The management of maturity-onset diabetes in general practice

C. H. STEWART-HESS, M.D., F.R.C.G.P., M.R.C.P.
Cheriton Fitzpaine, Devon

WELL over 30 years ago during those first impressionable years of general practice, I found myself waiting on a patient's doorstep with the Vicar of our Parish. He was corpulent, rotund and elderly, a Canon of the Cathedral and looked every inch of it. The household was never very brisk about answering the door and we had time to exchange a few words. During this pause, my eyes wandered over his expansive middle and then below. My gaze became rivetted on the physical sign that had been taught to me so recently in student days—white spots on boots and trousers. Diabetes!—I had not seen it before and do not believe that I have since. He followed the advice to see my partner who looked after his health, and he enhanced my reputation as a spot diagnostician with his parishioners without knowing about the give-away spots.

Five years ago experience and maturity were both on my side. It came as a rude shock therefore to be told that an elderly woman whom I had been attending for nigh on a year was much better since her new doctor, into whose area she had moved, had discovered that she suffered from diabetes for which he was treating her. She had been very obese, alcohol dependent, moderately demented and micturated anywhere in the bedsitting room that she happened to be. The linoleum floor-covering was always sticky and the smell of urine met me at the bottom of the stairs. Visits were repugnant and she had a list of the tablets which she required. To acquiesce meant brevity but bad medicine. The stickiness of the floor had obviously been due to glycosuria, and, as a physical sign, was unusual. To miss this pointer was forgiveable but to fail to test the urine certainly not so.

These two incidents are related in detail to illustrate the singular circumstances in which diagnoses are made or missed in general practice and how they contrast with the techniques of the consulting room or the hospital bed. They serve, too, as an illustration of the average detection rate of diabetes in the community. For every case revealed it is said that there is one concealed.

Detection

Detection is inseparable from management in an account of diabetes mellitus. The management in the second case was a miserable failure due to lack of detection. Emphasis will be made on the diagnosis of diabetes in this essay for good reason and where possible relevant cases will be quoted. No one would disagree with the view that its detection is primarily the responsibility of the general practitioner.

It is, therefore, surprising that with varying standards for investigating patients in this and other countries it has been shown that the number of new cases revealed on wide-scale screening surveys approximates closely to the number of cases already known. Malins (1962) quotes figures from four separate investigations in England and one in each of Canada, the United States of America, Germany and Sweden. The highest incidence figure is shared between a survey in the USA and one in England (Walker and Kerridge, 1961) at a figure of 1·4 per cent. The lowest incidence comes from another

English survey at 0·95 per cent (Redhead, 1960). About half these percentages represented cases already known and the rest were new discoveries.

The background

My urban practice grew between 1936 and 1964 to over 3,000 patients. The known diabetic population of the practice then was 15 (0·5 per cent). In 1964 I moved to a single-handed rural practice of 1,300 patients which by 1972 had risen to almost 1,600. The diabetic population is 18 (1·1 per cent).

The discrepancy between these two figures suggests an improved technique of investigating patients as opposed to a geographical difference in incidence or an increased proportion of the higher age groups. These figures reflect the lack of pressure through reduced numbers of patients and hence a better opportunity for clinical examination. Better technique and additional ancillary help would have probably raised the figure of incidence in the urban practice to approximately that of the rural practice.

Between 1936 and 1972 the treatment of diabetes has become more refined and more specialised. The notable discoveries that have been responsible for this change include the new types of insulin which cater more effectively for the varying manifestations of the disease. The time of onset, peak activity and duration of the action of insulin are the factors which have occupied the minds of pharmacologists. These improvements are continuing and, at present, research is concentrating on reducing the local reactions of insulin.

The oral hypoglycaemic agents were discovered in the 1950s and represented a great step forward. Advances in the 1960s included the investigation of insulin antagonists and the chemical assay of blood insulin which is replacing the older and less accurate bioassay (Catt, 1971). The fractions of a milligramme in which these substances are measured defeat the imagination of the practising doctor but open up new and exciting discoveries about diabetes. One recent discovery comes from the USA where oral hypoglycaemic drugs are being discredited as it is reported that they are doubling the death rate from cardiovascular complications compared with treatment by diet alone or by diet with insulin (Catt, 1971).

Considering the few diabetic patients in each general practice and the increasing complexity in tailoring the treatment best suited to every patient, it is not surprising that some general practitioners refer their patients to hospital for investigation and continuing supervision once the diagnosis has been suspected. The hospital physician might, with good reason, take the view that the few diabetics in each practice do not provide enough experience for moderate skill in dealing with the difficult problems of diabetes because the majority are in a mild form of the disease. This is a controversy that will be referred to later but what follows lends some support to both these attitudes.

The 18 cases detected and supervised in the present practice can be divided into those who are treated by diet only (five), those treated with diet and oral hypoglycaemic agents (eight), and the remainder (five) which are insulin dependent. The role of the general practitioner for those cases which are referred to as ' maturity onset ' will be described and views expressed on the essential and valuable role played by the hospital service and the specialist physician.

Definition of maturity-onset diabetes

The term ' maturity onset ' in relation to diabetes was first coined in 1939 by Himsworth. It was used to distinguish a mild form arising in adult life and usually in obese individuals who were described as insulin insensitive. They require treatment by diet with weight reduction as the aim. The insulin-dependent diabetic, as we now term it, was described as insulin sensitive.

All patients with diabetes have a relative or absolute deficiency of insulin activity but the plasma-insulin response to oral glucose differs in the various types from the normal and from each other (Catt, 1971). In all diabetics this plasma-insulin response is delayed but in true insulin deficiency it fails to reach the level of the normal response. In mild diabetes it may reach the normal level but fails to reach the resting state after three hours. In the obese diabetic the plasma response which starts at an elevated basal level of insulin rises to considerable heights and at three hours is still much above the normal resting level. Obesity, which is defined as ten per cent above the average weight for age, sex and height, appears to increase this relative insulin deficiency. Whether the insulin in these circumstances exists in a changed and less effective form or its action on receptor sites is interfered with by antagonists is not established. However, if this compensatory hyper-secretion of insulin breaks down, due to failure of the beta cells of the pancreas, then diabetes has become established.

