

## Fortnightly Review

### Managing lower urinary tract symptoms in older men

Paul Abrams

The *BMJ* recently published an article on the place of transurethral resection of the prostate for benign prostatic hyperplasia in the "Controversies of Management" series.<sup>1</sup> Although the debate focused on the active management of benign prostate disease, with drug or surgical treatment, for most patients management begins in the general practice surgery. It is the task of urologists to provide a logical scheme of investigation, diagnosis, and treatment that spans the community and hospital sectors and contributes to an overall management plan.

Before discussing the management systematically it is necessary to dwell a little on the semantics of the subject. In an editorial published by the *BMJ* last year I suggested a rather stricter use of terms than we have been hitherto accustomed.<sup>2</sup> The leader argued that the term "benign prostatic hyperplasia" should be reserved for what it is, a histological diagnosis. Benign prostatic hyperplasia is prevalent in elderly men in that it is evident on microscopic examination in 70% of men over 70 years old. Some patients with benign prostatic hyperplasia will develop benign prostatic enlargement but only a minority will develop benign prostatic obstruction. The only way that benign prostatic obstruction can be diagnosed accurately is by urodynamic studies—that is, by the pressure flow analysis of micturition. The leader also argued that, in order to extricate ourselves from the current confusion of terminology, we should abandon the term prostatism and substitute lower urinary tract symptoms. This was argued because it is well established that one third of all men with lower urinary tract symptoms have no element of bladder outlet obstruction.

In this article I will attempt to be honest about what is fact, what is reasonable supposition, and what is merely wishful thinking or indeed could be categorised as "old wives' tales."

#### Initial assessment

Patients present to the general practitioner for three main reasons. They may have lower urinary tract symptoms and these may or may not be interfering with the quality of their lives. Their symptoms may be uncovered by the general practitioner asking directly about lower urinary tract symptoms during a consultation for another reason. Increasingly, patients see their general practitioner for reassurance, having read about prostate disease in the popular press (some urologists are keen to make themselves available for press interviews).

The interpretation of lower urinary tract symptoms is fraught with difficulty. Symptoms can be categorised into filling symptoms and voiding symptoms, previously known as irritative and obstructive symptoms, even though there is generally little "irritation" in the

#### Summary points

- The presence of lower urinary tract symptoms does not indicate bladder outlet obstruction
- Size of the prostate does not correlate with bladder outlet obstruction: small prostates may cause severe obstruction
- Bothersomeness and effect on quality of life are the preferred indicators for treatment
- Conservative treatment is justified by the long clinical course of the conditions
- Drugs are of some help and are becoming safer
- Transurethral resection of the prostate is the only procedure known to give good long term results
- New alternatives to transurethral resection of the prostate should only be used within the context of randomised controlled trials at present

lower urinary tract in such patients and the so called obstructive symptoms show no statistical association with urodynamically proved bladder outlet obstruction. Only the concurrence of the symptoms of urgency and urge incontinence give any clue to an individual patient's bladder dysfunction. A patient with both these symptoms has a high chance (85%) of having detrusor instability (detrusor contractions during bladder filling which the patient is unable to inhibit).<sup>3</sup> Large series of patients have failed to show any other association between a urodynamic diagnosis and other lower urinary tract symptoms, either singly or in groups. Symptom questionnaires only measure symptoms at a particular time, and do not have any diagnostic importance. Indeed the best validated questionnaire, the international prostate symptom score (IPSS; fig 1), gives identical readings in men with and without obstruction, and indeed in age matched women.<sup>4</sup>

Of most importance in assessing symptoms is to evaluate their degree of bothersomeness and the impact of the symptoms on the patient's quality of life. Several questions can be used to assess bothersomeness and the effects on quality of life.

- If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?
- Thinking about how your symptoms have been in the last four weeks, how do you feel about them?
- How much do your symptoms stop you from doing what you want to do?

