Current Practice

MEDICINE IN THE TROPICS

Diabetes in the Tropics

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Diabetes is no longer a rare disease syndrome in the tropics, and in many parts it is being diagnosed with increasing frequency. Improved medical supervision, a greater awareness of the disease among the general population, and the improved life expectancy account for the increasing number of patients with recognized diabetes. These changes have occurred to a greater extent and at a faster rate in the towns and cities, and consequently the upward trend in the incidence of diabetes is more striking in hospital practice in the urban areas than in the rural districts. Other factors, such as change in dietary habits, may also play a part, but it is more difficult to establish the role of these as a cause of the increased incidence.

Prevalence

Few prevalence surveys have been done among the general population in tropical areas, but the limited information suggests that in most areas a prevalence rate of 0.2–1% of the general adult population may be expected. This is lower than the rates recorded for most European countries; but the figures are not comparable until a correction has been made for the difference in the age distribution of the populations concerned. After making such a correction the prevalence rate of diabetes in Jamaica was found to be very similar to that in Britain, but lower than the comparable figure for the United States of America.[1]

Diagnosis

In many urban areas in the tropics the "sugar disease" is now well known among the general population, and about 20% of diabetic patients reporting for the first time to the Korle Bu Hospital in Accra had already confirmed their suspicion of diabetes by tasting their urine. Occasionally diabetes is discovered in patients with septic skin lesions, tuberculosis, pruritus vulvae, paraesthesiae, or gangrene of a toe who were not aware that they had diabetes. This emphasizes the need for routine urine-testing as a part of the clinical examination of every patient, and the newer glucose-oxidase impregnated paper strips (Clinistix) offer a quick and reliable screening procedure for the purpose. These strips retain their potency, if their container is continuously capped, for the stated shelf life of two years. However, after the bottle is opened for clinical use, their sensitivity diminishes rapidly after two to three months under tropical conditions. It must also be remembered that patients receiving therapeutic doses of ascorbic acid may return false negative tests to the glucose-oxidase impregnated strips.

Clinitest tablets and the Benedict's test may be reserved as semi-quantitative tests useful for the known diabetic or for patients with a positive Clinistix test. Clinitest tablets are highly hygroscopic and deteriorate quickly if left uncovered; patients who are careless about capping the bottle may thus produce misleading results from the use of insensitive tablets. For such patients tablets packaged singly in strips of foil are available but are more expensive.

In over 90% of the patients the diagnosis of diabetes is easy because polyuria and thirst are prominent symptoms. Most of these patients have additional complaints of loss of weight, failing vision, or weakness. In male patients the complaint of "weakness" should arouse the suspicion of impotence, which is a common and sometimes early symptom of diabetes. A hurried or impatient interpreter may fail to grasp the full meaning of the patient's "weakness" or the patient himself may deliberately give the vague impression of weakness to the nurse, hopefully expecting that the doctor would glean its hidden meaning. Unless this possibility is appreciated the diagnosis of diabetes is likely to be delayed unnecessarily, for the patient may not return to the clinic until he has tried and failed to cure his impotence elsewhere.

Many diabetic patients even on first attendance have heavy glycosuria, and their fasting blood sugar at the time of diagnosis is invariably over 200 mg./100 ml. A glucose tolerance (provocative) test is not necessary for the diagnosis of these cases, though it may be useful at a later stage, if indicated, to determine the renal leak-point and hence the extent to which glycosuria can be relied upon to reflect the level of the blood sugar as a guide to the adequacy of diabetic control.

When a glucose tolerance test is necessary for a definite diagnosis, the conventionally accepted criteria for non-tropical populations have been found in practice to be reliable. The usual precaution of ensuring a good carbohydrate intake during the three or four days preceding the test is equally applicable, and it is essential to know the type of blood samples taken (whether capillary or venous) and the method of estimation employed (whether for "true" glucose or for total reducing substances). The normal upper limit of capillary blood sugar, estimated as "true" glucose "fasting," is accepted as 120 mg./100 ml.; after the oral administration of 50 g. glucose, the peak of the blood sugar curve should not exceed 180 mg./100 ml. and at two hours the blood sugar should be back to the pre-test level.

Blood sugar levels in some African communities have been shown to be significantly lower than those of Europeans living in the same geographical area, and it is also known that certain liver and gastrointestinal diseases can modify the shape of the oral glucose tolerance curve; but in general these factors have little application to the diagnosis of overt diabetes in the individual patient who attends a clinic in the tropics.

