- 3 Hobel CJ, Youkeles L, Forsythe A. Prenatal and intrapartum high risk screening. *Am J Obstet Gynecol* 1979;135:1051-6.
- 4 Guzik DS, Daikoku NH, Kaltreider DF. Predictability of pregnancy outcome in preterm delivery. *Obstet Gynecol* 1984; 63:645-50.
- 5 Holbrook RH Jr, Laros RK, Creasy RK. Evaluation of a risk scoring system for prediction of preterm labour. *Am J Perinatol* 1989;6:62-8.

Authors' reply

EDITOR,—A J Lyon and colleagues mention interesting data that they, in common with others, have obtained about the association between neonatal infection and genital mycoplasmas and chronic lung disease. It seems reasonable to speculate that the existence of these organisms in a neonate at least partially reflects bacterial vaginosis in the mother since both organisms are associated with bacterial vaginosis—*Mycoplasma hominis* more strongly than the ureaplasmas. On the assumption that this is the case, giving antibiotics that are active not only against the ureaplasmas but against the other bacteria found in bacterial vaginosis seems prudent.

Our responses to the concerns of Ann Yoong and of Cecilia J F Priestley and colleagues are as follows. We are continuing to look at our data, and in our current analysis there are 238 primigravidae. Four of the 197 women with normal (grade I) flora delivered before term compared with one of the nine with grade II flora and five of the 32 with grade III flora. Thus, as for other women with abnormal flora, primigravidae with grades II and III flora were significantly more likely to have a preterm delivery (odds ratio 6.7 (95% confidence interval 1.35 to 35.05); $P < 0.01$ (Fisher's exact test)).

We do not agree with Priestley and colleagues that bacterial vaginosis often has an identifiable underlying cause, and, as we pointed out, sexually transmitted infections, including those due to *Chlamydia trachomatis*, were rare in our pregnant population. We agree with Yoong that bacterial vaginosis is a chronic recurrent condition, but only in some women, not in all. We have seen women with bacterial vaginosis who miscarried and then, in a subsequent pregnancy with a normal vaginal flora, proceeded to term. In the initial analysis, however, only 25 women had a history of preterm birth, so it is difficult for us to draw conclusions about them. Nor does the strong association between bacterial vaginosis and late miscarriage or preterm birth enable us to prove causation.

We have been conscious throughout our work that the condition might be merely a marker for an underlying change, perhaps hormonal, that causes preterm birth, as Priestley and colleagues mention. That is why current investigations involving treatment of bacterial vaginosis in pregnant women are important. At the moment, if a doctor is aware that a pregnant woman has bacterial vaginosis it seems reasonable to discuss the condition and treatment with her, but we are not formulating a policy that would lead to unnecessary antibiotic treatment. Indeed, only if controlled trials of antibiotic treatment are shown to reduce the incidence of premature delivery would we recommend screening and treatment in pregnancy.

Finally, Yoong worries about generating a false sense of security in women with normal flora. Crude univariate analysis in our study shows that 96% of women with normal flora go to term compared with 83% of women with bacterial vaginosis. If this produces a false sense of security in women with normal flora we believe it to be misplaced.

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Haematuria clinics

Cystoscopy of little value in children

EDITOR,—In the editorial on haematuria clinics, Philip Marazzi and Roger Gabriel do not refer explicitly to children under 15 years old.¹ It would be unfortunate if unwary readers assumed, by default, that the problems of diagnosis and management in children are similar to those in adults; they are not.

Surgically remediable causes of haematuria in children are generally confined to the upper urinary tract and can be diagnosed by ultrasonography combined with plain abdominal radiography.² Bladder causes are rare and cystoscopy is generally unnecessary,^{3,4} yet paediatric nephrologists still see children referred with haematuria in whom cystoscopy has yielded normal results.

Once urinary tract infection, surgical causes, and rare medical disorders have been excluded most children with haematuria will be found to have a glomerulopathy. The most common causes are IgA nephropathy, Alport's syndrome, and thin membrane nephropathy,² but incompletely resolved poststreptococcal nephritis and unrecognised Henoch-Schönlein nephritis, with minimal rash, are occasional causes. The haematuria in thin membrane nephropathy and in girls with Alport's syndrome is usually only microscopic and should not be dismissed as necessarily benign.

When haematuria is persistent, familial, or accompanied by proteinuria or granular casts, renal biopsy will be required to determine the cause, and processing for immunofluorescence and electron microscopy is crucially important.² Not all patients, however, need a biopsy, at least immediately, and selection demands the skill and experience of a paediatric nephrologist, to whom these children are best referred.

