

<sup>7</sup> Bookman, J. J.; Drachman, S. R.; Schaefer, L. E.; and Adlersberg, D.: Steroid diabetes in man. The development of diabetes during treatment with cortisone and corticotropin. *Diabetes*. 2:100-111, Mar.-Apr., 1953.

<sup>8</sup> Conn, J. W.; Louis, L. H., and Wheeler, C. E.: Production of temporary diabetes mellitus in man with pituitary adrenocorticotrophic hormone; relation to uric acid metabolism. *J. Lab. & Clin. Med.* 33:651-661, 1948.

## INSULIN RESISTANCE

Insulin resistance may or may not be associated with the visible manifestations of allergy to insulin. Although the majority of patients with minor, transitory, allergic reactions to insulin are not noticeably resistant to insulin, one rightly looks for allergy to insulin as a possible cause of severe insulin resistance. In the last decade, the study of insulin resistance has been advanced by the application of several new methods. Lerman<sup>1</sup> and Lowell,<sup>2,3</sup> selecting patients because they were insulin resistant (with or without associated local allergy) have presented strong evidence for an immunologic mechanism. The same immunologic methods have indicated that antibodies to administered insulin may be produced in rabbits.<sup>4</sup> Insulin recrystallized six times is much less antigenic than commercial insulin<sup>5</sup> and the use of insulin prepared from human pancreas may be normally effective in the presence of resistance to the usual commercial insulin.<sup>3</sup> Such results indicate that the allergy to administered insulin is due either to some contamination of the protein hormone, or to differences in the actual structure of insulin from different sources, to which these few patients are susceptible.

Further evidence of the part which allergy may play in insulin resistance has appeared since the control of allergic reactions by corticotropin (ACTH) has been possible. Howard<sup>6</sup> treated a patient, who had marked resistance and allergy to insulin, with corticotropin and was able to restore the patient to a stage of mild diabetes for which no insulin was needed. Sera of this and of other insulin resistant patients were examined for their effect on the action of insulin on the isolated rat diaphragm.<sup>7</sup> There was striking inhibition of the effect of insulin *in vitro* by the sera of patients requiring 300 units of insulin per day or more. In the patient who had been treated with corticotropin, this inhibitory action of the serum was no longer present. Finally, Marsh and Haugaard<sup>7</sup> have shown that the serum of insulin resistant patients behaves differently from the hormones which inhibit the action of insulin *in vitro*. Thus in the presence of antibodies, less insulin is bound to the rat diaphragm: antagonistic hormones appear not to pre-

vent this binding of insulin to tissue but to inhibit its subsequent metabolic action. These results emphasize the importance of immune reactions in insulin resistance. The preliminary differentiation of immunological and hormonal types of insulin resistance by new methods suggests that this obscure corner of diabetes may be considerably enlightened in the future.

F. D. W. LUKENS, M.D.

<sup>1</sup> Lerman, J.: Insulin resistance. The role of immunity in its production. *Am J. Med. Sci.* 207:354-360, 1944.

<sup>2</sup> Lowell, F. C.: Immunologic studies in insulin resistance. I. Report of a case exhibiting variations in resistance and allergy to insulin. *J. Clin. Invest.* 23:225-31, 1944.

<sup>3</sup> Lowell, F. C.: Immunologic studies in insulin resistance. II. The presence of a neutralizing factor in the blood exhibiting some characteristics of an antibody. *J. Clin. Invest.* 23:233-240, 1944.

<sup>4</sup> Franklin, W.; and Lowell, F. C.: Experimentally induced insulin resistance and allergy in the rabbit. *J. Allergy* 20:400-403, 1949.

<sup>5</sup> Paley, R. G.; and Tunbridge, R. E.: Dermal reactions to insulin therapy. *Diabetes* 1:22-27, 1952.

<sup>6</sup> Howard, J. E.: Proceedings of the Second Clinical ACTH Conference, edited by Mote, J. R., New York, The Blakiston Co., 1951, Vol. I, p. 318.

<sup>7</sup> Marsh, J. B.; and Haugaard, N.: The effect of serum from insulin-resistant cases on the combination of insulin with the rat diaphragm. *J. Clin. Invest.* 31:107-110, 1952.

## A PRE-DIABETIC STATE IN PARENTS OF OVERWEIGHT BABIES

It is widely recognized that maternal diabetes bears a close relationship to production of abnormally large babies as well as to hydramnios, a high fetal mortality and perhaps toxemia. It has been clearly shown by Miller, Kriss and Fitcher and others, that abnormally large children may be born to mothers who have no evidence of diabetes at the time of birth (as judged by existing methods) and who later develop diabetes.

W. P. U. Jackson,<sup>1</sup> in his recent article in the *British Medical Journal*, offered fresh, carefully studied and convincing evidence along these lines. He found that 62 per cent of women who developed overt diabetes after childbearing claimed to have had before becoming diabetic at least one baby over 10 pounds in weight at birth; 31 per cent of the babies of these women were over 10 pounds as compared with 4.6 per cent of the babies of women in the control group. One of the most internal maternal environment must be the dominant engaging parts of Jackson's studies and one which appears to be a new contribution to the knowledge of