MEDICAL PRACTICE

Contemporary Themes

Metabolic Disorders in Diabetes*

RUSSELL FRASER

British Medical Journal, 1972, 4, 591–596

Introduction

Diabetes is the persistent tendency to high blood sugar, especially evident after oral glucose, and I shall discuss here how to distinguish an abnormally high blood sugar regardless of age. Obviously behind this end result may be several causes, mostly awaiting definable diagnostic criteria. We have known since earliest times that both heredity and overindulgence in sweet-foods are possible causes, which, however, still need diagnostic criteria. Here my concern is not causes but those disorders apparently common to all types of diabetes mellitus, especially their manifestations in the adult-onset type and those facets in which this unit has made some studies.

From a clinic survey among mild adult-onset diabetics data are presented on the insulin, glucose, and lipid levels seen at 0 and 1 hour after a 50 g oral glucose load. Also recorded are the findings of some in-vitro metabolic studies on adipose tissue biopsy specimens and some studies of diabetic lipaemia and its basis.

Hyperglycaemia

It may seem simple to define the normal levels of blood sugar both fasting and after glucose from a group of chosen normals, but as with hypertension symptomless hyperglycaemia is often found in older age groups, and especially in some populations. Should our standards for diagnosing diabetics be dependent on age and population as some suggest? For example, among the Pima Indians Bennett *et al.*[1] found that conventionally defined hyperglycaemia is as common in the older decades as normal levels.[2]

From Wellborn's population survey,[3] if we measure both blood sugar and insulin levels one hour after 50 g of oral glucose we find enough borderline and higher blood sugar values for us to assess when insulin secretion is apparently failing. This can be defined by a plot of the mean values at 60 minutes for serum insulin against those of concurrent blood sugar (Fig. 1). For blood sugars up to 160-180 mg/100 ml the serum insulin rises with blood sugar but thereafter it falls, suggesting that this is the level above which insulin lack or diabetes is implied. Similar data are plotted in Fig. 2 for 45 chosen healthy non-obese normal London adults and 120 subjects presenting at the diabetic clinic with mild and non-ketotic diabetes mellitus as yet untreated with insulin. It is evident that these two groups confirm the population survey finding that the blood sugar range 160-180 mg/100 ml one hour after 50 g of oral glucose separates

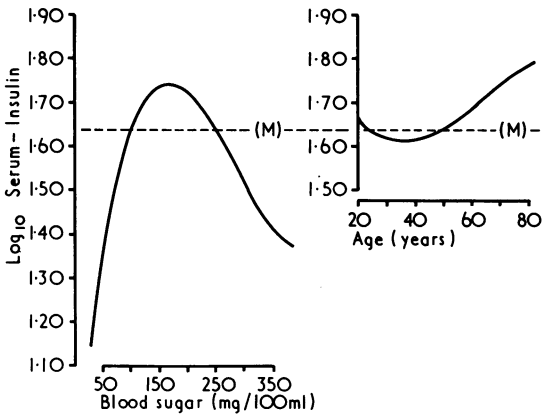

FIG. 1—Data from normal population survey[3] showing correlation one hour after 50 g of oral glucose between serum insulin and simultaneous blood sugar and age (corrected for blood sugar). M = Mean of whole group.

*From the H. D. Rolleston lecture delivered at the Royal College of Physicians on 2 February 1972.

Endocrine Unit, Department of Medicine, Royal Postgraduate Medical School, London W12 0HS
RUSSELL FRASER, M.D., F.R.C.P., Professor of Medicine

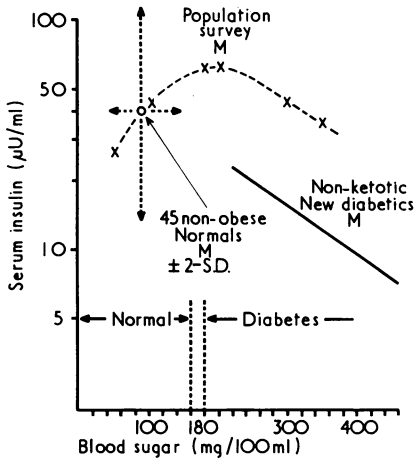

FIG. 2—Correlation between 60 min serum insulin (log) and 60 min blood sugar after 50 g oral glucose in a normal population survey (1,200 subjects)[3] and 120 new mild or non-ketotic diabetics compared against range seen in 45 chosen non-obese normal adults. M = Mean.

normals from those with a failing insulin response or diabetes. The normals fall to the left of the division and fit on the initial section of the survey curve where a rising blood sugar means also rising insulin levels. But above this blood sugar level, as in the population survey, the clinic diabetics show declining insulin levels as the blood sugar rises further. Presumably, therefore, blood sugar values above this division reach these levels because of a defective insulin response and so imply diabetes mellitus.