The blood-glucose curve demonstrated by the glucose tolerance test, is a measure of this breakdown. When it occurs the resting glucose is usually higher than normal and rises further as a result the challenge of oral glucose to above the point at which the kidneys leak it into the urine; glycosuria thus occurs. Later the return of the blood sugar to basal levels is delayed.

An understanding of the insulin secretion in conjunction with the glucose tolerance test has resulted in a more useful classification of maturity-onset diabetes. ' Maturity onset ' and ' adult onset ' are synonymous terms and the former is no longer confined in the narrow sense which Himsworth originally intended.

Adult-onset diabetes can be divided into:

(1) The mild thin type which usually requires oral hypoglycaemic agents for control,

(2) The obese type which is largely controlled by diet but may require oral hypoglycaemic agents in addition,

(3) The insulin-dependent type,

(4) The latent type (described below).

Prevention of maturity-onset diabetes—prediabetes

In medical practice prevention should be included in management and this especially applies in diabetes where the dividing line between prediabetes, chemical diabetes and overt diabetes is so ill-defined. The following case history provides an illustration:

Mrs K., a famer's wife aged 52 years was accepted as a patient in 1964 and was described as a mild diabetic. Two sisters and one brother were diabetic. Glycosuria had been reported. She had had nine children, the weights at birth rising from 2·70 kg (six pounds) in the first to 4·50 kg (ten pounds) in the last. Dietary treatment (100 gram carbohydrate) had reduced her weight from 102·60 kg (16st 4lb) to 81·45 kg (12st 13lb). Her height was 5′ 4″. Since 1964 she had been a poor attender and random tests for glycosuria were negative. In 1972 when her weight was 90·00 kg (14st 4lb) she was persuaded to undergo a glucose tolerance test:

Fasting blood glucose			84	mgm/100ml	
½ hour	,,	,,	162	,,	
1 hour	,,	,,	186	,,	glycosuria.
1½ hours	,,	,,	98	,,	
2 hours	,,	,,	74	,,	

The curve is that of the lag storage or steeple type which carries a 14 per cent likelihood of developing diabetes in five years (Malins, 1962). The family history, obstetric history and clinical findings here increase this likelihood of developing overt diabetes in the future. Plasma insulin levels might clarify the situation still further but as a routine procedure these are impractical. However, the prednisone-glycosuria test (Joplin *et al.*, 1961), which is simpler, might clinch the matter.

The hypothesis that both prediabetes and obese maturity-onset diabetes result from a defect in glucose uptake by the muscles so that glucose is deposited in the form of fat implies that obesity is the result and not the cause of the disorder (Lowly *et al.*, 1961). In our present state of knowledge a reduction of the body mass by limiting the carbohydrate intake prevents insulin hypersecretion and either arrests or delays progress of the disease. There is thus good reason for a reducing diet and lifelong weight control for Mrs K.

Chemical diabetes is the term which describes the state before overt symptoms of the disease show themselves but when the diabetic type of glucose tolerance curve is found. This should be distinguished from prediabetes which, of course, implies predisposition to diabetes. Individuals with a strong family history and women who have borne children weighing 4·50 kg (ten pounds) or more at birth, particularly if they are obese themselves, would be so classified. Blood insulin curves have been responsible for this classification.

The way in which one type of diabetes can progress into another and the variety of terms used to describe each type have caused confusion. To illustrate this interrelationship a diagram showing circles of various sizes representing chemical, diet controlled, oral agent controlled (both obese and thin types), insulin dependent and latent forms of the disease has been drawn. Diabetes mellitus may arise in middle life or at a late age in any one of these forms. On the other hand it may change from one type to another as the intersecting circles are intended to convey. Transition from an excess insulin type into an insulin deficient type is a one way process and naturally cannot be reversed.

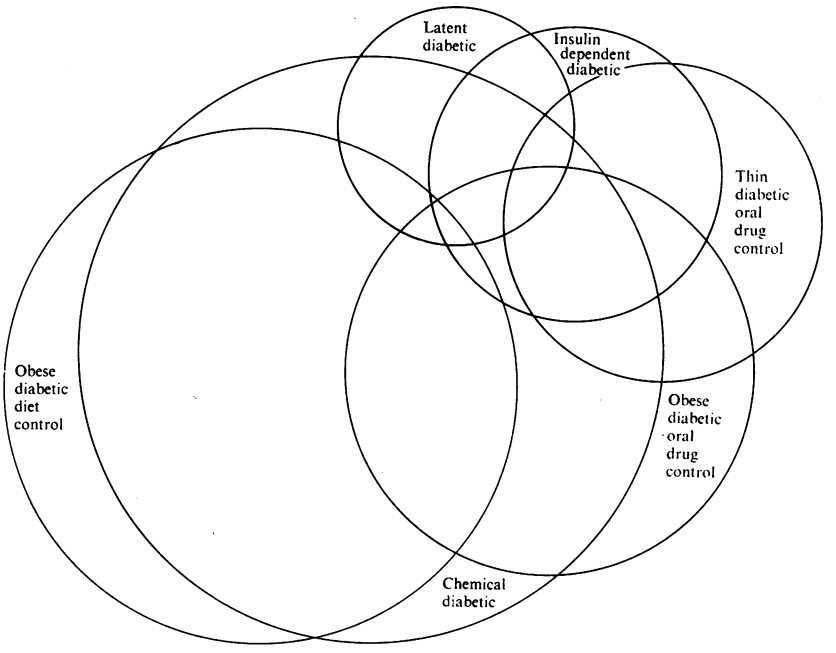

Figure 1.—Diagram of adult-onset diabetes.
The size of the circles does not represent the proportion of each type.

First consultations

Glycosuria is the physical sigh which starts a whole train of action as described below. It is routine practice when requesting urine specimens for screening tests, excluding those for antenatal examinations, to ask that they should be passed one and a half hours after the main meal of the day which preferably should contain a good carbohydrate load.

The examination proceeds as follows:

(1) ' Clinistix ' screening test. This is glucose specific.

(2) ' Clinitest ' quantitative test.

(3) ' Acetest ' (or ' Ketostix ') especially if glucose measures of two per cent or more are found.

