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Gestational Diabetes

Though the natural history of the patient's state preceding overt diabetes mellitus remains mysterious, it nevertheless has acquired a classification. "Latent diabetes" defines the situation in which a normal glucose tolerance test becomes abnormal temporarily during some kind of stress. When this is pregnancy and the glucose tolerance test returns to normal post partum, the latent diabetes is termed "gestational diabetes."

Women with gestational diabetes have a considerably increased risk of developing diabetes in subsequent years.[1] However, the more immediate risk is to the fetus. With overt diabetes perinatal mortality is high, though much decreased by improvements in medical, obstetric, and paediatric care.[2] Retrospective analysis of the prediabetic period in women—that is, the time before diagnosis of overt diabetes—has shown a high average perinatal mortality rate among their babies and an increased incidence of babies of high birth weight.[3] These challenging findings remain unexplained.

J. B. O'Sullivan and colleagues[4] studied prospectively a group of gestational diabetics and observed a higher fetal mortality than in a group of women with normal glucose tolerance. However, it was not possible to regard the abnormal glucose tolerance as solely responsible for the excess mortality, for there were other differences between the two groups of patients. Recently O'Sullivan and colleagues[5] have reported on another prospective study comparing gestational diabetics with a control group having normal glucose tolerance in which they also examined the possible effects of age and obesity. In the control patients the perinatal mortality was significantly lower, and age and degree of obesity had little or no effect. In the gestational diabetics the increased perinatal mortality was confined to the babies of mothers above the age of 25, with a small additional effect of overweight. But the authors are careful to point out that the absence of risk to the babies of the younger mothers may be true only when obstetric care is optimal. Whatever the aetiological implications of these results, they do offer some practical guide in determining the mothers who should be carefully screened in pregnancy.

If the risk of perinatal mortality is higher in cases of gestational diabetes, can anything be done to lower it? The answer at present must be "perhaps." O'Sullivan and colleagues[6] studied 603 patients who were found to have abnormal glucose tolerance during pregnancy. Half were treated with insulin and diet and all were followed for 15 years post partum. The perinatal mortality was higher in the control group receiving only routine obstetric care, but it was only so in the babies of those mothers who subsequently developed diabetes, about one-third of the total. On this evidence, therefore, only the babies of truly prediabetic women may expect benefit from treatment of the mother, and there is no way at present of recognizing her. Even so, if the possibility of giving benefit is confirmed, it may be justifiable to treat all gestational diabetics for the benefit of one-third, particularly if the treatment itself is neither unpleasant nor hazardous. A trial of treatment is in progress at Aberdeen, and the results will be awaited with interest.

Another problem of gestational diabetes is screening. H. W. Sutherland and colleagues[7] compared the yield of abnormal intravenous glucose tolerance tests derived from patients having a variety of indications for carrying them out: glycosuria detected in a second, overnight fasting specimen; family history of diabetes; obesity above the 85th percentile; previous large-for-dates baby; previous unexplained stillbirth; previous unexplained neonatal death; two or more abortions unexplained; presence or history of major congenital defect; presence or history of unequivocal polyhydramnios; and history of hyperplasia of the islets of Langerhans in the baby, particularly if unassociated with rhesus isoimmunization.

Of 62 women with fasting glycosuria 15% had abnormal glucose tolerance compared with none of 50 women with random glycosuria. Fasting glycosuria also enhanced the significance of the other indications.

The urine testing in this study was done with Clinistix, but because of possible false negatives a dual test with Clinistix and Tes Tape might be safer in practice.[8] N. G. Soler and J. M. Malins[9] also found random glycosuria to be a poor indicator of abnormal (oral) glucose tolerance. When more than one indication exists and a glucose tolerance test is normal early in pregnancy, it is advisable to retest during the last trimester.

The type of confirmatory glucose tolerance test—oral or intravenous—remains a controversial topic. Each has its advocates. Unfortunately in the same individual the two tests may give disparate results. Most of our present information on gestational diabetes stems from the work of O'Sullivan and his colleagues, who have used the 100-g oral glucose tolerance test. With venous sampling and using the Somogyi-Nelson method of blood sugar estimation they have defined normal values based on testing large numbers of unselected pregnant women. There are no comparable studies with the 50-g oral glucose tolerance test, but T. Lind and colleagues[10] have

suggested that the British Diabetic Association criteria[11] are applicable to pregnant women. Criteria for the intravenous test during pregnancy have been published by F. A. Silverstone and colleagues.[12]

The case for screening in pregnancy rests not only on the chance of discovering gestational diabetes but also on that of finding chemical or overt diabetes. Only a postpartum test can confirm that the diabetes is gestational. Apart from any risk in the current pregnancy, gestational diabetes means that the woman has a greater risk of developing permanent diabetes, and it is an indication for an early glucose tolerance test in subsequent pregnancies.