Thus a blood sugar value above 180 mg/100 ml one hour after 50 g of oral glucose implies a failing insulin response or diabetes mellitus unless it can be attributed to rapid absorption and is associated with the expected correspondingly higher insulin levels.

How Best to Show Insulin Deficiency

To define the diagnostic limits of normal blood sugar we have just assumed that diabetes always implies insulin deficiency. The necropsy data of Wrenshall *et al.*[4] and much other data strongly hint that insulin deficiency is a feature of all diabetics. But how is this insulin deficiency best indexed in vivo, and is it a demonstrable feature in all diabetics? Obviously it is a deficiency of insulin action that we wish to index. For example, in states of known insulin resistance, such as obesity or acromegaly, high serum insulin levels may only reflect defective insulin action. Since apart from such secondary diabetic states an

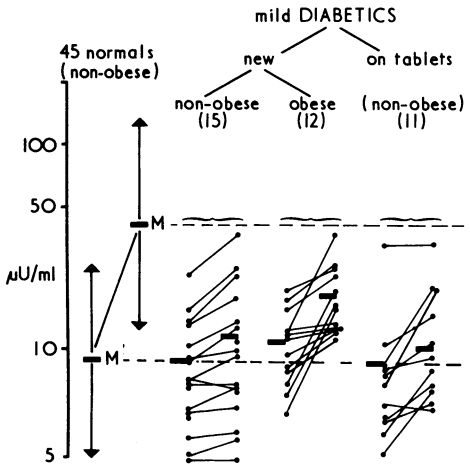

FIG. 3—Serum insulin fasting and one hour after a 50 g oral glucose tolerance test in clinic survey of mild diabetics—that is, non-ketotic diabetics with fasting blood sugar of 150-330 mg/100 ml. M = Mean

insulin deficiency is least evident in non-ketotic diabetes of adult onset we can usefully test any index on insulin deficiency in these cases.

The insulin levels at 0 and 60 min after a 50 g oral glucose load for the chosen normals and also for the clinic's mild diabetics are shown in Fig. 3. Firstly, note the variability of normal insulin levels. At 0 or 1 hour after the glucose load, while we know the normal blood sugar varies only twofold these insulin levels vary tenfold. Hence as the diagnostic guide to deficient insulin action we should be wise to retain blood sugar rather than the circulating insulin level needed to achieve it. This variable normal insulin level must imply variable insulin sensitivity, which can be displayed by plotting log values of the insulin against the blood sugar, as in Fig. 1. From data on the non-ketotic diabetics surveyed in the clinic (Fig. 3) it is seen that while fasting insulin levels are normal the early or one-hour insulin response to the glucose is low. This early increment should be a good index of secretory reserve and also more independent of tissue insulin resistance than the absolute insulin level.

If for these same subjects we correlate this early or one-hour insulin increment—that is, the rise over the fasting level—against the fasting blood sugar as an index of the degree of diabetes we see an inverse relationship (Fig. 4). For fasting blood sugars above 150 mg/100 ml this absolute increment is

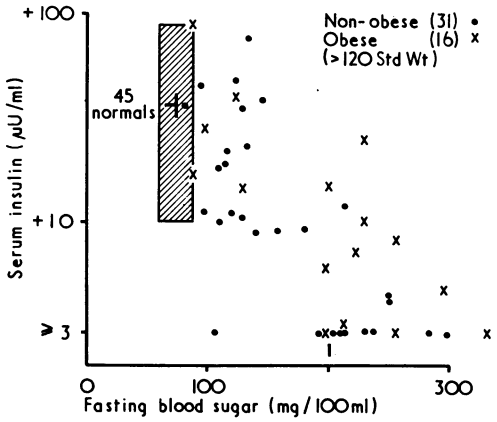

FIG. 4—Serum insulin response (increment one hour after 50 g oral glucose load over fasting value) correlated against fasting blood sugar for mild or non-ketotic subjects and contrasted with range for normal subjects. Note clearly defective increment where fasting blood sugar is above 150 mg/100 ml

clearly deficient, while those with lower fasting blood sugars also have a probably deficient increment. When we examine these same one-hour increments in insulin level in relation to the individual's fasting level of serum insulin we see that the normals generally have increments of two to three or more times their basal value, while the diabetics rarely have an increment as high as the fasting levels. Thus the ratio of the level one hour after glucose to the fasting level might prove a good index of insulin deficiency, since recognizable diabetics rarely as much as double the serum insulin level after oral glucose.