(4) Routine clinical examination including testing for proteinuria, blood pressure, fundal examination with mydriatic drops and presence or absence of deep reflexes.

(5) Blood for glucose estimation while fasting is sent to the laboratory requesting a glucose tolerance test. A glucose tolerance test before treatment is started is always worthwhile but is occasionally omitted when the fasting glucose is very high or when ketonuria exists.

(6) X-ray examination of the chest.

Assuming that the diagnosis of diabetes mellitus has been established and that it is not in association with concomitant disease such as acromegaly or haemochromatosis, some idea of the type of the diabetes should be clear. Whatever the type, however, the following advice is given:

1. Membership of the British Diabetic Association is urged.
2. Education about the disease is started.
   (a) *Almost all about Diabetes*, a Family Doctor booklet gives much information. *The Diabetic Life* and *The Diabetic A.B.C.* by R. D. Lawrence once covered this adequately but these publications are both out of date and out of print.
   (b) The publication of the British Diabetic Association called *Balance* covers a wide range of subjects. A collection of the most important of these is the *The Diabetic's Handbook*. Experts in the individual fields have written the articles which are excellent and up to date.
   (c) The area hospital where a diabetic clinic is held often publishes its own booklet. *Advice to Diabetics* is one and is very good.
3. The patient's own record of his disease is started with a diabetic progress book. In this he records—and the emphasis is on *he*—the details of his diet, drug dosage and urine tests and he notes any special symptoms. The aim is to strike a balance between intelligent supervision and morbid introspection. The progress book must be brought to every consultation.
4. The doctor starts to record his own observations and his instructions to the patient. A standardised insertion card for diabetics such as is issued for obstetric patients would be a useful addition to the National Health Service medical record. Much time, however, and trouble can be saved by ruling columns on the plain continuation cards indicating such essential items as weight, diet, urine tests, blood glucose, ketonuria, drug dosage and remarks.
5. The patient is told how to test the urine for glucose, qualitatively and quantitatively, and also for ketone bodies.
6. Identification as a diabetic should be on the person in the form of a card or stainless-steel bracelet. The card may be obtained in a plastic cover through the hospital

service and indicates the essential details of the individual's treatment and conveys warnings regarding emergency treatment.

It might be thought that the 18 patients under supervision at present are meagre material on which to form opinions. Nevertheless, wrapped up in their case histories it is possible to reveal many of the complexities and the problems of management of maturity-onset diabetes in particular. These case histories are illustrative and provide a means of expressing the experience gained in diabetic management during the last 36 years.

Mild maturity-onset diet treated diabetics

These number five and table 1 shows their essential details:

TABLE 1

Patient number	*Sex and age*	*Age at onset*	*Weight at onset*	*Mode of onset*	*Diet prescribed*	*Associated conditions*
1	M 67	65	90·00 kg (14st 4lb)	Mild symptoms	Marriott's	Hypertension 165/90 Myocardial infarction 1969
2	M 54	52	109·35 kg (17st 5lb)	Mild symptoms	100–120 gram carbohydrate	Hypertension 170/100
3	F 62	59	91·35 kg (14st 7lb)	Pruritus vulvae	100 gram carbohydrate	Hypertension 210/110
4	F 39	37	60·75 kg (9st 12lb)	Pregnancy glycosuria	100 gram carbohydrate	Mild toxaemia of pregnancy at 38 weeks
5	F 87	59	94·50 kg (15st)	Cataract extraction	Avoidance of excess carbohydrate	Hypertension at age 59 240/110 Pernicious anaemia age 74 Stroke age 81 Pancreatic diarrhoea age 85

All five patients had suffered minimal diabetic symptoms at the time of discovery when they had glycosuria but no ketonuria. All had glucose tolerance curves of the diabetic type. Four were overweight at onset and had some degree of hypertension. The one whose weight was normal (number 4) requires special mention. Two of the four overweight patients have suffered from cardiovascular illnesses (numbers 1 and 5).

All five patients have remained free from glycosuria except on rare occasions. They keep their own records and use ' Clinistix ', testing their urine 1½ hours after the heaviest carbohydrate meal. Fasting blood glucose estimations have remained sufficiently low, the highest reading being 145mgm/100ml which, it must be admitted, leaves something to be desired.

Obesity, must be abolished and a treatment which allows its persistence is bad. Reference has been made to the high insulin levels in this type of diabetes and the presence of obesity as an aggravating factor. To emphasise this fact and the likelihood of cardiovascular complications in later life to an individual who feels well and can demonstrate negative tests for glycosuria is often unavailing. Patients 1 and 3 are all losing weight, but too slowly. Patient 4 does not need to do so and number 5 is described below.

Diet

In theory the diet for these obese individuals should not contain more than 100 grams of carbohydrate. The protein content at 70 grams and fat at 25 grams keeps the calorie value at 1,000 or below. At the start of treatment weighing of the food is required but later this can be substituted by measuring. A bread slice measure is useful.

In practice two diets are used and both are adequate. First, the Lawrence line ration diet which emphasises the accurate measurement of carbohydrate but fat and protein are not restricted. It is found that with a strict control of carbohydrate the fat, particularly, is unacceptable. Secondly, the Marriott weight reducing diet which is practical and simple. Vitamin supplements are desirable with this. It outlines food which may be eaten without restriction, what should be limited and what is forbidden. A loss of weight of about a kilogram a week is usual of this diet is followed. Weekly attendance and weighing is carried out in the early stages and as success is achieved the intervals between visits can be increased. On reaching average weight as shown on weight charts a cautious relaxation of carbohydrate restriction can be allowed. Frequent and regular consultations have proved essential to success.

Theory and practice often conflict and nowhere is this more evident than in dieting for loss of weight. Marriott's diet has been used extensively in simple non-diabetic obesity and many patients have been well disciplined. The results have varied from crowning success to hopeless failures. Among the failures there are undoubtedly both the irresolute and the cheat. There are, in addition, patients whose diligence seems unquestionable but who fail to lose weight adequately. Among obese diabetics similar cases occur and patient 2 appears to be an example. How far obesity itself can be classed as an endocrine disease has not yet been established. The discoveries about insulin blood levels in obese diabetics support this approach in this one form of obesity. There is good reason to think that the obese individual, diabetic or not, can anticipate further discoveries in the aetiology of his complaint in the near future. They are likely to relieve him of much of the burden of conscience as well as bulk. It is possible that patient 2 would benefit by treatment with a biguanide which augments the action of insulin on muscle and helps with weight loss (Clarke and Duncan, 1968). The action of the biguanides is discussed below.

