

adenine and uracil. 3. Desoxyribonucleic acid was inactive as the factor, but became active after depolymerization by desoxyribonuclease. 4. The lack of uniformity of Group A streptococci with respect to dependence on this factor shows that nutritional studies performed on a single strain cannot be regarded as representative of the entire group.

Acknowledgement of indebtedness to the many

individuals who have supplied materials for this investigation will be found in the text, in the footnotes and in the tables of this paper. A word is appropriate here concerning the generosity of those who have these rare materials in their possession and who lend them so freely. An undertaking of this sort would be impossible without it. The author wishes further to thank Dr. A. E. Mirsky for his interest and for his many suggestions.

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Diabetes in a Totally Depancreatized Man.*

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We wish to report observations on the diabetes of a totally depancreatized man. The surgical aspects of the case have been described elsewhere.¹ The patient in question had had spontaneous diabetes, known for 9 months before he entered the hospital, and his father also had had the disease. His presenting complaints were abdominal pain and diarrhea of 2 years' duration and, recently, thirst, polyuria and loss of weight. The symptoms, except for the diarrhea, were largely ameliorated by diet and insulin. While under treatment he developed jaundice and at operation was found to have a carcinoma of the pancreas with infiltration of the neighboring organs. The entire pancreas, duodenum, stomach, spleen, left adrenal and most of the omentum were removed. The liver appeared normal. Histologic examination of the uninvolved head and neck of the pancreas (Dr. George Gomori) showed insular changes characteristic of diabetes. At the conclusion of the operation there was no gross evidence of remaining neoplasm. The postoperative course was uneventful and the patient was out of bed on the sixteenth

day. For 6 weeks he was maintained on both protamine zinc and crystalline insulin, but thereafter, in order to facilitate studies, was given crystalline insulin alone. He also received vitamin preparations parenterally, atropine to control diarrhea, and at intervals large doses of powdered pancreas. He survived for 14 weeks after operation, death being due to recurrence of the carcinoma and, terminally, to the withdrawal of insulin.

Insulin Requirement. Before operation, on a diet of C 398, P 200, F 12 g (glucose equivalent 511 g), the amount of insulin necessary to keep the urine nearly sugar-free was from 40 to 65 units per day. The body weight at this time was 72 kg (158 lb). Two months after operation, when the patient was up and about, the diet was C 401, P 102, F 11 g (glucose equivalent 459 g) and the insulin requirement was about 40 units per day. The body weight was now 56 kg (123 lb). The apparent reduction in the demand for insulin may have been due to 2 factors: first, the lower glucose value of the postoperative diet, and second, the loss of 16 kg of weight. The striking fact, however, is not that the insulin requirement was lower, but that it was no higher.

Sensitivity to insulin was marked, the patient showing frequent hypoglycemic reactions.

Withdrawal of Insulin. Approximately 3

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¹ Brunschwig, Alexander, and Ricketts, Henry T., *Surg. Gyn. and Ob.*, 1945, in press.

months after operation all insulin was withdrawn for a period of 4 days. On the first day, glycosuria, previously less than 10 g per day, rose to 112 g. On the second day, the value was 143 g and ketosis appeared. On the fourth day, all food was withheld and the urine showed a D/N ratio of 2.42. Insulin was reinstituted that evening because of severe thirst and discomfort. The patient had lost 4.5 kg of weight during this period.

Six days later, with the patient's appetite failing, insulin was again withdrawn. Marked glycosuria and ketosis promptly appeared. Two days later, the urine contained 108 g of glucose and the patient stopped eating entirely. On the fourth day of this period, the blood sugar was 570 mg %, and between the fifth and sixth days the urine showed a D/N ratio of 3.59. Death occurred on the sixth day in typical diabetic coma.

Fasting respiratory quotients were determined daily for 5 days when the patient was in relatively good health and was receiving crystalline insulin 3 times per day, the last dose being given before supper. The values varied from 0.77 to 0.80. Fasting blood sugars on the same mornings were in the neighborhood of 100 mg per 100 cc. Determinations of the R.Q. during the complete withdrawal of insulin were unsatisfactory.

Fat Metabolism. The serum lipids, which before operation ranged from 800 to 1260 mg

per 100 cc, slowly declined after pancreatectomy but never sank to subnormal levels, the minimum being 707 mg per 100 cc. At autopsy the liver was grossly fatty, probably owing to the patient's death in diabetic coma.

Conclusions. (1) The pancreas, or its hormone, insulin, is necessary to life in the human. (2) On the basis of the present case and others previously reported,²⁻⁵ the insulin output of the normal human pancreas must be considerably smaller than has been believed and seems to lie in the range of 30 to 50 units per day. Therefore, (3) in diabetic patients requiring more than this amount, an extra-insular factor must be contributing to the diabetic syndrome. (4) The D/N ratio of from 2.42 to 3.59 indicates that a fasting, depancreatized man deprived of insulin converts protein to carbohydrate at a rate commensurate with that observed in the dog under the same conditions⁶ or when treated with phloridzin.⁷

² Roockey, Eugene W., *Ann. Surg.*, 1943, **118**, 603.

³ Goldner, Martin G., and Clark, Dwight E., *J. Clin. Endocrinol.*, 1944, **4**, 194.

⁴ Priestley, James T., Comfort, Mandred W., and Radcliffe, James, Jr., *Ann. Surg.*, 1944, **119**, 211.

⁵ McClure, R. D., *Ann. Surg.*, 1944, **120**, 416.

⁶ Minkowski, O., *Arch. f. exp. Path. u. Pharmacol.*, 1893, **31**, 85.

⁷ Lusk, Graham. *The Science of Nutrition*, Philadelphia and London, W. B. Saunders Co., 1928.

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Effect of p-Aminobenzoic Acid on the Growth of Typhus Rickettsiae in the Yolk Sac of the Infected Chick Embryo.*

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The search for chemical compounds having possible therapeutic effects on typhus fever, which centered first on sulfonamide derivatives, has been extended to include all kinds of substances having effects on pathogenic bacteria and protozoa. Snyder, Maier, and Anderson¹ tested the activity of a large number of drugs (sulfonamides, anti-luetic, anti-malar-

ial, and trypanosomicidal compounds) on the

* Report to the Director of the United States of America Typhus Commission, December 16, 1943, withheld from publication. Since this time two other papers dealing with the therapeutic effect of P.A.B.A. were published.

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