Thus these data confirm the common impression that a defective early response of insulin to a standard stimulus can characterize all but the mildest or the very obese diabetics. Since insulin deficiency is thus recognizable in most diabetics as well as their hyperglycaemia we may regard lack of insulin action as the primary core of diabetes mellitus, with hyperglycaemia as its best diagnostic index.

Complicating Compensatory Responses

We can expect to find in diabetes some features which are compensatory responses to the insulin defect and others which by impairing insulin action or insulin production have contributed to the development of the diabetic state.

(1) A common aggravating factor is obesity. It is well recognized that even non-diabetic obese subjects show resistance to insulin action and probably for this reason they have abnormally high insulin levels. The insulin resistance is evident, for example, on an intravenous insulin tolerance test.[5] Many other studies have shown high insulin levels in non-diabetic obese subjects. We have found that urinary insulin levels reflect the serum insulin levels and are relateable to body weight; and in non-diabetic obese subjects the urinary insulin excretion corrected for body weight lies in the normal range.[6] The urinary insulin levels in the obese diabetics when so corrected are subnormal basally and also in response to insulin and so again show an insulin deficiency even among these obese diabetics.[5,0]

(2) A probably similar aggravating factor is age, which in the normal population is associated with steadily increasing levels of insulin, probably to compensate an associated increasing insulin resistance. This was well shown in Welborn's population survey[3] (Fig. 1).

(3) The hyperglycaemia itself is probably a compensatory response mediated from the liver induced by insulin lack, glucagon, and other reponses. This reaction to withdrawing insulin is well shown when an animal is injected with insulin antibody which also acutely induces other aspects of the diabetic syndrome.[7]

(4) In the diabetic syndrome there is another probably compensatory or associated disorder of some recent interest which may well be important in relation to the development of diabetic microangiopathy—an overproduction of growth hormone. It has proved difficult to establish the growth hormone secretory status in diabetics, but studies by Hansen and Lundbaek,[8] of Aarhus, have recently established its levels in untreated juvenile diabetics. Frequent samplings through the 24 hours have shown clearly raised levels in these untreated juvenile diabetics, and these workers have also found that they show an excessive rise in growth hormone level in response to a standard exercise stimulus (Fig. 5). Further, they have also been able to show that

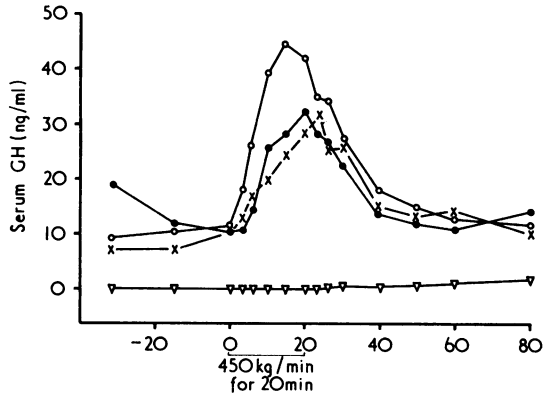

FIG. 5—Serum growth hormone (GH) response among three groups of diabetics to a standard exercise which is insufficient to alter normal serum GH levels. (From Hansen.[8]) Flat curve indicates normals. o = Untreated diabetics. ● = Diabetics treated 1-8 years. × = Diabetics treated 12-30 years.

these raised growth hormone levels and responses can be restored to the normal range by three weeks of careful diabetic regulation. Hypophysectomy may help restrain the development of diabetic retinopathy[9] by eliminating this growth hormone response to insulin lack.

Cellular Metabolic Disorder in Diabetes

The diabetic's hyperglycaemia reflects his tissues' defective uptake of glucose due to either tissue defects or lack of insulin action or both.

ADIPOCYTES

Biopsies of adipose tissue from adult-onset diabetics, as well as from juvenile diabetics, have shown a subnormal glucose uptake or evidence of insulin deficiency.[10] The main actions of insulin have been shown in vitro with incubated rat adipose cells,[11] and corresponding defects are seen when these rat cells are insulin-deficient and also in biopsy specimens from human diabetics. The smallest insulin doses have an antilipolytic effect, while the larger doses promote glucose uptake both for its transformation into glycerol and fatty acids in stored triglyceride and its oxidation and disposal and other pathways. This primacy of the antilipolytic action could be the basis of the glucose and fatty acid cycle, a mechanism postulated by Randle *et al.*[12] to explain the tendency for conditions with excessive fatty acid mobilization and oxidation to be associated with impaired glucose utilization, possibly apart from insulin availability.