The unweighed diet first described by Lawrence in *The Diabetic Life* where carbohydrate containing foods are classified into those with negligible, those with five per cent, and those with ten per cent carbohydrate content has much to commend it. Little use has been made of this diet, no doubt because habit dies slowly. Dietary instructions on broad lines are more suited to general practice and the detail involved in accurately calculating calorie requirements is not practical and seldom necessary.

Patient 5

The female now 87-years old presents a wealth of clinical interest. Diabetes was discovered during routine testing because of cataracts. She then weighed 94·50 kg (15st) and was treated by diet. This was 18 years ago. Her blood pressure was then 240/110 mm Hg. Twelve years ago she developed Addisonian anaemia and eight years ago a stroke which left some disability. She is now partially sighted, the blood pressure is unchanged, her weight is below 63·00 kg (10st) and she is mentally alert. There is no glycosuria or proteinuria. When she came to this practice three years ago she was beginning with diarrhoea which increased in severity until it created a night and day disturbance for herself and her family. The stools had the features of a steatorrhoea. She was reluctant to enter hospital and her family supported her. In view of the mild form of diabetes and the symptoms which suggested a deficiency of the exocrine secretion of the pancreas she has been treated for 14 months with pancreatic extract. The diarrhoea has become manageable and the stools are much more normal.

Association of the multiple pathology has not been attempted here but on clinical grounds it is likely that her diabetes belongs to the pancreatic type and although it could be also classified as maturity onset, insulin antagonism is not considered to play a part in its aetiology (*British Encyclopaedia of Medical Practice*, 1968). The management of her diabetes namely diet, has had the desired effect of reducing weight and abolishing glycosuria but the vascular complications of retinitis and a stroke have added to her disability notwithstanding.

Patient 4

This female now aged 39 years was detected as a result of her first and only pregnancy which started in

her 36th year. Throughout her pregnancy she had glycosuria noted during her first antenatal visit at the 12th week. There were no symptoms of diabetes and she proceeded to term. During the 40th week there was a rise of blood pressure to 140/90mm Hg and minimal oedema. Artificial rupture of the membranes resulted in a ten-hour labour with a normal delivery of a healthy female child weighing 3·5 kg (7lbs 9ozs).

A glucose tolerance test carried out six weeks after delivery because of persistence of the glycosuria, revealed a mild diabetic curve. Her weight was 459·85 kg (9st 7lb) and her height 1·60m (5′ 4″). For two years she has reduced her carbohydrate to 100 grams per day with resulting abolition of glycosuria but no alteration in weight.

Interest here centres round the pregnancy which was essentially normal, the freedom from diabetic symptoms which pregnancy would be expected to precipitate and the normal baby of average weight. She can be regarded as a thin maturity-onset diabetic who has just passed from the stage of ' chemical diabetes '. Experience of diabetes in pregnancy is usually associated with the juvenile type, a combination fraught with hazards and requiring the close co-operation of consultant physician and obstetrician. The combination of an elderly primigravida with early maturity-onset diabetes must be unusual and the future progress and management of this patient makes for interesting speculation.

During the last 205 consecutive pregnancies in this practice there have been 28 mothers with glycosuria on two or more occasions. One was a known juvenile-type diabetic. The remainder, disregarding the patient described above, were regarded as examples of a low renal threshold. It is interesting that patients who show glycosuria in one pregnancy do not necessarily do so in a subsequent pregnancy.

Treatment with oral hypoglycaemic drugs

No account of treating diabetic patients with oral hypoglycaemic drugs in general, or in any other type of practice, is complete without reference to their mode of action. Better understanding of this has resulted in a change of attitude towards them individually and this change is reflected in an alteration in treatment routines of individual patients. The ability to monitor blood levels of insulin as opposed to blood glucose referred to above, has provided an explanation to many problems which had previously puzzled physicians. There is still much, however, to be learned.

The sulphonylureas stimulate the beta cells of the islets provided they have some secretionary function left, the so called insulinogenic response. The heightened blood insulin lowers the blood glucose level and if this is enough it abolishes both glycosuria and symptoms. The carbohydrate normally taken up by muscle tissue apparently is blocked from so doing and glucose is deposited as fat. An increase in body fat in the diabetic has in itself an aggravating effect upon glucose tolerance (Catt, 1971). It is this lipogenic result of the sulphonylurea drugs that has had much to do with the changed attitude towards their use. A majority of maturity-onset diabetics are already obese.

An additional drawback arises from a recent discovery about death rates. Evidence is accumulating that sulphonylurea treatment doubles the death rate from remote cardiovascular complications compared with treatment by diet alone or by diet and insulin (Prout and Goldiner, 1970). The view had been held previously that good control of hyperglycaemia by oral treatment would reduce the incidence of long-term complications—cardiovascular, retinal, renal, and neuropathic. The case against the sulphonylurea drugs however, is not proved and authorities in Britain are critical of the method of planning the trial by the Universities Group Diabetic Program in the USA (*British Medical Journal*, 1970; *The Lancet*, 1971).

The biguanide drugs did not receive the same popularity in the early days as the sulphonylureas and formed a second line of defence. In the light of the hyperinsulinism that is now known to exist in the obese maturity-onset diabetic, a drug which did not so aggravate would be welcomed. The biguanides are thought to act by enhancing the

action of insulin, and increasing the peripheral uptake of glucose by the muscles. In addition they may inhibit glycogenesis by the liver. Hyperglycaemia is reduced, the glucose available for conversion to fat is reduced and the stimulus for further release of insulin by the pancreas is removed (Butterfield *et al.*, 1971). Studies carried out on the effect of the biguanides in obese diabetics have tended to show a reduction in weight. One such study (Stowers and Bewsher, 1969) was inconclusive regarding the mechanism of weight loss but appeared to favour the view that impaired absorption by the gut was responsible.

