insulin to cover meals there is likely to be sufficient B cell failure for continuation of a sulphonylurea to be of marginal benefit, and it can be withdrawn. Simple guidelines on the use of tablets and insulin⁴ can cater for most patients until long term studies show a different regimen to be particularly beneficial.

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- 1 UK prospective study of therapies of maturity-onset diabetes. Effect of diet, sulphonylurea, insulin or biguanide therapy on fasting plasma glucose and body weight over one year. *Diabetologia* 1983;24:404-11.
- 2 Holman RR, Turner RC. A practical guide to basal and prandial insulin therapy. *Diabetic Medicine* 1985;2:45-53.
- 3 Holman RR, Steenson J, Turner RC. Sulphonylurea failure in type 2 diabetes: treatment with a basal insulin supplement. *Diabetic Medicine* 1987;4:457-62.
- 4 Holman RR, Turner RC. Optimizing glycaemic control in type 2 diabetes: an approach based on fasting blood glucose measurements. *Diabetic Medicine* (in press).

In vitro fertilisation

SIR,—Mr David Barlow and others (12 March, p 751), Mr Peter Bromwich and others (12 March, p 759), and subsequent correspondents (9 April, p 1064) discussed means of improving oocyte collection and pregnancy rates and methods of cutting costs. The emphasis has been on various methods of oocyte collection and on the practicalities of sharing the cost between the public and private sectors. We have improved cost effectiveness at the Lister Fertility Centre by routinely using a luteinising hormone releasing hormone analogue before oocyte collection by either the laparoscopic or an ultrasound directed trans-vaginal route.

One hundred and twenty consecutive patients receiving in vitro fertilisation and gamete intrafallopian transfer were treated with intranasal luteinising hormone releasing hormone analogue four hourly from the first day of their cycle until ovulation was induced with 10 000 IU of human chorionic gonadotrophin. Ovarian stimulation was achieved using two ampoules of human menopausal gonadotrophins daily from the third day of the treatment cycle. The mean number of ampoules used in each cycle was 20.7 (SD 9.2). The follicular development was monitored by vaginal or abdominal ultrasound studies without hormonal monitoring.

The cancellation rate because of inadequate ovarian stimulation was 6%, but no cycles were cancelled because of spontaneous ovulation. The flexibility provided by the analogue enabled us to perform an average of 15 procedures in only four operating sessions each week, with no weekend service. The mean number of oocytes collected at each procedure was 8.5 (5-9). The clinical pregnancy rate for in vitro fertilisation was 39% (14 out of 36 cases) and the pregnancy rate for gamete intrafallopian transfer was 41% (35 out of 84 cases). The early miscarriage rate was 14%. These pregnancy rates are higher and the early miscarriage rate lower than those commonly reported.^{1,2} These improvements may be the result of reduced maternal serum concentrations of luteinising hormone at the time of conception after the use of luteinising hormone releasing hormone analogue.

Although using the analogue is associated with a small increase in the amount of human menopausal gonadotrophin needed in each cycle, it obviates the need for serial assays of serum oestradiol or luteinising hormone, reduces the number of cancelled cycles, and allows oocyte collections to be performed on planned lists during normal working hours. These factors, coupled with increased pregnancy rates and reduced miscarriage rates,

suggest that using the analogue will increase the cost effectiveness of in vitro fertilisation programmes.

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- 1 Seibel MM. A new era in reproductive technology. *N Engl J Med* 1988;318:828-34.
- 2 Lancaster PL. *In vitro fertilisation pregnancies. Australia 1980-1986.* Sydney: Commonwealth Institute of Health, 1987.

Induced ovulation in underweight women

SIR,—We were concerned by the recommendations of Mr Z M van der Spuy and others to withhold induction of ovulation and advocate weight gain in underweight anovulatory women (2 April, p 962).

We have compared their analysis of 41 singleton pregnancies resulting from induction of ovulation with our data from 71 singleton pregnancies, 12 induced with pulsatile gonadotrophin releasing hormone and the rest by human menopausal gonadotrophin. Our overall risk of delivering a baby with a birth weight below the 10th centile was 20% compared with 25% in their study, and our risk for underweight women was only 43% compared with theirs of 54%. The risk for women of normal weight was 13%, slightly above their figure of 11%. We found an overall abortion rate of 30%, with 27% in women of normal weight, 50% in the overweight, but only 22% in the underweight group.

It must be emphasised that having a baby whose weight falls below the 10th centile does not necessarily imply intrauterine growth retardation and the dire problems cited by Dr van der Spuy and others. Few of the small babies in our study even required neonatal intensive care.

We have been impressed by the beneficial effects of a successful pregnancy in underweight women on their subsequent weight gain, with the restoration of menses and spontaneous conception. Some of these women respond better to the responsibilities of motherhood than to exhortation to gain weight alone.