Insulin can be shown to bind to cell membranes and to promote glucose entry by effects interlocked with electrolyte shift. It also reduces the cyclic adenosine monophosphate released by adenyl cyclase in the membranes in response to noradrenaline, presumably the mechanism of its antilipolytic effect. Much of the diabetic defect may arise from disorders in these membrane

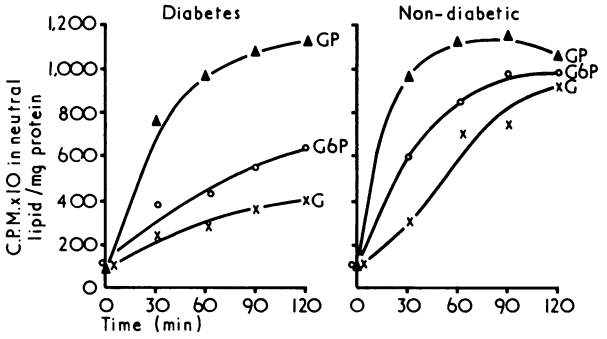

FIG. 6—In-vitro adipose tissue homogenates. Rate of incorporation of ^{14}C-palmitate into triglyceride in diabetic contrasted with non-diabetic chosen normals showing impairment in diabetics when the only source of glycerol-P (GP) is glucose (G) or other glycolytic precursor. (From Galton.[13])

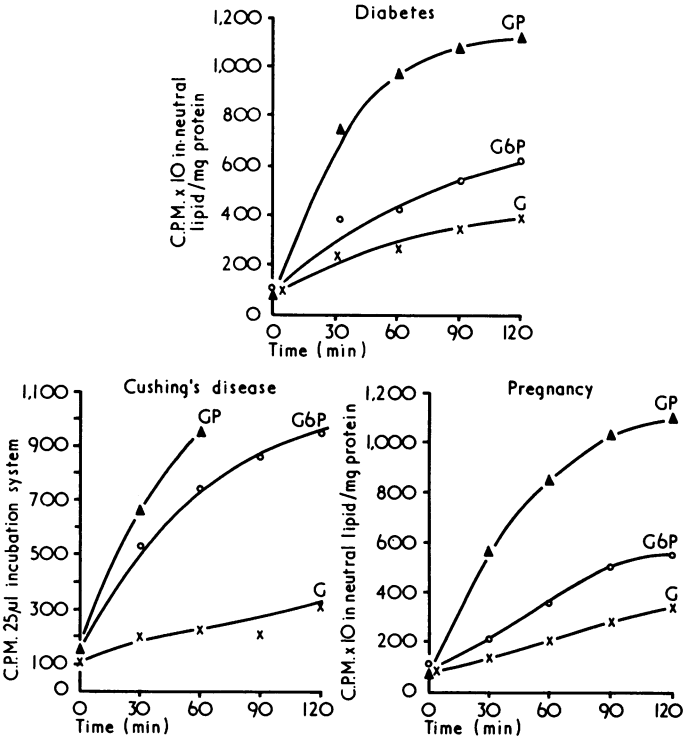

FIG. 7—In-vitro adipose tissue homogenate studies as in Fig. 6. Note similar need for glycerol-P rather than glycolytic precursors in Cushing's disease and pregnancy as well as in diabetes. (From Galton.[13])

responses but other defects are also seen in the diabetic tissue. Galton *et al.*[10] in this laboratory found that there are demonstrable enzyme defects in the homogenates from diabetic adipose cells. Fig. 6 shows that homogenates from normal cells can support triglyceride synthesis from ^{14}C-palmitate equally well whether supplied with glycerol phosphate or with glucose as a precursor for the glycerol, or alternatively that the normal homogenate can supply glycerol phosphate by glycolysis from glucose. Also, in the diabetic this triglyceride formation is seen to be defective unless the glycerol is supplied as glycerol phosphate. In other studies Galton showed that there is defective enzyme activity in the diabetic homogenate, notably defective phosphofructokinase activity.[13]

Galton has now made similar assessments on the adipose tissue of several diabetogenic states, such as obesity, pregnancy, and Cushing's syndrome—that is, states without hyperglycaemia but which may precipitate diabetes in about 25% of cases. Again these homogenates (Fig. 7) have shown a similar defect—that is, an impaired ability to supply glycerol phosphate from glucose for triglyceride formation. Thus some of the cellular metabolic disorders characteristic of diabetes may arise in states merely apt to precipitate diabetes in about 25% of subjects. Here then is a mechanism whereby insulin resistance can arise from disordered cell metabolism. There is, of course, good evidence of this insulin resistance in these states known to be liable to precipitate diabetes (in obesity, in pregnancy, in Cushing's syndrome, and in acromegaly)—for example, as produced by an intravenous insulin tolerance test. Doubtless similarly varying cell responsiveness to insulin explains some of the tenfold variations in normal serum insulin levels.

