prostatic obstruction. Alternative techniques will be developed and may eventually come to supplant transurethral resection of the prostate. However, until adequate information on the effect of new treatments with respect to relief of obstruction, short term and long term morbidity, mortality, cost effectiveness, quality of life, and reoperation rate is available, these techniques should be regarded as experimental.

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Lesson of the Week

Insulin dependent diabetes in nonagenarians

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Insulin dependent diabetes should always be suspected if appreciable weight loss and ketonuria are found, irrespective of age

The National Diabetes Data Group's definition of insulin dependent diabetes misleadingly talks of "predominant onset in youth."¹ Over 40 years ago Lawrence wrote that many diabetic patients aged over 70 were insulin deficient.² It has recently been shown in Denmark that the annual incidence of insulin dependent diabetes after the age of 30 is 8.2 per 100 000 and is remarkably constant from the fourth to the ninth decade; thus at least 44% of all cases are diagnosed after the age of 30.³ We report on two patients who developed insulin dependent diabetes at the ages of 88 and 93.

Case reports

CASE 1

An 88 year old woman presented with a five month history of lethargy, weight loss, and nocturia. She was found to be hypothyroid, with a high titre of thyroid autoantibodies. One of her seven siblings had developed diabetes of uncertain type at the age of 75 and a granddaughter had Graves' disease. A month later she became thirsty, was found to have diabetes, and was treated with glibenclamide 5 mg twice daily by her general practitioner. She was referred to us three months later with a random blood glucose concentration of 15.1 mmol/l and a haemoglobin A1 concentration of 11.6% (normal range 5.0%-7.5%). Apart from bilateral cataracts there were no diabetic complications, but she had a body mass index of 23 kg/m² and was positive for islet cell antibodies. A senior registrar diagnosed late onset insulin dependent diabetes but continued treatment with oral hypoglycaemic agents.

Over the next three years she had persistent hyperglycaemia but remained well and regularly walked about 3 km. Her weight gradually decreased, however, from 62 kg to 51 kg (body mass index 19.0) and, at the age of 92, she started taking Human Ultratard insulin 20 units once daily, the injections being given by her daughter. Within three months she had regained all her lost weight and was described as being like "a new person." One year after taking insulin her treatment was changed to bovine lente insulin because of nocturnal hypoglycaemia. At the age of 97 she could still walk to the shops, and in five years of taking insulin she had not required admission to hospital or developed any diabetic complications. Paradoxically, diabetic control has been worse while taking insulin (haemoglobin A1 concentrations being in the range

12-14%), probably because the diabetes nurse allows her to have chocolate biscuits with her coffee and banana sandwiches for lunch, which according to the patient "make life worth living."

CASE 2

A 93 year old woman with no family history of diabetes presented to a geriatric unit with a one week history of thirst and polyuria. In the 24 hours before admission she had become increasingly drowsy and confused. She had been wheelchair bound for four years because of osteoarthritis but had no other illnesses and was taking no drugs. She was dehydrated and cachectic with a Glasgow coma score of 3/14. She had moderate ketonuria, a blood glucose concentration of 44 mmol/l, and a serum osmolality of 396 mmol/kg. Blood gas pressures and bicarbonate concentration were not measured. Blood cultures, a chest radiograph, and an electrocardiogram showed nothing abnormal. Hyperosmolar non-ketotic coma was incorrectly diagnosed. After treatment with intravenous insulin and fluids she recovered full consciousness within 24 hours. Because she was thought to have non-insulin dependent diabetes she was discharged taking gliclazide 120 mg twice daily.

Over the next three months she did not see her general practitioner but had persistent symptoms, lost weight, and never felt well. She was then readmitted with heavy ketonuria, a blood glucose concentration of 31.3 mmol/l, and a blood bicarbonate concentration of 13 mmol/l. She was positive for islet cell antibodies at a titre of 1:64. Twice daily Human Mixtard insulin produced a rapid and sustained improvement in her symptoms and general wellbeing. The insulin was given by her daughter, with a district nurse providing holiday cover. Two years later she was well, had had no acute diabetic problems, and had no microvascular complications.