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Patient name : \_\_\_\_\_ DOB : \_\_\_\_\_ ID : \_\_\_\_\_ Date of assessment : \_\_\_\_\_  
 Initial assessment ( ) Monitor during \_\_\_\_\_ Therapy ( ) after \_\_\_\_\_ therapy / surgery ( ) \_\_\_\_\_

INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)							
	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating ?	0	1	2	3	4	5	
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating ?	0	1	2	3	4	5	
3. Over the past month, how often have you found you stopped and started again several times when you urinated ?	0	1	2	3	4	5	
4. Over the past month, how often have you found it difficult to postpone urination ?	0	1	2	3	4	5	
5. Over the past month, how often have you had a weak urinary stream ?	0	1	2	3	4	5	
6. Over the past month, how often have you had to push or strain to begin urination ?	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 or more times	
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning ?	0	1	2	3	4	5	
<b>Total I-PSS Score S=</b>							
QUALITY OF LIFE DUE TO URINARY SYMPTOMS							
	Delighted	Pleased	Mostly satisfied	Mixed about equally satisfied and dissatisfied	Mostly Dissatisfied	Unhappy	Terrible
1. If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that ?							
<b>Quality of Life assessment index L=</b>							

If available enter data for  $Q_{max}$  (cc/sec),  $R_{res}$  (residual urine) and  $V_{post}$  (prostate volume) : S \_\_\_\_\_ L \_\_\_\_\_ Q \_\_\_\_\_ R \_\_\_\_\_ V \_\_\_\_\_  
 (Code for R and V : TA = Transabdominal, TR = Transrectal Ultrasound, MRI, CAT = CT scan, IVU, DRE = Digital rectal examination, END = Endoscopy, I&O = Catheterization, X = Other).

FIG 1—International prostate symptom score

- Are your symptoms sufficiently bad for you to want to take treatment on a regular basis?
- Are your symptoms bad enough for you to consider having an operation in an attempt to improve them?

#### INVESTIGATIONS

A "focused examination" follows evaluation of the symptoms. This consists of an abdominal and rectal examination, and though the clinical information gleaned is relatively small this physical examination aims to exclude those few patients with a palpable bladder or a hard, craggy, irregular prostate. Unfortunately the association between prostatic size as assessed by rectal examination and benign prostatic obstruction is extremely poor. Hence it is possible to have very large glands with no element of obstruction, and quite small glands with obstruction severe enough to cause renal impairment. In addition, a midstream specimen of urine should be examined microscopically to exclude the presence of red cells or white cells, or indeed neoplastic cells that might come from an unsuspected bladder tumour. Serum creatinine measurement will exclude significant renal impairment. Whether or not to test for prostate specific antigen is extremely contentious as there is as yet no evidence that early diagnosis of prostate cancer or the timing of the treatment of prostate cancer makes any difference to the length of the patient's life. It seems

logical to diagnose prostate cancer as early as possible and to treat it at an early stage, so there is considerable pressure to test for prostate specific antigen in younger men. I believe that a prostate specific antigen should be tested only in men under the age of 70 who, if discovered to have localised prostate cancer, could then be included in a randomised controlled trial of radical prostatectomy against delayed treatment. The extraordinarily slow development of prostate cancer makes this tumour different from other cancers.

Having talked to the patient and performed a focused physical examination and some laboratory tests, the general practitioner should be in a position to exclude three groups of patients—those who have come seeking reassurance, those with suspected prostate cancer, and those patients who require immediate referral because of complications such as recurrent urinary infections, bladder stones, haematuria, chronic retention, and upper tract deterioration with the consequent risk of renal impairment.

#### Treatment options

If the patient wants treatment and, after discussion, the doctor believes this to be reasonable, because of a significant impairment in quality of life, then the treatment options can be discussed. These consist of conservative treatment, drug treatment, established surgical techniques, and alternative surgical techniques (fig 2).

#### CONSERVATIVE TREATMENT

Unless the symptoms are greatly impairing the quality of his life, most patients are happy to accept a period of non-medical, non-surgical treatment. Con-