LIVER CELL DISORDER

One function of the liver is the supply of fuels to the tissues during fasting. The normal mechanism of glucose uptake into the liver is different from that in the adipose cell, being based on glucokinase and glycogen synthetase activity. But the liver glucose uptake nevertheless is also enhanced by insulin as well as by raised levels of glucose circulating through the liver. As Tulloch *et al.*[14] showed by in vitro perifusion of liver tissue, the rate at which liver tissue transforms perifused ^{14}C-glucose into fatty acid is enhanced not only by higher glucose concentrations but also by addition of insulin, the only hormone they found to produce this effect.

Abnormal liver metabolism is evident in diabetes in at least two ways—(1) the raised fasting blood sugar, which is probably maintained by increased hepatic glucose output and by increased gluconeogenesis from amino-acids released from muscles, and (2) the ketosis seen especially in severe diabetes, which probably reflects both increased free fatty acid mobilization from fat tissue and also abnormal liver metabolism due to decreased availability of glucose and insulin.

One of the striking features of obese diabetics is the responsiveness of their high fasting blood sugar to starvation. Since this change is not accompanied by any corresponding change in either glucose intolerance or insulin resistance it implies a correction of some disorder of liver metabolism. Welborn[3] performed insulin tolerance tests before and after 7-14 days of starvation in both diabetic and non-diabetic obese subjects. He found that after fasting the non-diabetics there was a slight fall in fasting blood sugar but no discernible change in insulin sensitivity, while the fasting blood sugar halved in diabetic patients. We have also compared the glucose tolerance tests done before and after similar fasts on similar groups of patients.[15] Again with the diabetics the striking change after starvation was the fall of the fasting blood sugar (Fig. 8), while after oral glucose neither the rise in glucose level nor the insulin response was very different, both being still diabetic in comparison with the non-diabetic obese responses. Presumably on starvation, therefore, the diabetic liver reduces its previously excessive fasting gluconeogenesis and hepatic glucose output, and these diabetic disorders are evidently not dependent either on glucose intolerance or on peripheral insulin insensitivity.

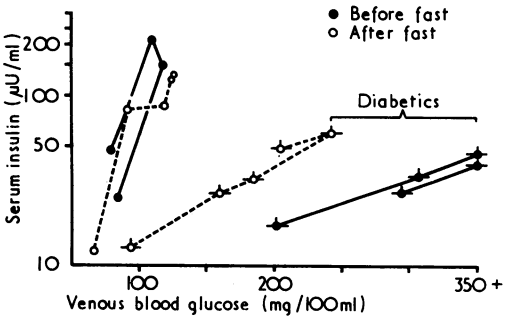

FIG. 8—Mean serum insulin versus blood glucose insulin during a glucose tolerance test both before and after a two-week fast in 7 obese non-diabetic subjects contrasted with 7 diabetic subjects.

Tendency to Lipaemia and Ketosis

KETOSIS

Probably all uncontrolled diabetics show raised free fatty acid levels,[16] doubtless from lack of antilipolytic effect of insulin on adipose tissue. Free fatty acids arriving at the liver provide the precursors of ketone bodies, and lack of insulin in the liver cell promotes this transformation. In severe juvenile diabetics with severe insulin lack the associated urinary ketosis with its basis in the liver is familiar. But in surveys at this clinic the more

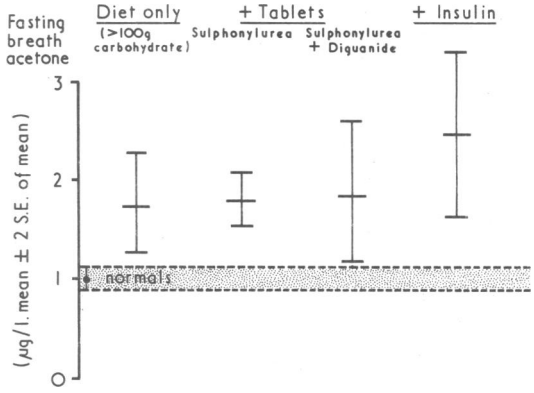

FIG. 9—Morning fasting breath acetone levels in controlled diabetics (fasting blood sugar 120-200 mg/100 ml). Note raised levels even in mildest group. (From Tassopoulos *et al.*[17])