Clinical Picture

Diabetic Types.—The concept of the natural history of diabetes, through the stages of potential diabetes, latent

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diabetes, asymptomatic diabetes, and overt or clinical diabetes is applicable to the diabetic syndrome wherever it occurs; but the evolution of the disease may take a variety of courses, and it is possible to recognize certain patterns of presentation. The two well-known types of (*a*) "juvenile" insulin deficient diabetes and (*b*) "maturity onset" lipoplethoric, insulin non-dependent diabetes[2] occur in the tropics also; but experience has shown that it is not always easy to assign diabetic patients neatly into one or other of these classical groups.

In certain parts of the tropics there are young and often underweight diabetic patients whose clinical behaviour to insulin treatment suggests that they are not insulin deficient; occasionally, also, certain lipoplethoric females develop diabetes in their 20s and yet show the characteristics of "maturity onset" diabetes. Furthermore, in some patients the evolution of the disease in time occasionally necessitates a revision of the initial categorization of their diabetes. For these reasons the classification simply into Type 1 and Type 2 diabetes[3] as follows is preferable.

Type 1 Diabetes.—Patients in this category are insulin dependent and require it to remain healthy. Without insulin they quickly become ketotic and succumb in diabetic coma. At the same time they are sensitive to the effects of insulin and are apt to develop hypoglycaemic reactions during treatment. Type 1 patients are usually young and underweight.

Type 2 Diabetes.—This type of diabetes is typically "mild" and shows little tendency to ketosis. The patients are often overweight; they are not insulin dependent, except during periods of stress, and they may be adequately controlled with diet and oral hypoglycaemic agents. Type 2 diabetics are usually over 40 years of age and are relatively insensitive to the effect of injected insulin.

In addition to these two main types, several sub-types have been described to give expression to observed regional variations in Ceylon,[4] Jamaica,[3] Indonesia,[5] Kampala,[6] Natal Indians,[7] and in East Pakistan.[8] It is probable that these sub-types merely reflect aspects of the normal variability of the diabetes syndrome or stages in its evolution that are conditioned by the degree of effectiveness of treatment or by a combination of unknown extraneous factors, rather than any inherent variability in the syndrome itself.

The best known sub-type is Type J diabetes, which was described in Jamaica[3] to embrace young diabetics who are not insulin dependent, do not tend to become ketotic without it, and are relatively resistant to its effects.

Frequency of Diabetic Types.—The usual experience in the tropics is that over 85% of diabetics are of the Type 2 variety, 10–15% are Type 1, and the remaining "residue" is made up of Type J and other variants.

Other Forms of Diabetes

Pancreatic Lithiasis.—In Europe and America diabetes associated with pancreatic lithiasis is occasionally found in older male patients who give a history of alcoholism and have steatorrhoea. This syndrome is also seen in the tropics, but in addition there is a group of young diabetics in whom pancreatic calcification may be found if looked for. These patients are often underweight and require insulin (up to 80 u. per day); over half of them have enlargement of the parotid glands (Figs. 1 and 2). Alcoholism is not a factor, but a past history of recurrent abdominal pain suggesting pancreatitis may be obtained. Estimation of stool fat content often reveals a defect in exocrine pancreatic function, but frank steatorrhoea is generally not a troublesome feature of this type of diabetes. In Ibadan Kinnear *et al.*[9] found pancreatic lithiasis in 12.6% of 325 consecutive Nigerian diabetics.

"Temporary Diabetes."—The transient lowering of carbohydrate tolerance in susceptible persons during periods of stress is well known, but practitioners in the tropics must keep the concept of temporary diabetes in mind for yet another reason. In many parts, potent herbal concoctions are taken as medicine or given as enemata, and it is possible that transient or temporary diabetes may be related to abuses of this sort. Unless this possibility is kept in mind the rare chance of discovering the cause of a potentially preventable type of diabetes might be missed.

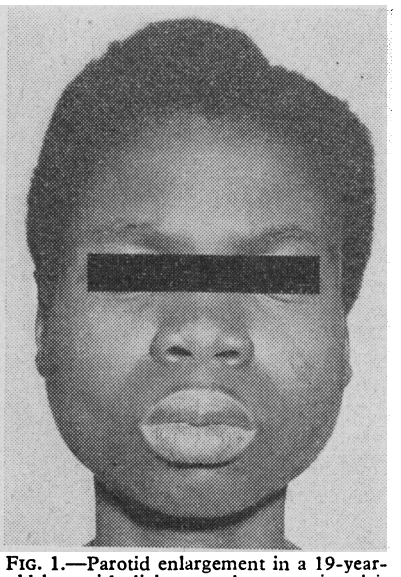

FIG. 1.—Parotid enlargement in a 19-year-old boy with diabetes and pancreatic calcification (Fig. 2).