[1] O'Sullivan, J. B., and Mahan, C. M., *Diabetes*, 1964, **13**, 278.
[2] Baird, J. D., *Journal of Endocrinology*, 1969, **44**, 139.
[3] Malins, J. M., and Fitzgerald, M. G., *Diabetes*, 1965, **14**, 175.
[4] O'Sullivan, J. B., Gellis, S., Dandrow, R., and Tenney, B., *Obstetrics and Gynecology*, 1966, **27**, 683.
[5] O'Sullivan, J. B., Charles, D., Mahan, C. M., and Dandrow, R. V., *American Journal of Obstetrics and Gynecology* 1973, **116**, 901.
[6] O'Sullivan, J. B., Charles, D., and Dandrow, R. V., *Journal of Reproductive Medicine*, 1971, **7**, 45.
[7] Sutherland, H. W., Stowers, J. M., and McKenzie, C., *Lancet*, 1970, **1**, 1069.
[8] Feldman, J. M., and Lebovitz, F. L., *Diabetes*, 1973, **22**, 115.
[9] Soler, N. G., and Malins, J. M., *Lancet*, 1971, **2**, 724.
[10] Lind, T., Cheyne, G. A., Billewicz, W. Z., and Fairweather, D., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1968, **75**, 540.
[11] Fitzgerald, M. G., and Keen, H., *British Medical Journal*, 1964, **1**, 1568.
[12] Silverstone, F. A., Solomons, E., and Rubricius, J., *Diabetes*, 1963, **12**, 398.

Drugs Causing Weight Gain

Body weight is amazingly well regulated in the normal adult. Within a daily variation of about a kilogram it may remain constant for weeks, months, years in spite of changes of diet, climate, and activity. Regular weighings over the years form a valuable health check. Deviation from the individual's norm may signal serious disease, and this is true of gains in weight as well as losses. The speed of gain or loss may point to the type of lesion. Even by stuffing oneself with food it is probably impossible to gain more than 2 kg per week—or by total starvation to lose more than 3 kg. At these rates the gain or loss of body water must be the main question at issue.

Apart from physical illness certain changes in life style may impinge on weight. Taking to drinking or giving up smoking may both lead to obesity—such every-day facts that possible pharmacological mechanisms are ignored. In the last 20 years long-term drug treatments have become important in psychiatry and some of these give rise to troublesome gains in weight. Chlorpromazine, the first of the phenothiazine drugs so useful in treating schizophrenics, sometimes causes a steady rise of perhaps 0·75 kg per week, levelling off when 7 to 10 kg have been added to the bodyweight. This could be partly due to fluid retention as well as to increased appetite and deposition of fat. The weight may decline again rapidly when the drug is stopped, without immediate behavioural change. Other phenothiazines and butyrophenones affect the weight only rarely if at all.

Lithium carbonate taken over months in the prophylaxis of manic-depressive disorders is another drug which may lead to gain in weight. Again the mechanisms at work are unknown, but there is some evidence that an increase in weight is more likely when the lithium is given in combination with other drugs which by themselves would not cause an increase, such as haloperidol.

The latest addition to the list is amitriptyline, another drug now coming to be used in the prophylaxis of recurrent depressive illness, and E. S. Paykel and his collaborators[1] have studied the mechanism in the setting of a prophylactic trial. Their patients were all women who had recovered from a depressive illness three months before, so that any weight losses due to the illness should have been made up in the recovery and post-recovery periods, and they were taking regular amitriptyline daily. In essence, half of them continued on this drug for a further six months and half did not. Those on the drug gained an average of 2·5 kg in this time, whereas the weights of the others remained level. Further, those drug-takers who then stopped lost their excess weight again, like the chlorpromazine-takers noted above. Some of the individuals on amitriptyline gained 6 kg or more in a few months, again like patients on chlorpromazine.

Paykel and his colleagues found that the patients gaining weight on amitriptyline had a craving for carbohydrate foods. The severity of craving seemed to be dose-related and disappeared altogether when the drug was withdrawn. This led them to test the response of serum glucose and free fatty acids, insulin, and growth hormone to an intravenous dose of insulin in some of these patients, but they found no abnormalities except perhaps in one respect. Patients with greater carbohydrate craving showed a greater growth hormone response to the hypoglycaemia. The authors suggest that this might mean that amitriptyline had altered the hypothalamic monitoring of plasma glucose. This seems a point at which animal experiments could take over for further clarification of appetite control. The results may be useful in the rapid fattening of pigs and beef as well as in clinical medicine.

From a practical point of view the patient who complains of weight gain while on long-term psychotropic drugs needs a physical check for cardiac, renal, or thyroid disease, a review of medication in case the gain is due to drug combinations, and possibly a lowering of the dose if a single drug is clearly responsible. Dieting, the use of diuretics, or a trial of an anorectic such as fenfluramine, might be appropriate in special circumstances.

[1] Paykel, E. S., Muelter, P. S., and de la Vergne, P. M., *British Journal of Psychiatry*, 1973, **123**, 501.

Suicide by Private Pilots

From time to time we read about a lone pilot handling his aircraft in a way which could almost certainly lead to disaster. The immediate reaction of the public is often one of admiration, and it is usually interpreted as a defiant if somewhat foolhardy reaction to authority. Flying low under bridges may be an exhilarating experience and a great spectacle, but such behaviour could lead easily to tragedy.

It is not widely appreciated that pilots who undertake such circus acts are often under considerable stress in their own lives. There is even the possibility that it may be the immediate prelude to suicide. This is one of the reasons why doctors responsible for the medical supervision of private pilots should be careful to expose any psychiatric history which may suggest irresponsible behaviour under stress. Emotional instability during childhood and immature personal relationships need careful assessment, while frequent changes of job, financial difficulties, minor skirmishes with the law, and recent car accidents all suggest behaviour which may be inappropriate for a pilot. Individuals with this kind of personal history find it difficult to cope with the stresses of their lives, and this in-