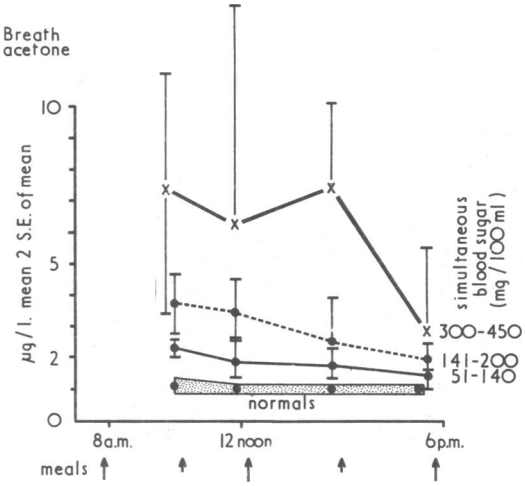

FIG. 10—Breath acetone measurements before meals in insulin-controlled diabetics. (From Tassopoulos *et al.*[17])

sensitive measure of breath acetone[17] showed on morning fasting samples a lower degree of ketosis also in all mild diabetics (Fig. 9) even when the diabetes was reasonably well controlled by various means—that is, with the fasting blood sugar between 120 and 200 mg/100 ml. This ketosis is also evident on breath acetone measurements throughout the day, as shown by the pre-meal samplings in Fig. 10—more abnormal as expected according to the severity of the simultaneous hyperglycaemia but gradually lessening through the day even for the same blood sugars; a good argument for twice-daily insulin.[18]

LIPAEMIA

Hypertriglyceridaemia is also a universal feature of severe uncontrolled ketotic diabetes.[19 20] It is also a feature found commonly in untreated diabetic children[18 21] and is found in about half of our untreated adult mild diabetics—that is, half of those non-ketotic on urine testing. But why in only half?

Among our non-ketotic or mild diabetics we find that lipaemia is especially common among those with higher blood sugars and least insulin deficiency (Fig. 11). This association with higher blood sugar and minimal insulin lack suggests that in overfed subjects with some but minimal insulin lack there is overproduction of triglycerides by the liver. As noted above our perifusion studies showed that the liver's formation of triglyceride was increased by the addition of either glucose or insulin to the perifusate. When by appropriate antidiabetic treatment the blood sugar of these mild diabetics and also that of the insulin-dependent diabetics is controlled this triglyceride level is usually restored to the normal range, suggesting that hyperglycaemia is a major factor.

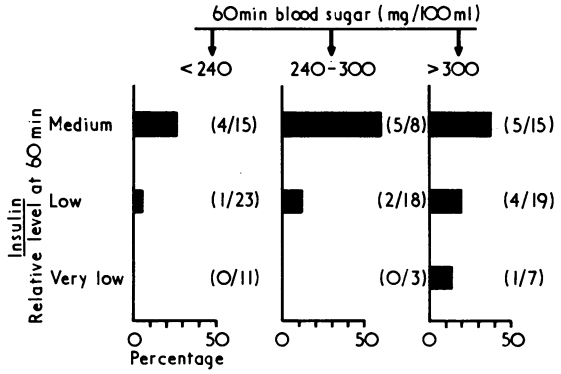

FIG. 11—Percentage of subjects with high triglycerides (over 150 mg/100 ml) among 119 mild and non-ketotic diabetics (48 untreated, 71 controlled on diet with or without tabs.) subdivided first according to 60 min blood sugar (oral glucose tolerance test) and then by relative insulin level at 60 min. Note few raised triglycerides with low insulin unless blood sugar high. (From Fraser and Rabinowitz.[5])

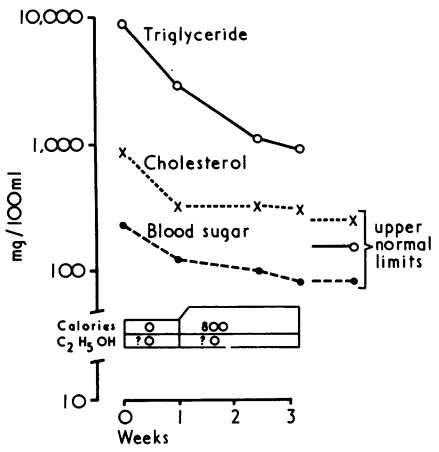

FIG. 12—Lipid and blood sugar responses in a newly diagnosed severely lipaemic diabetic man aged 28 on instituting caloric and alcohol restriction.

Studies of our patients using intravenous fat tolerance tests[16] have suggested that impaired triglyceride removal was also an important factor in this lipaemia of diabetes. Other studies suggest that this diabetic triglyceride removal defect may arise from an impaired lipoprotein lipase release in adipose tissue in states of hyperglycaemia or insulin deficiency or both.[22] Occasionally in some mild diabetics the lipaemia is extreme, and we then have to seek an associated disorder as well as the diabetes, which sometimes proves to be chronic alcoholism with its tendency to hepatic overproduction of triglycerides. Fig. 12 shows a rapid fall in lipids as well as in blood sugar when both the calories and the alcohol intake of a young patient were reduced.