High levels of serum cholesterol and triglycerides are closely related to obesity. Diabetes is known, especially in the obese form, to be associated with high blood lipids. The connection between atherosclerosis and increase in the lipids of the blood is supported by much convincing evidence. The biguanides, through their lipolytic effect may reduce blood lipids and in addition it is claimed that they exert a direct effect in lowering blood cholesterol.

These apparent advantages of the biguanides have not been fully exploited and some patients in this series being treated with sulphonylureas might be transferred to the biguanides with benefit. The difficulties of enforcing a diet regime on some patients has been referred to and then a drug allowing a less stringent regime may be welcome.

A preliminary report on the biguanide phenformin by the Universities Group Diabetic Program (*Journal of the American Medical Association*) suggests that it too has a similar liability to double the death rate from cardiovascular complications, despite good control of hyperglycaemia, as had been suggested with the sulphonylureas. Opinions on this investigation in Britain are also likely to be cautious and the full report will be awaited with interest.

New attitudes towards treatment in any disease process penetrate slowly into general practice. A revolution in the treatment meted out to patients in diabetic clinics will have to occur first before there is a universal change in the same direction among those treated outside the clinics. A review of diabetic clinics up and down the country would more than likely reveal a great diversity of views, attitudes and policies. It is this lack of standardisation that renders case histories the only means of illustrating treatment trends and management as they affect an individual doctor.

At present there are eight patients who have been treated orally. These are those patients in whom glycosuria has not been controlled by diet alone for one reason or another.

PATIENTS TREATED WITH ORAL HYPOGLYCAEMIC DRUGS

Patient number	*Sex*	*Present age*	*Age at onset*	*Obese at onset?*	*Drugs used*	*Mode of onset*
6	M	44	38	Yes	Chlorpropamide	Retinal haemorrhage
7	M	60	50	No	Chlorpropamide → phenformin	Thirst, polyuria—3 weeks
8	M	57	55	Yes	Chlorpropamide	Balanitis—4 weeks
9	M	66	56	Yes	Phenformin → Chlorpropamide	Loss of weight, thirst —6 weeks
10	M	65	58	No	Chlorpropamide ——→ insulin	Thirst, polyuria —6 weeks
11	M	78	67	Yes	Tolbutamide	Treatment with steroids for rheumatoid arthritis
12	F	79	72	Yes	Chlorpropamide	Admitted for cataract operation
13	M	93	87	Yes	Chlorpropamide	Thirst, polyuria—months

Patient 6

Heavy manual labourer. Retinal haemorrhage was discovered by an optician. He was referred to an ophthalmic consultant and then to a general physician. The G.T.T. showed a diabetic curve, there was no glycosuria. His weight was 229·95 kg (36st 7lb); he was given a 200 gram diet and chlorpropamide 100 mgm daily. The weight reduced to 67·50 kg (10st 10lb). Chlorpropamide was stopped after two years. He has maintained dietary restriction and average weight. The retinae are now clear.

Here the ' diabetic lesion ' was a first manifestation and eventually a full picture of retinitis is likely. The administration of a sulphonylurea by a hospital physician was probably a compromise as he was a manual worker. Maybe his continued dieting and the regular review of weight and urine will postpone the islet decompensation.

Examination using a mydriatic of the fundi of all diabetic patients is carried out annually. There is now no exudative retinopathy among these patients but haemorrhages and microaneurysms are often seen. Regular review of the retinae is worth while because of evidence that when hard exudates first appear and visual acuity is beginning to deteriorate, treatment with clofibrate 500mgm twice daily will arrest deterioration (Nolan and Cullen, 1969). The outlook is otherwise so hopeless and hypophysectomy so drastic, that a simple measure such as this is worth doing.

Patient 7

This patient was a farmer of average weight at onset. He was treated elsewhere at first and was liable to ignore his diet and rely on oral drugs. His weight is nearly 75·60 kg now (12st) and fasting blood glucose maintained at 115mgm/100ml. Owing to increasing weight he has been advised to curtail his diet to 100 grams and phenformin (50 mgm twice daily in slow-release capsules) exchanged for chlorpropamide. At the time of writing he has reported a reduction in appetite and a loss of 1·80 kg (4lb) weight.

Patient 8

He was a road worker and presented with an inflamed prepuce and balanitis which should always arouse suspicion. A diet of 100 grams of carbohydrates failed to abolish glycosuria after two weeks. Chlorpropamide 100 mgm daily was effective. The weight was reduced by 7·65 kg (17lb) which has been maintained for 18 months. The fasting blood glucose is 90mgm/100ml. There is no reason to change the regimen for this patient.

Patient 9

A moderately obese farmer who was first treated elsewhere with phenformin 100 mgm daily and simple carbohydrate reduction. After five years the drug was changed to chlorpropamide 250 grams daily. He has neither gained nor lost weight after five years' treatment with each type of oral agent. He is, however, still obese and a resumption of phenformin is under consideration with a higher dosage than before.

Patient 10

A builder's labourer, height 1m70 (5′ 8″) whose weight at onset was 68·40 kg (10st 12lb). Diet alone failed to control glycosuria. Chlorpropamide 250mg daily with 100-gram diet was successful but there was a gradual return of glycosuria. These patients make urine tests routinely on rising and one half an hour after the heaviest carbohydrate meal of the day. The fasting blood glucose rose to 162mgm/100ml. Chlorpropamide was increased to the maximum dose of 500 mgm daily with disappearance of gylcosuria. During the last few months glycosuria is again appearing.

This is an example of secondary failure. In such circumstances these questions are asked: (1) Is this ' patient failure '? i.e. breaking the diet.

(2) Is this ' drug failure '?

(3) Is there intercurrent disease? He is a diligent dieter and in his effort to control glycosuria has reduced his carbohydrate intake to 90 gm daily. There is no evidence of intercurrent disease. His weight has reduced by 8lbs since treatment began. The stringent treatment is creating hardship as the present winter approaches and he is fearful of the cold he experiences. The fasting blood glucose is 222mgm/100ml. Here are

indications for increasing his carbohydrate to 150 or 200 grams and treating him with insulin. This is now being done and should earn his gratitude.