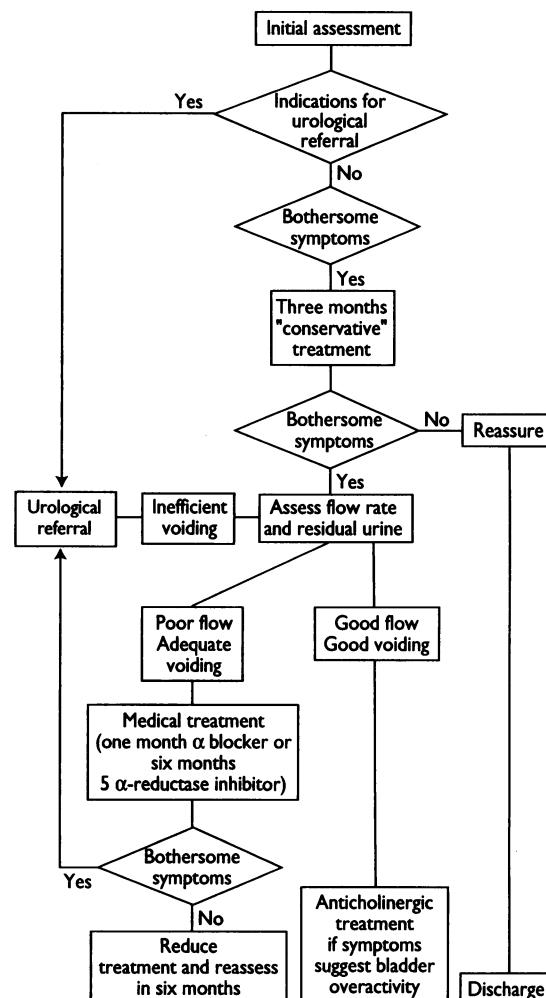


FIG 2—Patient management in general practice

### Initial assessment of lower urinary tract symptoms

Lower urinary tract symptoms have a poor correlation with the presence or absence of obstruction

- Only urgency and urge incontinence show any consistent association with a micturition abnormality (detrusor instability)
- Use the international prostate symptom score to quantify symptoms
- Rectal examination helps exclude carcinoma
- Test for prostate specific antigen if a diagnosis of carcinoma will influence treatment
- Identify patients who require urgent urological referral

servative treatment is readily justified by the fact that there is usually a good response to such treatment and that there is no evidence that important deterioration will occur over three to six months without active intervention. In the days of three to five year waiting lists, patients were rarely admitted from the prostate waiting list in acute retention of urine as an emergency, and this has been borne out by the limited studies on the clinical course of lower urinary tract symptoms and benign prostatic obstruction.<sup>5,6</sup>

Conservative management is based on the patient's completion of a frequency-volume chart, arguably the most useful test in lower urinary tract symptom dysfunction. The patient records intake and output over seven days. The chart gives important data, both for the patient and for the doctor. The patient may realise that the acquisition of a tea maker on retirement was counterproductive as regards his urinary symptoms. He may also realise that his nocturia can be moderated by reducing his intake during the evenings. Part of the considerable placebo effect seen in treatment of patients with lower urinary tract symptoms probably relies on the patient adjusting the timing and quantity of his fluid intake. Indeed in the ongoing International Continence Society benign prostatic hyperplasia study a quarter of patients reported that they restrict their fluid intake.<sup>7</sup>

If the patient has troublesome filling symptoms, including frequency, urgency, and urge incontinence, then formal bladder training can be instituted on the basis of the frequency-volume chart. Kadow showed that patients treated in this way have an excellent response.<sup>8</sup> During bladder training the patients are asked to increase both the intervals between voids and the voided volume. It may also be useful to teach the patient pelvic floor exercises so that any unwanted detrusor contractions can be counteracted by a more effective holding mechanism, during which the pelvic floor is contracted. Lastly, in some patients, drinks containing caffeine and alcoholic beverages may be usefully reduced or regulated as they can produce a disproportionate increase in symptoms.

It is reasonable to continue conservative treatment for three to six months, monitoring the effect with

### Conservative treatment

- Symptoms, and indeed obstruction, have a long clinical course
- Use the frequency-volume chart and international prostate symptom score to chart the patient's progress
- Advise on fluid intake
- Teach bladder training and pelvic floor exercises when necessary
- Reassess in three to six months

frequency-volume charts. If improvement is insufficient or if symptoms deteriorate, more active treatment can be instituted.