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- 1 Marazzi P, Gabriel R. The haematuria clinic. *BMJ* 1994;308: 356. (5 February.)
- 2 White RHR. The investigation of haematuria. *Arch Dis Child* 1989;64:159-65.
- 3 Glasgow EF, Moncrieff MW, White RHR. Symptomless haematuria in childhood. *BMJ* 1970;iii:687-92.
- 4 Bullock N. Asymptomatic microscopic haematuria. *BMJ* 1986;292:645.

Open access is useful if rapid treatment is available

EDITOR,—Haematuria is often worrying for patient and doctor alike; it is the single most important symptom in urological practice. It should be taken seriously and investigated promptly to exclude an underlying malignancy. In this context, the concept of haematuria clinics¹ has become popular over the past 15 years. With the advent of flexible cystourethroscopy all the necessary investigations can be completed relatively quickly. Undoubtedly the provision of "rapid" haematuria diagnostic services will allay patients' anxieties, and there may be an associated survival benefit. The effectiveness of haematuria clinics was the subject of a recent review that concluded that such a service may result in an improvement in prognosis.² This also depends, however, on being able to provide rapid treatment after diagnosis.

We established an open access haematuria clinic 14 months ago and recently published the results.³ There is little point in running such a service if communication with general practitioners is inadequate. We encourage referrals by fax or telephone and see all patients within one week of referral. If the general practitioner has already sent urine specimens for microbiological and cytological examination then the diagnostic work up is finished within 24-36 hours of the patient being

seen in the clinic. Patients should undergo flexible cystoscopy only in a sterile theatre environment; therefore theatre time and space have to be available. A disadvantage of flexible cystoscopy is that biopsy specimens of suspicious areas cannot be obtained for histological examination. A concern that tumours might be missed that would be diagnosed with conventional rigid cystoscopy seems to be unwarranted.⁴ In addition, cystological examination of the urine is mandatory and, in particular, is a key investigation in carcinoma in situ of the bladder. Finally, the ability to provide such a service depends heavily on support services.

Two issues remain unresolved. Firstly, to avoid swamping such a service a sensible referral policy from primary care needs to be established and encouraged. Secondly, precisely what constitutes an appropriate diagnostic protocol varies among patients and remains a matter for debate.

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- 1 Marazzi P, Gabriel R. The haematuria clinic. *BMJ* 1994;308: 356. (5 February.)
- 2 Nathan MS, Naseem MS, Morgan RJ. Same day haematuria diagnostic service. *Journal of One Day Surgery* 1993;3(2):12
- 3 Britton JP. Effectiveness of haematuria clinics. *Br J Urol* 1993;71:247-52.
- 4 Walker L, Liston TG, Lloyd-Davies RW. Does flexible cystoscopy miss more tumours than rod-lens examination? *Br J Urol* 1993;72:449-50.

Human gonadotrophin preparations

Patients can't afford new drug

EDITOR,—Recently, a drug company launched a new gonadotrophin preparation and at the same time discontinued its previous product, which itself had been hailed as a major breakthrough on the basis that preparations containing low concentrations of luteinising hormone or follicle stimulating hormone alone were considered better at inducing ovulation. What concerns us is the sudden discontinuation of a product that many specialists had previously been encouraged to use. Though we believe in the advantage of preparations containing low luteinising hormone concentrations or follicle stimulating hormone alone,^{1,2} we are concerned for patients seeking treatment of infertility as many have to pay for their drugs.

We run a busy fertility clinic offering simple treatments such as superovulation with intra-uterine insemination,³ transvaginal ultrasound monitored egg release and insemination (follicles are lanced to ensure ovulation), and direct oocyte transfer, a modification of gamete intrafallopian transfer (GIFT).^{3,4} These are carried out as outpatient procedures, offering couples the opportunity of active management locally (reducing the stresses of travel). Without the costly fertility drugs, these three treatments would be much less effective,² and would give us substantially less than the 10-15% delivery rates per cycle that we currently achieve.

Our patients currently pay between £200 and £400 per cycle for their drugs. Now that the follicle stimulating hormone preparation (the mainstay of our fertility programme) has been replaced with purified follicle stimulating hormone at twice the price some couples will effectively be barred from further active management of their infertility. Some couples will elect to be treated with an older preparation containing high concentrations of luteinising hormone, simply because it is cheaper. This is ironic because the drug company previously claimed this older preparation to be less effective than the follicle stimulating hormone preparation it has now discontinued.