Blood insulin levels in the thin maturity onset diabetic are low in contrast to those in the obese patient (*Advances in Internal Medicine*, 1967). The downward course of patient 10 and his drift into insulin dependency might well have been forecasted.

Patient 11

A retired farmer became severely disabled by rheumatoid arthritis involving most joints. Diabetes was precipitated by prednisone used in desperation to alleviate arthritis. The steroids have long since been abandoned but glycosuria returns when the tolbutamide is stopped. The misery of major disease is enough without adding that of a restricted diet. Phenformin might have been helpful but the risk of gastrointestinal effects resulted in the decision to leave well alone.

This effect of steroid administration is a reminder that all patients so treated must have regular urine tests for glucose. The challenge to the beta cells by cortisone and related drugs is, of course, the basis of the cortisone glucose tolerence and the prednisone-glycosuria test for detecting predisposition to diabetes (Malins, 1962).

Patient 12

This was the only woman. She was barely 1·5 m (5′) tall and naked weight 81·90 kg (13st) when she arrived in the practice 9 months ago. Diet control was haphazard, she was on chlorpropamide 100mgm daily and glycosuria was present. Both eyes had had cataracts removed. She had had a stroke in 1967, with no obvious sequelae. The retinae showed vascular changes but no exudates. She was treated with Marriott's diet and chlorpropamide in the same dosage. Weight loss to date is 13·50 kg (30lb) with marked clinical improvement and no glycosuria. It is intended to stop the oral drug soon as she is likely to remain well without it.

The regular screening for glycosuria in cataract sufferers continues to be normal practice but with less enthusiasm than before. Diabetes does, it is claimed, precipitate lenticular opacities of a certain type which are recognised as such by ophthalmologists. The commonly seen cataract does not appear to be connected with hyperglycaemia.

Patient 8

The interest in this very elderly male lies in his recent history. The onset of mild diabetes at 87 years was dealt with by a few practical hints about carbohydrate restriction and the administration of chlorpropamide 100mgm daily. On this regimen glycosuria was abolished. He had been overweight 75·60 kg (12st) at 1m 70 (5′ 8″) at the start of treatment. The latter abolished his symptoms but had no effect upon his weight. During recent months i.e., six years after the onset of diabetes, he developed an acute pulmonary infection and left ventricular failure. A long period of hospital treatment resulted in his recovery but he had lost a great deal of weight. He has been transferred to a geriatric unit as a long-stay patient. There is no glycosuria and he eats an unrestricted diet. Naturally he is not receiving hypoglycaemic drugs. The reduction in body bulk was the correct treatment for him as has been demonstrated by a severe acute illness.

This patient has developed a left foot drop since his admission to hospital. Peripheral mononeuritis is characteristic of diabetic neuropathy. I have seen this condition as a presenting symptom involving the anterior crural nerve in a middle-aged male. Treatment is what is appropriate to the diabetes and such mechanical measures and physiotherapy as are indicated. The prognosis in this condition for nerve function is poor which is not surprising as the lesion is considered to be an arteritis of the vasi nervorum.

Practical comments on the oral hypoglycaemic drugs

The sulphonylurea drugs in use in the practice are chlorpropamide and tolbutamide. There is not enough opportunity nor a need to gain experience with any others. The maximum dose of the former drug has been 500mgm daily and in latter the 1·5 grams daily. No gastrointestinal symptoms or skin rashes have been observed. Even more important has been the absence of hypoglycaemia. The possibility of this and its prolonged nature has been realised with the greater likelihood where renal function is impaired. Theoretically the blood urea should be estimated as a part of the investigation.

No proteinurea was observed in any patient so that significant renal disease was unlikely. Blood urea estimations were not done.

However, in patient 11 tolbutamide, which is eliminated rapidly, was the drug of choice because the enfeebled state of the patient might well have been associated with poor excretion. Hypoglycaemia would be expected more readily in such circumstances with chlorpropamide in view of its prolonged action.

Experience with phenformin used in the form of its hydrochloride has been too small to allow useful comment. Nevertheless, this is likely to be used as the drug of first choice in the obese diabetic if needed an oral drug is used at all. Sulphonylureas are likely to be retained for the thin patient and some patients at present treated with sulphonylureas are likely to be changed over to phenformin.

No case has had need of the combined treatment with sulphonurea and biguanide. Such a consideration would be referred to a specialist in diabetes, for advice.

A summary of the discussion of the treatment of the maturity-onset non-insulin dependent diabetic, with due regard for the varying circumstances of the 13 patients at present in the practice, who have been quoted as illustrations, would be as follows:

(1) Obese patients should be given a fair trial of diet only. Primary failure would be an indication for phenformin treatment.

(2) Patients of average weight would be dealt with similarly but a sulphonurea would be used and penformin substituted subsequently if considerable weight is gained.

(3) The thin patient would receive a higher carbohydrate allowance (from 150 grams) with a sulphonurea. Failure to control hyperglycaemia would be an indication for insulin.

(4) Where other diseases co-exist or heavy manual work is undertaken the treatment would be tailored more to the patient rather than to the book of rules.

Starting insulin

Patient 5, among those patients treated with oral hypoglycaemic agents illustrates the stage of secondary failure and insulin deficiency. At the time of writing he is about to start with insulin and to increase his carbohydrate allowance. The diet change will be clear to him owing to his previous experience. The administration of insulin requires a re-educating process. This can be summarised as follows:

(a) Syringes, needles, sterilisation, possession of a separate set, measuring of insulin by units, technique of administration by injection and sites for injection.

(b) The type of insulin selected with its time of onset, time of maximum effect and duration of action. A diagram on page eight of a booklet entitled *Diabetes—patterns of testing* published by the manufacturers of ' Clinitest ' tablets has proved invaluable as a means of illustrating insulin action. The insulins best suited for use in general practice consist of soluble, insulin zinc suspension (lente) and possibly protamine zinc types. These or combinations will cover most eventualities.

(c) A changed routine for urine testing. Quantitative testing with ' Clinitest ' is necessary and during the period of stabilisation, testing is required before each meal. The before breakfast test is carried out on an 0800 hours specimen having been urine voided at 0700 hours.