### DRUG TREATMENT

Before giving drugs or intervening surgically, more objective evidence of bladder outlet obstruction is desirable. This allows treatment to be more effectively directed and it has been shown to be cost effective,<sup>4</sup> as one third of patients with lower urinary tract symptoms have no bladder outlet obstruction. A one month course of an  $\alpha$  blocker costs £27, and a six month course of a 5- $\alpha$  reductase inhibitor costs £150—and urine flow studies cost only £30. Although urine flow studies have a higher diagnostic accuracy than symptom analysis, their usefulness is limited by their lack of specificity. This is because low flow is caused not only by bladder outlet obstruction but also by detrusor underactivity, and high flow may be associated with bladder outflow obstruction if the bladder is able to generate supranormal pressures to maintain a normal flow rate. The accuracy of flow studies is greatest at the extremes: nine out of 10 men with a maximum urine flow rate <10 ml (for a voided volume of greater than 150 ml) have bladder outlet obstruction, and 80% of men with a flow rate >15 ml have no bladder outlet obstruction.<sup>4</sup>

### Drug treatment

- Some objective evidence of bladder outlet obstruction should be sought before treatment
- Drug treatment gives moderate relief of symptoms
- Only  $\alpha$  blockers and 5  $\alpha$  reductase inhibitors have been shown to be effective
- Patients should be formally reassessed after one month with  $\alpha$  blockers and six months with 5  $\alpha$  reductase inhibitors

As general practice expands its range of facilities urine flow studies could be offered as a service. However, urinary flow studies are surprisingly difficult to interpret and there is a significant error rate in interpretation, so most companies organising large drug trials submit all flow rate data to a central quality control group. It is probably best that urological units offer an open access facility for urinary flow studies so that general practitioners are provided with a report including a likely clinical diagnosis. Urinary flow studies allow patients to be categorised (fig 2). The measurement of residual urine, which is a routine in many flow clinics, further helps this subdivision. Unfortunately, post-void residual, like maximum urine flow rate, fails to make an absolute diagnosis as it does not distinguish between a significant post-void residual secondary to bladder outlet obstruction and one due to detrusor underactivity. On the basis of urinary flow studies and post-void residual, patients can be divided into those who void efficiently—that is, empty at least two thirds of their bladder capacity—and those who do not. Patients with inefficient voiding should be referred to the urologist as there is no data to support drug treatment in these patients: such patients are always excluded from drug trials. As the algorithm shows, patients with adequate voiding and low flow rates (<15 ml/s) can be treated with an  $\alpha$ -blocker or a 5- $\alpha$  reductase inhibitor, the only effective classes of drug.  $\alpha$  Blockers work rapidly, but 10% of patients have significant side effects, usually lightheadedness; the 5- $\alpha$  reductase inhibitors show objective evidence of relief of bladder outlet obstruction only after the patient has taken the drug for six months. However, patients often feel better when taking a 5- $\alpha$  reductase

inhibitor thanks to the splendid placebo effect in this group of patients, which gives the patient the impression of early drug efficacy. New drugs will come on the market, and a more highly specific  $\alpha$  blocker ( $\alpha_{1c}$  blocker), available in some countries, seems to have as low an incidence of side effects as the 5- $\alpha$  reductase inhibitors (K Kawabe, 23rd congress of the Societ  Internationale d'Urologie, 1994).

Combination treatment with an  $\alpha$  blocker and a 5 $\alpha$  reductase inhibitor has not yet been shown to be more effective than either single agent. If after one month of treatment with an  $\alpha$  blocker or six months of 5- $\alpha$  reductase the patient's quality of life is still appreciably impaired the patient and the general practitioner should discuss the possibility of surgery.

#### SURGICAL TREATMENT

Transurethral resection of the prostate is still the most commonly performed surgical procedure for patients with lower urinary tract symptoms and benign prostatic obstruction. Good data exist on its mortality and morbidity, both in the short term and in the long term. Furthermore, data exist on the reoperation rate for transurethral resection of the prostate in comparison with open prostatectomy, which is now only performed in very large glands (about 5% of prostatectomies). Transurethral resection of the prostate is generally effective and safe, producing success rates of 90% with the best selection methodology.

In transurethral resection of the prostate tissue is rapidly removed under direct vision, at approximately a gram of prostate per minute. Sixty minutes is thought to represent a maximum safe resection time; during this time a gland of 60-100 g can be safely removed. Few glands are larger, and these are removed by retropubic prostatectomy. None of the currently available new techniques has either the surgical accuracy or this speed of tissue removal. In these respects the new techniques cannot compete with transurethral resection of the prostate. Morbidity from transurethral resection of the prostate is mainly due to bleeding and to the absorption of irrigation fluid, leading in extreme cases to the rare transurethral resection syndrome. This morbidity has spurred the search for alternative techniques.