Other Metabolic Disorders

Recent pathological studies have established that diabetic neuropathy is associated with a segmental type of demyelination[23 24] and also with histological abnormalities in Schwann cells, in the myelin, and in the axons, which suggest metabolic disorders in all three sites. And as a start diabetic nerves as well as lenses have been shown by Gabbay[25] to accumulate sorbitol and also to have abnormal levels of the enzymes producing and oxidizing this polyol, as has been confirmed by others.[26]

Regarding the angiopathy we also have only hints. Again histopathologists such as Norman Ashton have observed many microvascular lesions pointing to a metabolic disorder affecting particularly the capillary endothelial cells and associated with an overproduction of abnormal basement membrane. Spiro[27] showed abnormalities in the basement membrane polysaccharides of diabetic glomeruli and also in the enzymes related to their formation.

In seeking other clues to the metabolic disorders behind this retinopathy, from a survey of our patients we have compared the blood levels of glucose, insulin, and lipid seen in the retinopathy patients with those seen in other groups of diabetics. This as yet incomplete study hints that the insulin deficiency but not the other disorders may be more severe in the retinopathy subjects.

Conclusion

Diabetes is a disorder best hall-marked by its persistent hyperglycaemia but probably always involving lack of insulin action. Insulin deficiency is best shown by the proportionately small insulin increment after a standard stimulus such as at one hour after oral glucose. This deficiency also induces some complicating responses such as increased hepatic glucose output and hypersecretion of growth hormone. Further, diabetic cells show disordered functions of the cell membrane and of cell enzymes, probably not all dependent on insulin deficiency. The diabetic's ketosis and lipaemia are usually controllable by measures which control the blood sugar, but the more chronic disorders behind the neuropathy and the angiopathy await further definition.

I am indebted to many of my colleagues who obtained most of the data on which this review is based, in particular to Dr. David Galton, Dr. Clara Lowy, Dr. Brian Tulloch, Dr. T. Welborn, Dr. Barry Lewis, and Dr. Mario Mancini.

References

1 Bennett, P. H., Burch, T. A., and Miller, M., *Lancet*, 1971, 2, 125.
2 Rushforth, N. B., Bennett, P. H., Steinberg, A. G., Burch, T. A., and Miller, M., *Diabetes*, 1971, 20, 756.
3 Welborn, T. A., Ph.D. thesis, University of London, 1969.
4 Wrenshall, G. A., Bogoch, A., and Ritchie, R. C., *Diabetes*, 1952, 1, 87.
5 Fraser, T. R., and Rabinowitz, D., *Journal of Endocrinology*, 1962, 25, 299.
6 Fraser, T. R., in *Scientific Basis of Medicine. Annual Reviews*, British Postgraduate Medical Federation, p. 206. London, Athlone Press, University of London, 1968.
7 Wright, 1961. *American Journal of Medicine*, 31, 892.

[8] Hansen, A. P., *Journal of Clinical Investigation*, 1971, **50**, 1806.
[9] Panisset, A., Kohner, E. M., Cheng, H., and Fraser, T. R., *Diabetes*, 1971, **20**, 824.
[10] Galton, D. J., Wilson, J. P. D., and Kissebah, A. H., *European Journal of Clinical Investigation*, 1971, **1**, 399.
[11] Fain, J. N., Kovacev, V. P., and Scow, R. O., *Endocrinology*, 1966, **78**, 773.
[12] Randle, P. J., Garland, P. B., Hales, C. N., and Newsholme, E. A., *Lancet*, 1963, **1**, 785.
[13] Galton, D. J., *The Human Adipose Cell: A Model for Errors in Metabolic Regulation*. London, Butterworths, 1971.
[14] Tulloch, B. R., Dyal, K., and Fraser, T. R., *Journal of Endocrinology*, 1970, **48**, XLVIII.
[15] Jackson, R. A., *et al.*, *Diabetes*, 1971, **20**, 214.
[16] Lewis, B., Mancini, M., Mattock. M., Chait, A., and Fraser, T. R., *Lancet*, 1971, **2**, 947.
[17] Tassopoulos, C. N., Barnet, D., and Fraser, R., *Lancet*, 1969, **1**, 1282.
[18] Sterky, G. C. G., Persson, B. E. H., and Larsson, Y. A. A., *Diabetologia*, 1966, **2**, 14.
[19] Harris, L. V., Albink, M. J., Van Eck, W. F., Man, E. B., and Peters, J. P., *Metabolism*, 1953, **2**, 120.
[20] Tuller, E. F., Mann, G. V., Scherkenleib, F., Rochrig, C. B., and Root, H. F., *Diabetes*, 1954, **3**, 279.
[21] Lloyd, J. K., Fosbrooke, A. S., Wolff, O. H., and Salt, H. B., *Lancet*, 1962, **1**, 1329.
[22] Baghdade, S., Porte, D., and Bierman, E., *Diabetes*, 1968, **17**, 127.
[23] Thomas, P. K., and Lascelles, R. G., *Quarterly Journal of Medicine*, 1966, **35**, 489.
[24] Chopra, J. S., Hurwitz, L. J., and Montgomery, D. A. D., *Brain*, 1969, **92**, 391.
[25] Gabbay, K. H., *Diabetes*, 1968, **17**, 239.
[26] Ward, J. D., Barnes, C. G., Fisher, D. J., Jessop, J. D., and Baker, R. W. R., *Lancet*, 1971, **1**, 428.
[27] Spiro, R. G., *New England Journal of Medicine*, 1963, **269**, 566, 616.
[28] Fraser, T. R., *Proceedings of the 4th Congress of the International Diabetes Federation, Stockholm*, 1967, p. 206.