What concerns us particularly, however, about the insistence on weight gain and the withholding of stimulant treatment is the well documented evidence of the decline in natural fertility with age and the impairment of response to ovarian stimulants in women aged over 31.¹ By withholding treatment we could be denying them any possibility of fertility. Women requiring ovarian stimulant treatment for conception have a greater risk of a small baby even when they are of normal weight. Rather than denying treatment to the underweight we should be monitoring all such pregnancies closely.

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- 1 Ginsburg J, Bowes L, Osgood VM. Pregnancy in infertile couples. *N Engl J Med* 1984;310:1334-5.

Imaging of the urinary tract

SIR,—We endorse the conclusion by Dr G de Lacey and others (2 April, p 965) that routine urography is unnecessary in the assessment of patients with prostatism, but we are concerned that they make no mention of urine flow rates or

ultrasound measurement of residual urine. They imply that symptoms and, if necessary, cystoscopy are reliable guides to the severity of prostatic obstruction. This is not the case.

The assessment of prostatic size at endoscopy is often inaccurate.¹ The size of the prostate may be misleading as anatomical enlargement is only part of the pathophysiology of bladder outflow obstruction: dynamic and functional mechanisms are also important. The classical prostatic symptoms are a poor guide to the presence of severity of obstruction.^{2,3}

Multiple measures of the rate of urine flow and ultrasound studies of residual urine can differentiate the obstructed from the non-obstructed bladder and identify patients at risk from urinary retention or upper tract dilatation. Patients presenting with prostatic symptoms who do not have significant bladder outflow obstruction will not benefit from surgery, and others, with mild or moderate obstruction but little residual urine, can be managed conservatively.⁴ Objective assessment of patients tends to produce a low operation rate and improves the results of surgery.⁵ A urine flow rate clinic (incorporating a small real time ultrasound machine) is easily incorporated into a urology outpatient department and may be run by a nurse.

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- 1 Mitchell JP. *The principles of trans-urethral resection and haemostasis.* Bristol: J Wright, 1972.
- 2 Abrams PH, Feneley RCL. The significance of symptoms associated with bladder outflow obstruction. *Urol Int* 1978;33:171-4.
- 3 Andersen JT, Nordling J, Walker S. Prostatism I. The correlation between symptoms, cystometric and urodynamic findings. *Scand J Urol Nephrol* 1979;13:229-36.
- 4 Ball AJ, Feneley RCL, Abrams PH. The natural history of untreated prostatism. *Br J Urol* 1981;53:613-6.
- 5 Abrams PH. Prostatism and prostatectomy: the value of urine flow rate measurement in the pre-operative assessment for operation. *J Urol* 1977;177:70-1.

Drug addicts and the GP

SIR,—Dr Tessa Richards (16 April, p 1082) is too optimistic. Few general psychiatrists have much time for addicts, and it is unreasonable to expect general practitioners to be any more enthusiastic, especially when they will not be paid extra for their trouble. This is a pity because they could undoubtedly do a lot for drug addicts, including those addicted to "our favourite drug," alcohol.¹ In Denmark general practitioners routinely give supervised disulfiram.²

General practitioners could easily prescribe methadone for maintenance or withdrawal, and anxiety about diversion of supplies would be reduced if it were swallowed under the pharmacist's supervision. Most pharmacists are willing to supervise. However, general practitioners would need to understand that the success of a methadone programme is judged not only by how many addicts withdraw from opiates but also by how many are able, while taking methadone, to avoid lives of crime, degradation, and infection with the human immunodeficiency virus.

General practitioners should see their local drug dependency units as centres of excellence and expertise. Regrettably, the users say that the standard of service is frequently poor. Time consuming and repeated assessments of dubious value are often required, and clinic hours rarely cater for the many addicts working hard to rebuild their lives and finances. The lack of medical research in many such units is a disgrace.

"It is no longer justifiable for one physician to spend twice as much money as another on treating patients with similar diseases," yet it is almost embarrassing to report that only the private sector seems to be using well researched, humane, and acceptable techniques which reduce the duration of opiate withdrawal from the usual two to three weeks to two to three days or less.^{4,6}

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- 1 Royal College of Psychiatrists Committee. *Alcohol—our favourite drug*. London: Royal College of Psychiatrists, 1987.
- 2 Jensen E. A proper use of Antabuse: the Danish model of treatment. *Br J Clin Pract* 1984;38:10.
- 3 Stoll B. Balancing cost and benefit in treatment of late cancer. *Lancet* 1988;i:579-80.
- 4 Charney D, Riordan C. Clonidine and naltrexone: a safe, effective and rapid treatment of abrupt withdrawal from methadone. *Arch Gen Psychiatry* 1982;39:1327-32.
- 5 Kleber H, Topazian M, Gaspari J. Clonidine and naltrexone in the out-patient treatment of heroin withdrawal. *Am J Drug Alcohol Abuse* 1987;13:1-17.
- 6 Brewer C, Rezae H, Bailey C. Opioid withdrawal and naltrexone induction in 48-72 hours with minimal drop-out using a modification of the naltrexone-clonidine technique. *Br J Psychiatry* (in press).