#### ALTERNATIVE SURGICAL TECHNIQUES

In the United States all new modalities of treatment for benign prostate obstruction are subject to strict licensing regulations and control by the Food and Drug Administration. A similar scheme will come into force in 1995 in the European Union. This will prevent ad hoc trials of new treatments in patients with lower urinary tract symptoms. There have been a plethora of poorly controlled and scientifically inadequate studies on the various treatments—an unsatisfactory situation that, in some cases, may have delayed the implementation of effective techniques. It is becoming

#### Surgical treatment

- Only transurethral resection of the prostate and retropubic prostatectomy have proper data and outcome
- New treatments are in their infancy
- At present, new treatments should be offered only in the context of randomised controlled trials

recognised that new treatments must be exposed to rigorous scientific scrutiny; in many cases this has not happened.

Alternative techniques involve either tissue removal or the implantation of devices to stent open the prostatic urethra. Plastic or tubular metal stents have been used, but these have never been subjected to randomised controlled trials and are generally advocated for elderly and infirm patients in whom transurethral resection of the prostate is thought to be unacceptably risky. These stents are seen as second best treatment, to be used only in selected patients. Stents are associated with an appreciable early morbidity due to voiding discomfort, later complications of tissue ingrowth which may block the stent, and stone formation on the stent. There is no long term data on stents.

The most interesting possible new alternatives to transurethral resection of the prostate involve "removing" tissue. These techniques—laser, pyrotherapy, microwave, radio frequency—have attracted considerable interest. As with stenting, there has been very little proper scientific scrutiny, and no randomised controlled trials that include full preoperative investigation and postoperative assessment have been published. I believe that alternative therapies should be viewed as experimental: patients treated by these methods should be included in proper clinical trials. One such trial, of laser prostatectomy versus transurethral resection of the prostate versus conservative treatment, is being carried out in the departments of urology at Southmead Hospital and the Freeman Hospital, Newcastle, and is funded by the Research and Development Directorate.

Tissue can be destroyed by two main methods: heat and cold. Cryotherapy will not be dealt with here, although it was used successfully in elderly and infirm patients at Norfolk and Norwich Hospital in the 1970s and 1980s. This treatment might justify a new, properly conducted trial. The box lists the new methods of destroying the prostate by heat. Methods that use heat have the great advantage of causing blood vessel coagulation and reducing one of the main complications of transurethral resection of the prostate, which is blood loss. None, other than the contact laser, can accurately predict the amount of tissue destruction that will result from the application of energy. A variable zone of tissue necrosis results, depending on several factors: the nature of individual's prostatic tissue will determine the effect of the heat on the tissue and the degree of conductivity to neighbouring tissue, and the blood supply of the prostate and the ability of blood flow to increase in the prostate or in the periprostatic tissues will influence the effect of heat, as these vessels act as an efficient heat exchanger.

#### Conclusions

Many patients with lower urinary tract symptoms can be satisfactorily managed conservatively. Drug treatments may represent a step towards prostatic surgery, but in many patients it is acceptable long term. Transurethral resection of the prostate remains the most effective procedure for removing a benign

#### Destroying the prostate by heat

	Position of device	Means of directing energy	Immediate tissue removal
Laser:			
Non-contact	Urethral	Visual or ultrasound	No
Contact	Urethral	Visual	Yes
Needle	Urethral	Visual	No
Radiofrequency	Urethral	Visual	No
Thermotherapy	Urethral or rectal	Catheter balloon or ultrasound	No
High intensity focused ultrasound	Rectal	Ultrasound	No
Pyrotherapy	Extracorporeal	Ultrasound	No

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."<sup>1</sup> Over 40 years ago Lawrence wrote that many diabetic patients aged over 70 were insulin deficient.<sup>2</sup> 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.<sup>3</sup> 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/m<sup>2</sup> 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.<sup>4</sup> Insulin dependent diabetes can be diagnosed by clinical criteria. Kilvert *et al*<sup>5</sup> 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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