Would it not be possible to maintain supplies of urofollitrophin (Metrodin (Serono)) until further consultation? In addition, Organon has just launched a gonadotrophin preparation with low luteinising hormone concentrations (Normegon). Perhaps, Serono will reflect on the consequences of its unilateral action.

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- 1 Chappel SC, Howles C. Reevaluation of the roles of luteinizing hormone and follicle-stimulating hormone in the ovulatory process. *Hum Reprod* 1991;6:1206-12.
- 2 Mascarenhas L, Khastgir G, Davies WAR, Lee S. Super-ovulation and timed intercourse: can it provide a reasonable alternative for those unable to afford assisted conception? *Hum Reprod* (in press).
- 3 Davies WAR, Dhariwal HS, Lee S. GIFT and IUI in the district general hospital. *Hum Reprod* 1988;3:611-2.
- 4 Lee S. A simplified approach to the laboratory aspect of GIFT. *Hum Reprod* 1988;9(suppl):53-4.
- 5 Sterzik K, Rosenbusch B, Grab D, Lauritzen C. Pregnancies following direct oocyte-sperm transfer (DOST): a simple alternative to conventional in vitro fertilization (IVF). *Journal of In Vitro Fertilization and Embryo Transfer* 1991;8:241-2.

Manufacturer's response

EDITOR,—The human gonadotrophin preparations that have been used for 30 years are crude urinary extracts: 95-98% of the proteins are derived from serum and urine, and the hormone constitutes only 2-3% of the proteins.

The urine derived proteins in these preparations are uncontrolled and mostly unidentified; some are biologically active (uromodulin, IgG, epidermal growth factor, etc) (unpublished data). In analytical tests this heavy bulk of proteins masks the follicle stimulating hormone, which therefore is not characterised with respect to its isoform composition and profile. The only quality control is an in vivo animal bioassay developed in the 1950s, and this has a large inherent variability.

Recently, state of the art purification methods have been applied to obtain follicle stimulating hormone that is more than 95% pure, the other proteins being reduced to a minimum. To increase purity from 2-3% to over 95% entails severe losses during purification and expensive procedures. Stringent quality control of the highly purified follicle stimulating hormone preparation (Metrodin high purity (Serono)) is of a physico-chemical nature and guarantees batch to batch consistency of the hormone. This may reduce the intercycle variations in patients' responses that were observed with former gonadotrophin preparations.¹

The large amounts of extraneous proteins in gonadotrophin preparations have important clinical disadvantages. A recent report described severe local reactions to crude urinary gonadotrophins that did not reappear when the highly purified follicle stimulating hormone preparation was administered.² Further case reports from other countries confirm this observation.

Metrodin high purity is suitable for subcutaneous self administration, which appreciably reduces the stress and the financial burden of treatment as injections may be given at the patient's convenience without the need for frequent trips to a clinic or general practitioner's surgery. Thus the availability of a highly purified follicle stimulating hormone preparation may reduce the stress of infertility treatment, a factor linked to some cases of failure.³

In summary, Metrodin high purity is a state of the art drug whereas the old gonadotrophin preparations are obsolete crude urinary extracts. When a high purity drug is available the use of crude extracts cannot be justified. Serono has therefore discontinued Metrodin in the United Kingdom. Administration of a human gonadotrophin preparation such as menotrophin

(Pergonal (Serono)) is justified only in a small proportion of patients with hypogonadotrophic hypogonadism. In the near future the recombinant gonadotrophins that we are clinically evaluating should become available and replace all urinary preparations.

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- 1 Rector NA, Markusen TE, Stone BA, Marrs RP. Numbers and quality of oocytes after induction of multiple folliculogenesis in women and in mice with different lots of human menopausal gonadotrophins. *Fertil Steril* 1993;60:1082-7.
- 2 Li TC, Hindle JE. Adverse local reaction to intramuscular injections of urinary derived gonadotrophins: a case report. *Hum Reprod* 1993;8:1835-6.
- 3 Barnea ER, Tal J. Stress related reproductive failure. *Journal of In Vitro Fertilization and Embryo Transfer* 1991;8:15-23.