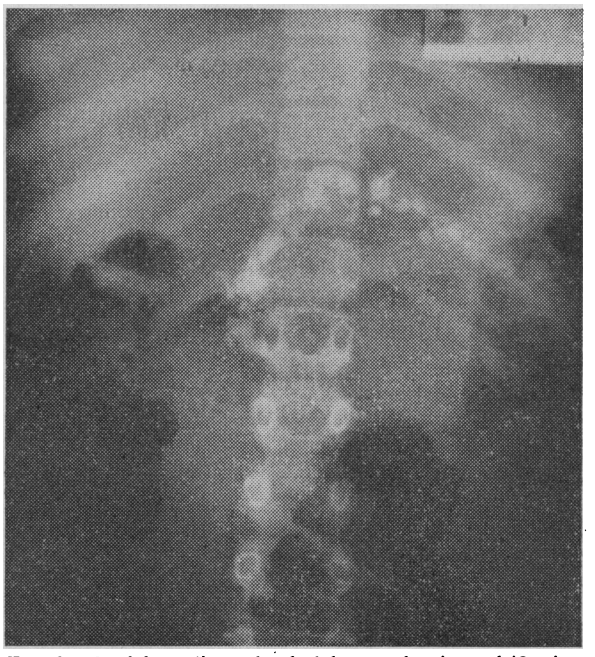

FIG. 2.—Straight radiograph of abdomen showing calcification of the pancreas.

Rare Forms of Diabetes.—Diabetes associated with various endocrinopathies such as Cushing's syndrome and acromegaly occurs, but is uncommon. Haemochromatosis is also rarely encountered, and in areas where haemosiderosis is common the combination of siderosis and diabetes, in the absence of a familial history, may be indistinguishable from idiopathic haemochromatosis.

Age and Sex.—The majority of diabetics in the tropics, as elsewhere, are over 40 years of age. Figures for Accra[10] show that only 33% of the males and 27% of the females are below that age. In the older diabetics there are almost twice as many

females as males, while below the age of 35 years there is hardly any difference between the sexes. Various reports have indicated that childhood diabetes is very uncommon in the tropics.

Complications

All the known complications of diabetes are encountered in the tropics also, but their recorded incidence is very variable. Hypertension, neuropathy, cataract, infections, and retinopathy are the more frequently seen complications, but peripheral vascular disease and gangrene and nephropathy (Kimmelstiel-Wilson syndrome) also occur.

Myocardial infarction resulting from ischaemic heart disease is distinctly uncommon among many tropical populations, but diabetes seems to play the expected role, and at least in the case of women it appears to be an important predisposing factor: only two cases of myocardial infarction in Ghanaian women have been treated in Accra during a five-year period—they were both diabetics aged 50 and 65 years respectively. Experience in the tropics as elsewhere suggests that the incidence of chronic complications increases with the duration of the diabetes, but it is not unusual to find that complications are present at the time that the diagnosis is first made.

The question of whether irregular or poor biochemical control of the diabetes increases the chances of the development of complications is still controversial, and it is possible that studies in the tropics where many patients are only marginally controlled may in future throw some light on this problem.

Treatment

The minimum objective of treatment in every case of diabetes is to relieve and prevent symptoms such as polyuria, thirst, or pruritus, and to prevent keto-acidosis, by means of a regimen of management which does not interfere unduly with the psychological, social, and occupational adjustment of the patient to his illness. In the majority of diabetics treated in the tropics this minimum objective is all that can be expected and it is fortunate that in many of these patients fairly simple measures are often sufficient to achieve it and at the same time maintain near normal fasting blood sugars and minimal glycosuria.

The management of the average case of diabetes in the tropics is not difficult and even in remote areas it is possible for the practitioner to manage the majority of his patients adequately without special knowledge of biochemistry or endocrinology. For the purpose of treatment, the categorization of patients into the diabetic types described earlier has little practical application and a better guide to therapy is to consider the extent of the biochemical abnormality and to group patients as follows:

(1) Patients with transient or stress diabetes which becomes manifest during infections, steroid therapy, pregnancy, surgery, chlorothiazide therapy, spironolactone therapy, or starvation.

(2) Patients with glucose tolerance diabetes in whom the fasting blood sugar is normal but the two-hour post-prandial blood sugar or glucose tolerance tests are abnormal.

(3) Diabetes mellitus with persistently elevated fasting blood sugar—that is, overt or clinical diabetes.

(4) Diabetes mellitus with ketosis.

(5) Diabetic precoma or keto-acidosis.