Discussion

Insulin dependent diabetes in elderly people is commonly diagnosed insufficiently early to prevent prolonged ill health, futile treatment with oral hypoglycaemic agents, or a potentially fatal admission with ketoacidosis.⁴ Insulin dependent diabetes can be diagnosed by clinical criteria. Kilvert *et al*⁵ found that diabetes in patients aged 64 years or over who needed insulin within the first year was distinguished by ketonuria at diagnosis, a history of autoimmune

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endocrine disease, and low body weight. We previously found that low body weight or appreciable weight loss, combined with moderate or heavy ketonuria, was an accurate indication of insulin dependent diabetes at any age.¹

The first patient had a normal body mass index, with subsequent appreciable weight loss despite maintaining reasonable glycaemic control. She also had autoimmune thyroid disease. In the second patient the onset was more dramatic: at presentation she was comatose with extreme hyperglycaemia and ketonuria. We believe that it is wrong to treat this type of patient without insulin irrespective of the islet cell antibody result since the mortality of recurrent hyperglycaemic coma in elderly people is high.⁶ Furthermore, elderly patients should not be allowed to languish in ill health when insulin could provide rapid relief of symptoms. Often the reluctance to start treatment with insulin in elderly patients arises from fears about possible hypoglycaemia and patients' ability to give injections. Our cases show that this should not be a problem: a relative or member of the nursing home staff can usually give it. If the patient can give the injection but not draw it up (a common problem in older people) a district nurse or relative can draw up a week's supply of syringes and leave them in the fridge.

If the aim of treatment is to control symptoms and restore vitality a once daily injection is usually adequate. It should nevertheless be noted that, as in case 1, human insulin is usually less satisfactory than bovine. Tindall *et al* found that, compared with bovine lente insulin, Humulin Zn (human insulin zinc

suspension, Lilly) produced excessively frequent nocturnal hypoglycaemia.⁷

Our cases raise the interesting question of whether late onset insulin dependent diabetes has the same pathogenesis as that developing in childhood. If it has, why were our patients "protected" until their old age. Our patients were not tissue typed, but in Denmark 94% of elderly patients with presumed insulin dependent diabetes were positive for HLA DR3 or DR4, or both, a proportion identical with that in young patients.³ Furthermore, the prevalence of islet cell antibodies in these elderly Danish patients was only slightly lower than that in patients under 30. It therefore seems that the underlying process of β cell destruction is the same irrespective of age at onset.

We thank Dr Jorn Nerup for letting us see a copy of his group's paper.³

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ANY QUESTIONS?

What is the rationale of using a combination of aspirin and warfarin in thromboembolic conditions?

The haemostatic system contributes platelet aggregates and fibrin deposits to occlusive thrombi. On the arterial side trials have shown that antiplatelet drugs (principally aspirin) or anticoagulants (heparin or warfarin, or both) on their own result in worthwhile reductions in the recurrence of major cardiovascular episodes. The value of thrombolytic agents in the early stages of myocardial infarction is also well established. An obvious question is whether modifying platelet behaviour and fibrin deposition simultaneously may be more effective than either approach on its own.

Until fairly recently, combined regimens have generally been avoided because of their expected effect on the risk of serious bleeding, but trials are now beginning to indicate that combined regimens may indeed be more effective than single regimens and that they do not necessarily lead to an unacceptable increase in serious bleeding—that is, requiring transfusion or surgery, or both). Thus the combination of aspirin and heparin followed by warfarin may lower the risk of major cardiac episodes in patients with unstable angina or non-Q wave infarction when compared with aspirin alone.¹

The clearest demonstration of the value of combined treatment is the concurrent use of aspirin and streptokinase in the early stages of myocardial infarction.² The use of 100 mg aspirin with warfarin to achieve an international normalised ratio of about 3.0 reduces major vascular episodes in heart valve replacement by over 70% compared with warfarin alone and at the cost of only a marginal increase in serious bleeding.³ Trials of combined treatment in the primary prevention of coronary heart disease in men at particularly high risk and in the secondary prevention of myocardial infarction are in progress.

More doctors are using combined treatment after myocardial infarction in advance of trial results. In the

light of encouraging findings in other settings this is probably justified, particularly in patients at high risk, provided that several precautions are observed. Firstly, any increased incidence of serious bleeding is likely to be more acceptable to those at high rather than moderately increased risk of thrombosis, and this balance needs to be discussed with patients. Secondly, there is no doubt about the increased incidence of less serious bleeding due to combined treatment, which takes the form mostly of bruising or nose bleeds but occasionally of haematuria. Thirdly, low doses of individual agents should generally be used in combined regimens—that is, not more than 75-150 mg aspirin daily and warfarin to achieve an international normalised ratio of not more than between 2.0 and 2.5, except in heart valve surgery, after which somewhat higher ratios are probably necessary. Fourthly, possible contraindications to antithrombotic treatment should be carefully assessed, although, because of the high risk of life threatening vascular episodes in those for whom combined treatment is likely to be considered, they may not rule it out altogether. For example, carriage of *Helicobacter pylori* can now be established and if necessary eliminated so that patients with dyspepsia are not automatically ineligible.

On the venous side it is now clear that aspirin (as well as warfarin) is effective in the prophylaxis of deep vein thrombosis and pulmonary embolism. It is therefore timely to consider whether combined treatment may confer further benefits in this context, too.—T W MEADE is a professor of epidemiology in London

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