

THE CORTISONE (AUGMENTED) GLUCOSE TOLERANCE TEST FOR THE DETECTION OF PREDIABETES

Cortisone is a steroid with diabetogenic properties by virtue of its ability to increase gluconeogenesis (Soskin and Levine¹) and decrease the rate of assimilation of glucose by the tissues (Frankson²). Zucher³ gave subdiabetogenic doses of alloxan to rabbits, followed by doses of adrenal cortical extract too small to modify the glucose tolerance in the normal rabbit. In these pre-treated rabbits, however, significant impairment of carbohydrate tolerance was produced. Somewhat similarly, Hoet⁴ showed that hydrocortisone, again in doses too small to affect a normal rabbit, would produce a diabetic state in a pregnant animal. All this suggested that the correct dose of cortisone might modify carbohydrate tolerance in prediabetic individuals, while not affecting normal people. Berger,⁵ in 1952, had already used corticotrophin (ACTH) to sensitize the glucose tolerance test, when Fajans and Conn,⁶ in 1954, reported results with the use of cortisone for the same purpose. Their method was to perform a standard oral tolerance test, followed the next day by a similar test which had been preceded by 2 doses of 50 or 62.5 mg. of cortisone, given 8½ and 2 hours before ingestion of the glucose. The normal degree of raising of the tolerance curve was estimated in control subjects with no family history of diabetes, and criteria for abnormality were established. They then investigated 152 healthy relatives of diabetic patients and found 19% of these to be unknown but unquestionable diabetics, as against 1 of 50 control subjects. They then tested 75 non-diabetic relatives of diabetics by cortisone-glucose tolerance test and found significant impairment in 24%, as against 1 of 37 normal controls (3.3%). They further demonstrated that 6 patients whose carbohydrate tolerance had apparently reverted to normal after they had lost weight nevertheless gave a positive response to the test when this was augmented with cortisone. It appeared, therefore, that 2 distinct groups of reactors to this test existed, and that a high proportion of positive reactors occurred in the relatives of diabetics. Were these people really prediabetics—the ones who would later themselves become diabetic? So far 4 out of 30 of such abnormal reactors who have been followed up have become grossly diabetic (Conn⁷).

West,⁸ with similar but somewhat modified techniques, confirmed the basic conclusion of Fajans and Conn. He claimed also that older healthy subjects tended to give more frequent positive responses than younger ones and that, among 14 subjects both of whose parents were diabetic, only 7 gave a positive result, a proportion no larger than was found when one parent, one sibling, or one child was diabetic. He also claimed that cortisone acetate was less active in producing changes in glucose tolerance than the equivalent doses of hydrocortisone, prednisone or pred-

nisolone. All this work, however, was concerned with single blood-sugar readings made 2 hours after the ingestion of glucose, so that more exaggerated effects at the maximum height of the curve would be missed.

Since there is a close, though somewhat indefinite, relationship between obesity and the development of mild diabetes, German⁹ investigated the response of obese subjects to the cortisone-glucose tolerance test, using the method of Fajans and Conn; 40 non-obese and 40 obese healthy individuals with no family history of diabetes were subjected to the standard glucose tolerance test followed next day by the augmented test. No significant difference was found to exist between the two groups as regards the 2-hour response on the standard test nor on the augmented test, and the two groups responded to cortisone priming in the same fashion. This result is perhaps unexpected, since it is generally believed that obesity, in at least a proportion of cases, is damaging to the individual's carbohydrate tolerance. German's subjects, however, were not so grossly fat (range 200-255 lb.). Moreover, according to Beaudoin *et al.*,¹⁰ there may be considerable difference in glucose tolerance between 'active' and 'static' obesity, and German does not indicate whether his subjects were actually gaining weight at the time of the test or had been obese for a long time.

It would therefore appear that this test, although of some value in indicating the potential diabetic, frequently fails to do so, while in older people it may appear falsely positive unless the criteria of abnormality are raised. Certainly we do not know for certain the best dose, the best steroid, or the best way of carrying out the test, or even the best way to interpret it (e.g. the total maximum rise of blood sugar over the control value may be more important than any absolute 2-hour figure); but it seems doubtful whether modifications on these lines will produce any great improvement.

Duncan¹¹ gives reasons for preferring to use intravenous glucose tolerance tests, with the change in increment index as the single-figure criterion of abnormality. He found a positive response in all mild diabetics and latent diabetics, and in 9 out of 19 suspected prediabetics. This would appear to be a more sensitive method of detecting prediabetes.

1. Soskin, S. S. and Levine, R. (1952): *Carbohydrate Metabolism*. Chicago: University of Chicago Press.
2. Frankson, J. R. M. (1953): *Acta endocr.*, **14**, 153.
3. Zucher, H. D. (1949): *Proc. Soc. Exp. Biol. Med. (N.Y.)*, **71**, 597.
4. Hoet, J. P. (1954): *Diabetes*, **3**, 1.
5. Berger, H. (1952): *J. Amer. Med. Assoc.*, **148**, 364.
6. Fajans, S. S. and Conn, J. W. (1954): *Diabetes*, **3**, 296.
7. Conn, J. W. (1958): *Ibid.*, **7**, 347.
8. West, K. M. (1957): *Ibid.*, **6**, 168.
9. German, J. L. (1958): *Ibid.*, **7**, 261.
10. Beaudoin, R., van Itallie, T. B. and Mayer, J. (1953): *J. Clin. Nutr.*, **1**, 91.
11. Duncan, L. J. P. (1956): *Quart. J. Exper. Physiol.*, **41**, 453.

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Op hierdie manier maak die mediese biblioteke dit dus moontlik vir dokters om met naslaanwerk en navorsing voort te gaan afgesien van waar hulle bly of werk.

The Secretary of the Medical Association of South Africa, the Editor of the South African Medical Journal, and the other members of the head office staff of the Association, extend hearty Xmas greetings to all members of the Association and all readers and supporters of the Journal, and wish them a happy and prosperous New Year.

Die Sekretaris van die Mediese Vereniging van Suid-Afrika, die Redakteur van die Suid-Afrikaanse Tydskrif vir Geneeskunde, en die ander lede van die hoofkantoorpersoneel van die Vereniging, stuur hartlike Kersgroete aan alle lede van die Vereniging, en alle lesers en ondersteuners van die Tydskrif, en wens hulle 'n gelukkige en geseëde Nuwe Jaar toe.