All patients require some form of dietary treatment, and this may be all that is necessary for patients in groups 1 and 2; those in group 3 usually require oral hypoglycaemic agents or insulin as well; group 4 patients need insulin and diet, and patients with keto-acidosis (group 5) require emergency treatment with soluble insulin and intravenous fluids. This classification only provides a guide to therapy, and appropriate changes in management must be considered when a patient moves from one category to another during the course of his illness or as a result of treatment.

The role of diet, oral hypoglycaemia agents, and insulin in the management of diabetes in the tropics follows the same broad principles that are already very well known, but local factors often alter the relative emphasis that must be placed on each. In a recent series, 2% of patients were receiving dietary treatment only, 65% diet and oral therapy, and 33% diet and insulin.[10]

Diet

Classical Type 2 diabetes is ideally best treated with dietary restriction and weight reduction, but in practice, particularly in the tropics, successful treatment is more likely if a sulphonylurea is prescribed with dietary restriction right from the start. In this way symptoms are more quickly relieved and it is then easier to obtain the patient's co-operation in other aspects of his management. At a later date it is possible in a small proportion of patients (about 2%) to withdraw the tablets and still maintain adequate control with diet only. Many less sophisticated patients are culturally well acquainted with the prohibition of certain foods as an adjunct to the treatment of disease, and they not only accept dietary restriction but also expect it. Unfortunately, the poor economic and educational background of such patients does not permit a dietary prescription along strictly orthodox lines. In many cases it is enough to prohibit sugar and all sugary foods completely and to advise a curtailment of starchy foods to half the amount of the patient's normal intake. A knowledge of the local staple diets helps to make these instructions more meaningful to the patient. Lean meat, fish, and vegetables are permitted without restriction. This form of simple, "relaxed," dietary restriction has proved satisfactory in conjunction with sulphonylureas for the majority of Type 2 diabetics. Previous attempts at a more "rigid" control tended to increase the proportion of defaulters at the clinic, and furthermore it was doubtful whether patients adhered strictly to the more rigid instructions.

Oral Hypoglycaemic Agents

The sulphonylureas have simplified considerably the management of diabetes and are particularly useful under the conditions now prevailing in many tropical areas. The usual criteria—mild, Type 2 diabetes without ketosis and of recent onset in an obese middle-aged patient—provide a useful guide and a reliable method of selection of patients for oral therapy. However, in the tropics the advantages of oral therapy are so overwhelming that in the absence of significant ketonuria or complicating infection it is permissible to accept the risk of some delay and to try the effect of sulphonylurea for two or three weeks in all patients except the young and obviously Type 1 insulin deficient diabetic.

Some patients initially fail to respond to sulphonylurea, but if their diabetes is then controlled with insulin it is occasionally possible to withdraw the insulin and to maintain control with the same or another type of hypoglycaemic agent.

Tolbutamide and chlorpropamide are both effective and safe. The following simple scheme using tolbutamide has proved suitable for outpatients and is particularly acceptable to those who have to travel long distances to reach a clinic. The patient is instructed to take tolbutamide 1 g. (2 tablets) t.i.d. for three days and then 0.5 g. t.i.d. thereafter and to report back to the clinic in a week. He is also given the simple dietary instruction mentioned earlier. The fasting blood sugar is estimated at the beginning of treatment and again at the second visit, and the urine is tested on each occasion for sugar and acetone. If the symptoms are relieved and the blood sugar and urine tests are satisfactory the dose is maintained; if not,

stricter dietary instructions are given and the dose of tolbutamide is increased from the 1.5 g. daily to 2–3 g. daily in divided doses. After two further weekly visits on the maximum dose oral therapy may be abandoned if still unsuccessful; it may also be abandoned earlier if significant ketonuria is found at the weekly visit.

Chlorpropamide in a single daily dose of 250 mg. (max. 500 mg.) is also efficacious, and is preferred by some. It is said to have a slightly higher incidence of side-effects.

Secondary failure to oral hypoglycaemic agents sometimes occurs, especially when patients who were previously well controlled begin to take liberties with their diet; conversely diabetics on minimal doses of oral hypoglycaemic agents who stick to their diet should occasionally be given a "therapeutic holiday" to establish whether or not diet alone is adequate to control the diabetes.