Fibre and patients with diabetes

SIR,—Ms V A Beattie and others (23 April, p 1147) state that viscous fibres have no therapeutic benefit for type II diabetic patients when added to a low energy, high carbohydrate, low fat diet. In their study the lack of washout periods between different treatments is unwise and could lead to misleading results, especially of concentrations of glycated haemoglobin. The method of giving the guar gum is not clear. Was it added to the main meals or given otherwise? Fasting blood glucose concentrations at the end of the run in periods were not grossly raised, an important factor for a beneficial effect from guar.

We have recently conducted an eight week randomised, non-crossover study of 15 g of guar mini tablets given daily before meals compared with placebo in 20 overweight non-insulin dependent (type II) diabetic patients who failed to respond to diet. Guar was well tolerated, although eight of 12 patients receiving guar experienced mild gastrointestinal upsets, which settled in one to two weeks in all but one patient.

Guar significantly reduced the fasting plasma glucose concentration (14.05 (SD 2.61) before treatment v 11.01 (2.02) mmol/l after treatment), postprandial glucose concentrations (17.50 (3.10) v 14.32 (3.60) mmol/l), glycated haemoglobin concentrations (9.96 (1.17) v 7.86 (1.00)), total cholesterol concentrations (7.44 (1.90) v 6.78 (2.20) mmol/l), and triglyceride concentrations (3.8 (2.18) v 2.99 (1.47) mmol/l) (in each case $p < 0.05$). No changes were observed in these variables with placebo.

Six out of nine patients in the guar group lost their symptoms of hyperglycaemia during the study compared with one of eight in the placebo group. Our results show a therapeutic benefit conferred by guar gum, and we conclude that it is effective in patients whose blood glucose concentrations remain high despite dietary measures.

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SIR,—Non-viscous, non-digestible materials in the diet have no important influence on the meta-

bolic control of diabetes. In contrast, viscous fibre, when intimately mixed with food, has been shown to delay carbohydrate absorption and lower serum concentrations of cholesterol. Many papers have been published to this effect.¹ Ms V A Beattie and others (23 April, p 1147) do not contribute usefully to them.

It is well recognised, for example, that guar, like many other treatments, must be started slowly. We prescribe half a satchet (2.5 g) with the evening meal for the first week of treatment and increase this slowly to a maximum of 10 or 15 g daily. If this is done over three to six weeks minimal bowel symptoms result and compliance is good. In contrast, a high proportion of patients begun on 15 g a day all at once will suffer from severe bowel symptoms.

For the best effect the gum needs to be mixed with the food.^{2,4} This is presumably because its effect is achieved through increasing the viscosity of the gastric chyme, preventing ingress of digestive enzymes and increasing the unstirred layer in the small intestine, both effects being likely to delay the absorption of nutriment. Indeed, drinking guar with a glass of water before the meal seems designed to frustrate its effective action by reducing mixing of guar with the food. The authors did not describe their mode of giving guar—a surprising omission.

If the optimal fasting blood glucose concentration is taken as 5 mmol/l the two groups on high fibre diets at 20 weeks were above this target by 1.8 and 1.5 mmol/l, while the low fibre group was above it by 2.8 mmol/l. This difference could be biologically important, and the lack of statistical significance might reflect the design of the trial and the small numbers of patients studied rather than a true lack of effect.

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- 1 Federation of American Societies for Experimental Biology. *Physiological effects and health consequences of dietary fibre*. Washington, DC: FASEB, 1987.
- 2 Fuessl HS, Williams G, Adrian TE, Bloom SR. Guar sprinkled on food: effect on glycaemic control, plasma lipids and gut hormones in non-insulin dependent diabetic patients. *Diabetic Medicine* 1984;4:463-8.
- 3 Fuessl HS, Adrian TE, Bacarese-Hamilton AJ, Bloom SR. Guar in NIDDM: effect of different modes of administration on plasma glucose and insulin responses to a starch meal. *Practical Diabetes* 1986;3:258-60.
- 4 Wolever TMS, Jenkins DJA, Nineham R, Alberti KGMM. Guar gum and reduction of postprandial glycaemia: effect of incorporation into solid food, liquid food, and both. *Br J Nutr* 1979;41:505-10.