Increasing rate of deliberate self poisoning

EDITOR,—We note with interest the recent figures highlighted by the Samaritans showing that the incidence of suicide in males seems to be increasing. Our experience indicates that this also applies to hospital admission for deliberate self poisoning. Since 1987 the Cardiff Poisons Treatment Unit has received more than 90% of all patients admitted with self poisoning in South Glamorgan (population 403400). The table shows the data on men and women.

Although violent methods and gassing are the commonest means of committing suicide or

Numbers of men and women admitted with self poisoning in South Glamorgan by year with ratio of men to women

	1987	1988	1989	1990	1991	1992
Women	513	464	537	582	537	629
Men	299	283	357	432	441	557
Total	812	747	894	1014	978	1186
Men: women	0.58	0.61	0.66	0.74	0.82	0.89

inflicting fatal self injury in England and Wales (36.8% and 30.4% of deaths respectively),¹ self poisoning is the cause of death in 22% of cases. Non-fatal incidents of deliberate self poisoning may identify men at risk of subsequent fatal events. A regional poisons unit, as advocated in a report of the Royal College of Psychiatrists in 1983,² enables psychiatric and social support to be coordinated for such patients as soon as they have recovered medically; we commend such an approach in tackling this difficult problem.

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- 1 Office of Population Censuses and Surveys. *Mortality statistics by cause*. Vol 17. London: HMSO, 1990. (OPCS series DH2.)
- 2 Guidance on the management of deliberate self-harm. *Bulletin of the Royal College of Psychiatrists* 1983;7:210-2.

HIV infection in Uganda

EDITOR,—In the Rakai district of Uganda, Maria J Wawer and colleagues have shown that, despite universal knowledge of AIDS, extensive education, and programmes for distributing condoms, the incidence of HIV infection remains high.¹ The failure of such programmes to curb the epidemic

may not be unique to Rakai, given that HIV continues to spread in many parts of Africa where prevention programmes exist.² Rather than intensifying programmes,¹ however, we must ask why the necessary behavioural change has not occurred. We therefore conducted in depth interviews about the context in which people have sex. We drew our sample—17 key informants from three villages in Rakai and 31 female prostitutes and 44 other residents from Kimwanyi, a poor neighbourhood of Kampala—from those used in two unpublished studies that required representativeness of the population.

Preliminary analysis suggests the importance of three themes. Firstly, despite knowledge that a man has died of AIDS the tradition of "widow inheritance" continues; secondly, technical knowledge of use of condoms is poor: 25 of 32 men expressed uncertainty about how to put on a condom; and thirdly, many places where sexual intercourse is practised lack privacy and this thus adds stress to sexual play. In Rakai all respondents were or had been living with their parents until marriage; as love making is prohibited in the parents' house they could have sexual intercourse only in the banana plantation and the bush. In Kimwanyi 31 of the 44 non-prostitutes had frequented public latrines, 19 had used back streets, and 22 had used the bush for sex with premarital or extramarital partners in the past five years. Most of the prostitutes (26 of the 31), however, took their clients to their rooms, regardless of the presence of others.

Several questions emerge from the above. Firstly, why do men sleep with widows of men who have died of AIDS and why do widows have new sex partners? Secondly, how can young people learn to use safer sex? Thirdly, how can people practise safer sex in the bush? There are no straightforward answers, but, clearly, information in itself does not make people change behaviour. Sexuality is deeply rooted in people and cannot be modified in isolation of sociocultural and emotional aspects of life. Sex education will continue to remain difficult, but, unless contextual factors are taken into account, studies like that of Wawer and colleagues are likely to continue to generate concerns about the adequacy of prevention of transmission of HIV in many parts of Africa.

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- 1 Wawer MJ, Sewankambo NK, Berkley S, Serwadda D, Musgrave SD, Gray RH, et al. Incidence of HIV-1 in a rural region of Uganda. *BMJ* 1994;308:171-3. (15 January.)
- 2 Way P. *Recent HIV seroprevalence levels by country*. Washington, DC: United States Bureau of the Census, 1993.

Women's reproductive health

Women left destitute by AIDS

EDITOR,—Though women's reproductive health in the developing world undeniably depends on a country's "social, economic, and cultural pressures,"¹ the profound additional influence of HIV infection and AIDS should not be forgotten. Uganda seems to be doing its best to wake up the world. With 20 years of unrest and civil war, a ruined economy, minimal healthcare equipment, a dearth of medical professionals, and a 12% prevalence of HIV infection in the adult population, Uganda may seem from the outside to have a problem too bewildering to contemplate. Yet with insight into Ugandan society it is possible to under-