Anaesthesia in Sickle-cell States: A Plea for Simplicity

K. A. ODURO, J. F. SEARLE

British Medical Journal, 1972, 4, 596–598

Summary

505 patients with various haemoglobinopathies were given a general anaesthetic between January 1970 and February 1972. One patient with haemoglobin SC disease and one patient with sickle-cell trait (HbAS) died postoperatively. Four other patients who were sickling positive, but whose genotypes were unknown, died, one from sickle-cell crisis precipitated by haemorrhage.

A simple anaesthetic technique together with good postoperative care can provide safe general anaesthesia for patients with sickle-cell states. A plea is made for simplicity in the anaesthetic management of these patients.

Introduction

Interest in the management of patients with sickle-cell conditions in the steady state, in crisis, and during anaesthesia has increased during the past seven years. It is generally accepted that general anaesthesia is hazardous in these patients, especially those with genotypes SS and SC. There have been reports from West Africa,[1 2] the West Indies,[3] and America[4] on the anaesthetic management of patients with haemoglobin S, although the total number of cases reported is relatively small. This paper concerns 505 patients with various haemoglobinopathies who were anaesthetized at Korle Bu Teaching Hospital, Accra, during the 26-month period January 1970 to February 1972.

Anaesthetic Technique

The anaesthetic management of patients with haemoglobin SS, SC, and S-beta-thalassaemia may be summarized as simple safe techniques, with adequate oxygenation, ventilation, maintenance of the circulating volume, and efficient postoperative care. Infections, malaria, helminthic infestations, and malnutrition are vigorously treated before operation. In elective patients folic acid is also given. If the haemoglobin concentration is less than 5 g/100 ml one or two units of blood are given about three days before operation.

Premedication is usually effected with atropine and promethazine. Promethazine provides sedation without respiratory depression. Respiratory depressant drugs are avoided. Preinduction oxygenation is given for at least five minutes. Induction is achieved with a sleep dose of thiopentone (except in very ill patients or children, where diethyl ether or halothane are used). If intubation is necessary this is performed after paralysis with a short-acting muscle relaxant. Breath-holding, laryngeal spasm, and struggling must be avoided during induction.

Anaesthesia is maintained with halothane or trichloroethylene and 50% nitrous oxide and oxygen. The patient is allowed to breathe spontaneously or ventilation is controlled, depending on the surgical procedure.

Adequate blood replacement is essential. In an earlier report[5] failure to maintain an adequate blood volume caused the death of two patients. This did not occur in the present series.

Early recovery of consciousness and of upper respiratory tract reflexes is important. Postoperatively oxygen is given through nasal catheters for 12 to 24 hours. The dangers of hypoxaemia in the postoperative period are well established,[6] and in patients with sickle-cell disease its importance cannot be over emphasized. Blood gas studies[7] in patients with abnormal haemoglobin syndromes showed that the arterial oxygen tension was significantly lower than in those with normal haemoglobin. This serves to emphasize the need for adequate oxygenation before, during, and after anaesthesia.

Present Study

During January 1970 to February 1972 inclusive 505 patients with haemoglobinopathies had a general anaesthetic. The distribution of the haemoglobinopathies is shown in Table I.

TABLE I—*Distribution of Genotypes among the 505 Patients*

	No. of Patients		No. of Patients
SS	17	SF high gene	1
SC	21	AS	257
S-beta-thalassaemia	2	AC	26
CC	1	Sickling positive, genotype unknown	180

Department of Anaesthesia, University of Ghana Medical School, P.O. Box 4236, Accra, Ghana
K. A. ODURO, M.B., F.F.A. R.C.S., Associate Professor
J. F. SEARLE, M.B., F.F.A. R.C.S., Senior Registrar