Neisseria gonorrhoeae resistant to tetracycline

SIR,—Dr M A Waugh and others (26 March, p 898) discuss the isolation of tetracycline resistant *Neisseria gonorrhoeae* in the United Kingdom. We have also encountered infections caused by these organisms in patients attending the Praed Street Clinic at St Mary's Hospital. Since our original report of eight such infections¹ we have isolated a further six strains of tetracycline resistant gonococci, all from heterosexual patients.

Recently we have encountered a strain of *Neisseria meningitidis* that also has high resistance to tetracycline (minimum inhibitory concentration > 8 mg/l). This was isolated from the pharynx of a homosexual man during screening for pharyngeal gonorrhoea. Analysis showed the presence of a plasmid of approximately 25.2 megadalton. A similar isolate of *N. meningitidis* (received from Dr M S Sprott at the Newcastle Public Health Laboratory) showed a plasmid of identical size. In gonococci the determinant for high level resistance

to tetracycline is integrated into the conjugal plasmid to give a plasmid of 25.2 megadalton.²

Plasmids are unusual in meningococci, although low molecular weight cryptic plasmids have been described.^{3,4} To our knowledge there has been only one report of plasmid mediated antibiotic resistance in a clinical isolate.⁵ This strain carried both a penicillinase encoding plasmid of 4.5 megadalton and a conjugal plasmid of 24.5 megadalton. Transfer of penicillinase plasmids between gonococci and meningococci has been achieved in vitro, but acceptance of the conjugal plasmid by the meningococci has not been shown.^{6,7}

The presence of a 25.2 megadalton plasmid in these two isolates of meningococci, which both exhibit high level resistance to tetracycline, is alarming. This plasmid may have been acquired from gonococci. If this is true the plasmid will be capable of self transfer,² allowing further dissemination of tetracycline resistance. Both of these isolates were associated with asymptomatic carriage. This means that the presence of the 25.2 megadalton plasmid could easily remain undetected. While tetracycline resistance is not of concern in meningococcal disease, the presence in the pharynx of meningococci that carry self transmissible plasmids is worrying. Meningococci should be screened for tetracycline resistance, particularly in areas where the 25.2 megadalton plasmid has been found in gonococci.^{1,8}

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- 1 Ison CA, Terry P, Bindayna K, et al. Tetracycline resistant gonococci in UK. *Lancet* 1988;i:651-2.
- 2 Morse SA, Johnson SR, Biddle JW, et al. High-level tetracycline resistance in *Neisseria gonorrhoeae* is due to the acquisition of the streptococcal tet M determinant. *Antimicrob Agents Chemother* 1986;30:664-70.
- 3 Verschueren H, Dekegel M, Dekegel D, et al. Plasmids in *Neisseria meningitidis*. *Lancet* 1982;i:851-2.
- 4 Ison CA, Bellinger CM, Glynn AA. Plasmids in throat and anogenital isolates of meningococci. *J Clin Pathol* 1984;37:1123-8.
- 5 Dillon JR, Pauze M, Yeung KH. Spread of penicillinase producing and transfer plasmids from the gonococcus to *Neisseria meningitidis*. *Lancet* 1983;i:779-81.
- 6 Genco CA, Knapp JS, Clark VL. Conjugation of plasmids of *Neisseria gonorrhoeae* to other *Neisseria* species: potential reservoirs for the β -lactamase plasmid. *J Infect Dis* 1984;150:397-401.
- 7 Ikeda F, Tsuji A, Kaneko Y, Nishida M, Goto S. Conjugal transfer of beta-lactamase-producing plasmids of *Neisseria gonorrhoeae* to *Neisseria meningitidis*. *Microbiol Immunol* 1986;30:737-42.
- 8 Anonymous. *Tetracycline resistant Neisseria gonorrhoeae*. Collingbourne: Public Health Laboratory Service, 1987. (Communicable Disease Report No 46.)

Meningococcal meningitis

SIR,—Dr G Venkat Raman (23 April, p 1141) stated that rifampicin is the prophylactic drug of choice for meningococcal meningitis. A 14 year old girl was admitted in the last week of March 1988 with what proved to be meningococcal meningitis. Rifampicin prophylaxis was given to all of her close contacts. It was shown subsequently by disc diffusion tests that this isolate was resistant to the sulphonamides and rifampicin, and these results were confirmed by the Meningococcal Reference Laboratory.

This strain was sensitive to the tetracyclines and ciprofloxacin, and ciprofloxacin was given prophylactically to the home contacts. We were told that this had been used successfully at a naval establishment (N Gaunt, personal communication) to protect adolescents. No adverse effects were reported, and so far no evidence of secondary meningococcal disease has occurred.