The results of these tests indicate whether the insulin dose is correct and in addition whether the type of insulin is suitable. When control is established, the early morning and before evening meal tests are usually adequate unless symptoms of hypoglycaemia are presenting or intercurrent illness occurs.

(d) Hypoglycaemia is explained and the need to carry sugar to counteract symptoms.

(e) Testing for ketonuria by 'Acetest' or 'Ketostix' should the urine glucose reach two per cent or more. The presence of ketonuria usually implies the need for medical advice.

Patient 10 is co-operative and a little time spent with him on this advice will render him independent—the aim in treatment of all diabetics. His membership of the British Diabetic Association will provide the answer to many side issues such as exercise, employment and motoring. For his wife a valuable handbook in cookery is available entitled *Diet without tears.*

The aim of treatment will be to produce a glucose free urine without hypoglycaemic symptoms and a blood glucose of 160mgm/100ml or below at one hour after food. This would be regarded as perfect control.

The long term control of the insulin dependent case (maturity onset)

It was stated earlier that a female patient, one of the five insulin-dependent group and now aged 67 years, had been under treatment with insulin since diagnosis at the age of 47. For the last eight years her details have been known. These show that neither diet (160 grams of carbohydrate) nor insulin dosage (PZI 16 units, soluble 20 units) have required modification. From her own evidence this has sufficed for much longer. She has maintained reasonable freedom from glycosuria before breakfast and the evening meal. She, however, provides an illustration of the acute complications of insulin treated patients that require emphasis.

In 1966, she suffered a chest cold with some bronchitis. Glucose tolerance was upset and she went rapidly into coma. When first seen she had been ill for three days and was in light coma. She had a dry tongue and skin, hyperpnoea and a heart rate of 128 per minute. The eyeball tension was reduced and the urine loaded with sugar and ketone bodies. A small quantity of urine was available for testing. She was given 50 units of soluble insulin intravenuously and admitted to hospital. A saline intravenous drip set up to run during the journey by ambulance would have been an improvement on the emergency treatment. Antibiotics and a coma regime in hospital were successful and she was discharged in seven days. Such is the responsibility of the general practitioner in a case of established diabetic coma but he has an even more important role and that is in its prevention.

The education of insulin dependent patients about intercurrent illness is an important step in the prevention of coma. This is especially so in conditions where vomiting is present. Should measures more complicated than substitution of carbohydrate into soluble form be required, admission to hospital where control by blood glucose estimations and intravenous therapy can be carried out is the treatment of choice.

Coma and glycosuria are often associated, the latter sign bring both misleading and inconsequential. A middle-aged man presented with such a combination many years ago. The diagnosis was established in 12 hours but he died shortly afterwards from cerebral malaria. The glycosuria did, for a time, detract from the true diagnosis and wasted valuable hours.

The coma and glycosuria seen in malignant malaria are not associated with ketonuria. It has been revealed in recent years that a further type of coma may complicate diabetes and because of the absence of ketones in the urine it could escape early recognition. It may arise in the mild adult-onset diabetic and is known as hyperosmolar non-ketotic hyperglycaemic coma and has a high mortality. Experience of this complication can be quoted.

The second acute complication occurring in the case of the female diabetic happened in 1970. Her husband reported one Sunday morning that she was unable to stand, was incontinent of urine and faeces and was shouting obscenities. Moreover, this in lesser form had occurred each morning for several days after which she had become normal as the day progressed. His account was no exaggeration. She was confused, incoherent and aggressive. The blood glucose estimated with 'Dextrostix' was less

than 45mgm per 100ml. Ten ml of 50 per cent glucose was injected intravenously with a rapid return to normal. When she could give an account of herself it transpired that she had, some days previously, broken both her insulin syringes. She is a farmer's wife and substituted a syringe which they used for the cows! Her guess at dosage was surprisingly overestimated but the experience proved salutary.

Hypoglycaemia presents in many forms but individual patients seem to take on the pattern peculiar to themselves. Lesser forms are a frequent experience and are dealt with by the patient who recognises the symptoms early. Oral treatment is, in any case, usually possible. No experience has been gained with glucagon. The importance of the symptom lies in the decision to modify the diet or insulin dosage or both.

The same 67 year-old female patient would be expected to show evidence of the long-term complications of the disease. The development of these seems to depend upon the duration of the disease, the degree of control which has been exercised, and the unknown factor referred to as the essential lesion. Histologically this is a thickening of the capillary basement membrane. The second of these factors is not easy to support with evidence. Nevertheless, it is an essential attitude to adopt by those in charge of diabetic patients. The genesis of complications does not seem to relate to the type of diabetes; it seems to be the duration that matters.

At the annual examination which all diabetic patients are encouraged to have, this patient showed a few microaneurysms and small haemorrhages in the retinae. There was neither evidence of proliferative retinitis nor hard exudates. Her visual acuity had, however, dropped to 6/24 and J2 in both eyes. There have not been any cardiovascular symptoms and the urine is free from protein. The ankle and knee jerks are absent and the vibration sense is absent from the knee downwards.

Thus she shows the inevitable drift towards the late diabetic disabilities, ocular and neuropathic. Among the adult-onset diabetic patients she is the nearest to disintegration. In past years most of the late complications have been encountered in other patients at one time or another. The perforating ulcer of the foot and gangrene of both superficial and deep type, have been the cause of great distress. Close co-ordination with the specialist in diabetes and the surgeon are required to achieve the best results. Nephrosclerosis as a cause of renal failure has, as far as is known, not been encountered.

Blindness is a more common hazard in the juvenile diabetic no doubt because of the duration of the disease. Aids provided by the welfare services for the blind including guide dogs seem to be the limit of our powers in this field. Reference has been made above to pituitary ablation and clofibrate treatment.

Latent diabetes

This unusual and mysterious form of diabetes has not been encountered in the series of patients presented. Some years ago, however, it was encountered in an alarming form and a brief account illustrates the features.

An elderly male first came for consultation with the information that he had diabetes. There were no symptoms or signs of the disease, his urine was negative for glucose and he was on a full diet. He was regarded by his associates as a glutton. Many months later a summons to his house revealed a man in a state of undoubted pre-coma with severe ketonuria. After admission to hospital he continued to deteriorate before finally responding to treatment. There was no concurrent infection and after a stormy illness he recovered. He recovered so well that no insulin was required after an interval of a few weeks and he resumed his gluttonous habits. The same circumstances recurred a year later without obvious cause and he again recovered. A glucose tolerance test carried out after the second episode showed a normal curve. He referred to " being cured ", and not unnaturally. After this, contact with him was lost.

