypophysectomy levels either by cortisone, thyroxin or by both these hormones administered simultaneously.

Ketonaemia in pancreatic diabetes in the baboon, therefore, can be dissociated from the hyperglycaemia and from the intense lipaemia.

¹ Departments of Physiology and Anatomy and Joint Nutrition Research Unit of the C.S.I.R. and of the University of the Witwatersrand, Johannesburg.

² Department of Surgery, University of the Witwatersrand, Johannesburg.

³ C. N. H. LONG and F. D. W. LUKENS, J. exp. Med. 63, 465 (1936).

Table showing the changes in the serum lipid fractions of the baboon following pancreatectomy and hypophysectomy and substitution therapy

Experiment No.	Number of baboons used	Operative procedure	Treatment	Total lipids mg%	Cholesterol mg%	Lipid phosphorus mg%	Total ketone bodies (in blood) mg%	Resting blood sugar* mg%
1	9	Controls (non-operated)	None	384- 512	117-155	7.0-11.3	0.6- 1.8	70- 80
2	9	Pancreatectomy	insulin	285- 458	94-156	5.6- 9.6	0.8- 3.2	102-588
3	9	Pancreatectomy	No insulin	1218-2184	218-780	12.3-34.6	13.2-113.2	363-588
4	3	Pancreatectomy	insulin + thyroxin	350- 382	98-112	8.75- 9.7	1.8- 4.4	260-596
5	3	Pancreatectomy	No insulin + thyroxin	1927-2136	396-624	32.0-47.4	102 -138	391-448
6	4	Pancreatectomy + hypophysectomy	insulin	384- 455	141-186	9.3-12.5	0.02- 3.0	170-588
7	4	Pancreatectomy + hypophysectomy	No insulin	423- 567	185-251	10.5-15.3	2.0- 5.4	519-666
8	2	Pancreatectomy + hypophysectomy	insulin + cortisone	406- 448	178-189	8.1-12.1	2.0	519-627
9	1	Pancreatectomy + hypophysectomy	No insulin + cortisone	1588	340	20.1	2.8	601
10	1	Pancreatectomy + hypophysectomy	insulin + cortisone	435	100	6.05	1.0	197-324
11	1	Pancreatectomy + hypophysectomy	insulin + thyroxin	437	126	5.95	1.6	510
12	1	Pancreatectomy + hypophysectomy	No insulin + thyroxin	831	292	13.75	2.6	150-247
13	1	Pancreatectomy + hypophysectomy	No insulin + cortisone + thyroxin	2003	544	27.6	9.8	666

* Blood sample collected at 9 a.m. 16 h after the last meal and after the last injection of insulin.

Investigations to elucidate the factors responsible for the ketonaemia in diabetic baboons are still in progress.

Résumé

Après ablation de la glande pituitaire, le dérèglement du métabolisme des hydrates de carbone persiste, tandis que l'intense lipémie est abolie. L'administration de la cortisone aux babouins pancréas- et hypophysectomisés privés d'insuline, rétablit la lipémie mais non la cétonémie.

Le dérèglement du métabolisme des hydrates de carbone dans les babouins diabétiques peut être dissocié de celui des lipides par un traitement approprié des glandes endocrines.

La cétonémie des babouins pancréas- et hypophysectomisés, contrairement à la lipémie, n'est pas rétabli par l'administration de la cortisone, thyroxin ou par une combinaison de ces hormones.

CONGRESSUS
GREAT BRITAIN

VIIth International Cancer Congress
London, July 6-12, 1958

The International Union against Cancer will shortly award a limited number of travel grants to facilitate young scientists to attend the 7th International Cancer Congress in London, July 6-12, 1958. Priority will be given to applicants under the age of 35, who do not yet hold senior appointments, but who have already made significant contributions to the cancer literature. The grants will cover part or all of the travel expenses from and to the country of residence, but will not include subsistence allowance. Application forms may be obtained from Dr. I. BERENBLUM (Chairman: Committee for Young Scientists, U.I.C.C.), The Weizmann Institute of Science, Rehovoth, Israel.

CONGRESSUS
CANADA

IXth International Botanical Congress
Montreal, August 19 to 29, 1959

The IXth International Botanical Congress will be held in Montreal, Canada, from August 19 to 29, 1959, at McGill University and the University of Montreal. The program will include papers and symposia related to all branches of pure and applied botany. A first circular giving information on program, accommodation, excursions, and other detail will be available early in 1958. This circular and subsequent circulars including application forms will be sent only to those who write to the Secretary-General asking to be placed on the Congress mailing list: Dr. C. FRANKTON, Secretary-General, IXth International Botanical Congress, Science Service Building, Ottawa, Ontario (Canada).