Insulin Therapy

Insulin is mandatory for all patients in groups 4 and 5 (i.e., patients with ketosis or keto-acidosis) irrespective of the type of diabetes or the nature of the previous therapy. It is also indicated in young, underweight diabetics with severe disease. The daily requirement of long-acting insulin at balance is usually between 32 and 60 u., and treatment can safely be started with 16–24 u. daily for an adult. Most patients in the tropics have to attend a special clinic to receive their daily injections, and for many of them this means several miles of tedious and sometimes expensive travelling. Under these circumstances control of the diabetes is likely to become irregular and haphazard, and in a few patients is reduced to periodic admissions to hospital for the control of symptoms and the treatment of ketosis or other complications. Although many patients can be taught to inject themselves, some, particularly women patients, do not wish to do so. Naturally, those who inject themselves take a greater interest in their management and as a group they maintain better control than the general clinic patients. However, even those who take their injections at home still need to make fairly frequent excursions to the hospital for their supplies of insulin; they can be given only a limited quantity at a time, because they cannot store it in a "cool place," and a larger quantity may deteriorate before it is used up.

Protamine zinc insulin (P.Z.I.) and mixtures of it and soluble insulin are still widely used, but the newer insulin zinc suspensions (Lente) are also available. The choice of insulin is often determined mainly by the availability as well as by the extent to which the continuity of supply can be assured.

Diabetic Keto-acidosis

Diabetic coma is not a common emergency in the tropics, and for that reason the unwary are likely to miss it in its early stages; the inexperienced practitioner is also inclined to expect a semi-comatose or comatose patient before "diabetic coma" comes to mind, and all too often it is only the result of the urine test that compels him to consider diabetes in the differential diagnosis.

The proper management of diabetic coma requires reliable laboratory support, and it is usually recommended that as soon as a firm diagnosis has been made the patient should be given 60–100 u. of soluble insulin (a third of the dose intravenously in a shocked patient) and transferred to a centre where such support is available. In the tropics this is not always possible, and if transport is likely to be delayed for more than four hours a district hospital should undertake the following procedures after the initial dose of insulin has been given:

Fluid Replacement.—In the first phase of treatment normal saline is given intravenously: the first litre is given over 30 minutes; the second over an hour and the third over two hours. Alkali therapy, though helpful, is not essential, but, if available, a litre of M/6 sodium lactate may be given after the first litre of saline. If insulin therapy has been adequate during this period ketonaemia (see below) will begin to fall by four to six hours and will usher in the second phase of treatment: glucose-saline may now be given as 4% glucose in one-fifth normal saline—one litre every six hours—until the patient is able to swallow.

Potassium chloride or citrate is best given by mouth or stomach tube 2 g. four-hourly for five doses during the recovery phase when urinary output is established. It is risky to administer potassium intravenously under circumstances where non-medical staff are permitted to keep the drip going, because attempts to run through the infusion fluid rapidly, to check whether it is going into the tissues, or for any other reason could produce a dangerous or even fatal local concentration of potassium in the heart.

Insulin Administration.—After the initial dose of 60–100 u. soluble insulin, subsequent insulin requirements are determined on the basis of blood sugar estimations where available or on the degree of ketonaemia. The latter is easily assessed by means of the Acetest or nitroprusside test on plasma.

A little blood is withdrawn into an oxalated tube and allowed to stand; 2 drops of plasma are later pipetted off into each of four tubes: tube 1 contains undiluted plasma and tubes 2, 3, and 4 are diluted to 50%, 25%, and 12.5% by adding 2, 6, and 14 drops of saline respectively. The ordinary Acetest tablet test is then performed on samples of undiluted and diluted plasma. The procedure is repeated two-hourly on fresh plasma, to guide therapy: a 4+ result (dark blue) on tubes 3 or 4 indicates severe ketonaemia with blood sugar greater than 600 mg. per 100 ml. and requires at least 100 u. of soluble insulin. If there is no change in the test two hours later a further 100 u. is injected; when only undiluted plasma shows a 4+ reaction to Acetest a dose of insulin is omitted until the next test.

Urine tests for sugar are conducted at the same time, and, provided the bladder is emptied on each occasion and renal function is adequate, the results of the urine test for sugar will reflect the blood sugar and help to avoid severe hypoglycaemia.

Associated Infection.—Pulmonary, renal, or gastrointestinal infections are well known to precipitate diabetic coma; occasionally a liver abscess may be the exciting cause, particularly in the diabetic who is also an alcoholic. Other forms of infection must be looked for and treated accordingly.

Conclusion

The management of diabetes mellitus by its very nature can play an important though unobtrusive role in the health education of many tropical communities. It teaches patients the system of diagnosis based on observable evidence, which they can check for themselves; illustrates how effective therapy can be tailored for each patient's special requirements; emphasizes the need for patient co-operation and regular supervision, and introduces what is perhaps a new concept to many patients, that not all diseases are immediately and completely curable. In this way patients begin to learn to live with their chronic disabilities. In spite of the many difficult circumstances consideration of these points seems to justify the effort of trying to manage diabetes mellitus on a sound basis, even in the tropics.

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