The hospital diabetic clinic

The function of the hospital in the treatment of diabetes mellitus is a subject about which no overall policy can be laid down. The following can be considered as guide lines:

(1) The hospital laboratory is invaluable for the initial diagnosis by blood glucose estimations and the glucose tolerance test. Subsequent control by blood glucose estimations carried out at the laboratory is equally essential.

(2) Routine supervision is desirable in the unstable (brittle) diabetic by the specialist at the clinic. Especially is this so in the case of children. The general practitioner can maintain his supervision in conjunction with the hospital.

(3) Diabetes associated with pregnancy is an absolute indication for co-operation with the hospital physician and obstetrician.

(4) On diagnosis, when there is the possibility of insulin treatment, the less well-educated or apprehensive patient is better in hospital for stabilisation. He can be trained to administer insulin under supervision and dieticians can educate him about calorie requirements and food values. Once this stage is over the management may be left to his general practitioner.

(5) The diabetic clinic has incalculable value for the family doctor when he has problems of management, and for the community, it is a focus for research and therapeutic trials.

Amongst the present practice population of diabetes (18 patients) all five of the insulin dependent type have, at some time, been referred to hospital for advice. Only one, a boy of nine years, with a highly unstable type of disease, attends the clinic for regular supervision. The remainder are supervised at the practice surgery. None of the remaining 13 patients (maturity onset) have been referred to hospital for other than glucose tolerance tests, except one who was referred by an optician.

Conclusion

This account has been written with the general principles of management in mind more than the minutiae of dosage, diet and directives.

It is intended to convey the idea that small numbers of patients suffering from the same disease, as occur in general practice, can provide a wide spectrum of experience in symptomatology, pathology and treatment.

The willing and friendly co-operation of the hospital staff in the laboratory and the specialists in the outpatient departments and wards is a pre-requisite for successful management.

Summary

The known diabetic patients of a small rural general practice are discussed in relation to their detection, form of disease and the treatment undertaken. ' Maturity onset ' as a section of diabetic patients is regarded as a synonymous term to ' adult onset '. This group may be further subdivided into the mild, who may be thin or obese, and the insulin dependent. Prediabetes and chemical diabetes are defined and their positions relative to the maturity onset form of the disease clarified.

The management of these various types is described with special emphasis on diet and the oral hypoglycaemic drugs. Case histories, which incorporate the complications of diabetes, are related and the present evidence that certain complications are aggravated if not caused by the oral drugs is presented. The start of insulin treatment and the continuing supervision required is described.

Emphasis throughout is laid on educating the diabetic patient to supervise his own treatment and time spent with him in this respect is well worth while. The small but invaluable role played by the hospital diabetic clinic in the management of patients in any one general practice is emphasised.

The management of maturity-onset diabetes is essentially the responsibility of the general practitioner.

Acknowledgements

To David Mattingly, F.R.C.P. Professor of Postgraduate Medical Studies, University of Exeter and Consultant Physician, Royal Devon and Exeter Hospital, Exeter, for his inspiration by example in the care of diabetic patients.

To Miss Chitty, Librarian at the Royal Devon and Exeter Hospital, for invaluable assistance in obtaining references.

To my wife without whose forbearance, interest and help this essay would not have been written.

REFERENCES

Advances in Internal Medicine (1967). **13,** Chicago: Year Book Publishers.
British Medical Journal. (1970). Editorial, **4,** 444–445.
Butterfield, W. J. H., Kelsey Fry, I. & Whichelow, M. J. (1961). *Lancet,* **2,** 563–567.
Catt, K. J. (1971). *An ABC of Endocrinology.* London: Lancet.
Clarke, B. F. & Duncan, L. J. P. (1968). *Lancet,* **1,** 123–126.
Joplin, G. F., Fraser, R. & Keeley, K. J. (1961). *Lancet,* **2,** 67–70.
Journal of the American Medical Association (1971). **217,** No. 6, 817.
Love, A. H. G. & McEvoy, J. (Edit.) (1968). *Medical Progress.* London: Butterworth.
Lowy, C., Blanshard, G. & Phear, D. (1961). *Lancet,* **1,** 802–804.
Malins, J. (1962). *Clinical Diabetes Mellitus.* London: Eyre and Spottiswoode.
Marriott, H. L. (1956). *Weight reducing diet.* London: Middlesex Hospital.
Nolan, J. & Cullen, J. F. (1969). *British Journal of Ophthalmology,* **53,** 9–15.
Prout, T. E. & Goldiner, M. G. (1970). *Diabetes,* **19,** Suppl. 1, 375.
Stowers, J. M. & Brewsher, P. D. (1969). *Postgraduate Medical Journal,* **45,** Suppl. 13–19 (May).
The Lancet. (1971). Editorial, **1,** 171–172.

MEDICAL EDUCATION AND MEDICAL CARE

Those responsible for providing medical education should know how many physicians are required to meet the needs of a country and the kind of training they should receive; in the light of this information the educational objectives should be established to provide the most effective delivery of medical care. While this was possible in the first quarter of this century, when the people needed all the care that the medical profession could offer, it is now extremely difficult to relate educational objectives to medical care since medical care cannot be evaluated accurately. Moreover, few countries have the resources to cover all the medical specialities and a choice of priorities must be made and a balance struck between quality and quantity. This choice will involve long-term predictions of future requirements and the rapidly changing social conditions in all countries and in medical science itself make such forecasting rather inaccurate.

Another factor to be borne in mind is the dependence of the success of medical education in all countries on public support, that is, on the confidence of the public in the physicians who graduate from medical schools. The recruitment of good students and high-grade teaching staff is largely influenced by the public image of medicine and medical education and of the medical schools themselves. In addition, all medical schools require the full co-operation of the public in their programmes of clinical teaching and in the practice of clinical methods by the students.

REFERENCE

World Health Organisation Chronicle (1973). **27,** 153–156.