Map showing distribution of significant leukaemia incidence ratios (incidence ratio >1.0 ; $p<0.05$) at ages 0-14 in 143 electoral wards in West Berkshire and Basingstoke and North Hampshire District Health Authorities. Figures are numbers of cases. Bold outlines indicate urban areas. (● = Atomic Weapons Research Establishment, Aldermaston, ■ = Royal Ordnance Factory, Burghfield, and ▲ = United Kingdom Atomic Energy Authority's Establishment, Harwell.)

ignores all other nuclear sites. The more extensive analysis of data from the Office of Population Censuses and Surveys by Dr Paula Cook-Mozaffari (in press) provides a geographically more complete but very different picture. Selecting only the sites with an excess incidence from the full set is bound to give a biased average for the selected group.

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AUTHORS' REPLY—Though there have been no systematic studies of the completeness of cancer registration in Britain, the Childhood Cancer Research Group estimated that during 1971-6 91% to 95% of all childhood leukaemias in Britain were registered in the national scheme.¹ Reliable data for more recent years are not available, and the studies quoted by Dr Harte do not provide sufficient information for assessing the completeness of childhood cancer registration.

Dr Wade suggests that the excess incidence of childhood leukaemia around the nuclear establishments in our study was confined to the area around the Royal Ordnance Factory at Burghfield and that this might be explained by differences in disease frequency in urban and rural areas. Our analyses were designed to test the specific hypothesis that the incidence of leukaemia was increased in children living in the vicinity of the nuclear establishments in the study area. We had no prior hypothesis concerning any individual establishment, but we did note that the relative excess around the Atomic Weapons Research Establishment at Aldermaston was of a similar magnitude to that around the Royal Ordnance Factory at Burghfield.

The figure shows the leukaemia incidence ratios for 1972-85 in children aged 0-4 years living within 10 km of the United Kingdom Atomic Energy Authority's Establishment at Harwell, the Atomic Weapons Research Establishment at Aldermaston, and the Royal Ordnance Factory at Burghfield and within 10 km of both the establishment at Aldermaston and that at Burghfield. Most of the

Map showing leukaemia incidence ratios (observed/expected cases) at ages 0-4 in the West Berkshire and Basingstoke and North Hampshire District Health Authorities. Circles of radius 10 km are drawn around each nuclear establishment. (● = Atomic Weapons Research Establishment, Aldermaston, ■ = Royal Ordnance Factory, Burghfield, and ▲ = United Kingdom Atomic Energy Authority's Establishment, Harwell.)

population, and thus most of the children with leukaemia, live in the urban area of Reading. In the remaining, largely rural, areas the population is smaller and there are correspondingly fewer children with leukaemia. The incidence ratio is, however, not highest in the urban area of Reading, and there are no significant differences between the incidence ratios shown in the figure. Finally, the data presented by Cook-Mozaffari *et al* are not at variance with ours.²⁻⁴

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Irritable bowel syndrome as a cause of chronic pain in women attending a gynaecology clinic

SIR,—Mr Patrick Hogston suggests that 60% of women with "unexplained pelvic pain" in his study had the irritable bowel syndrome (11 April, p 934). We find it hard to equate the findings of this study with our own.

Research among patients attending the pelvic pain clinic at the Samaritan Hospital does not as a rule show symptoms attributable to the bowel. All new patients attending the clinic are questioned directly, and in the past six months only five patients out of 130 have had symptoms suggestive of the irritable bowel syndrome, while in a study conducted in 1985 and 1986 only three of 35

women had such symptoms (unpublished findings). Mr Hogston's study relied solely on a questionnaire to make the diagnosis. Few clinical details of the patients are given with regard to their reproductive history and use of contraceptives. The only investigation reported to have been done was laparoscopy. Though some clinicians may find that the Manning questionnaire provides enough evidence to diagnose this condition, such an approach takes no account of recent work on pelvic pain in women.¹

Dyspareunia was reported in 41 of 50 patients. The author describes this as an association of the irritable bowel syndrome, attributing it to a "tender colon" while quoting from a paper describing a multitude of symptoms, including nocturia, frequency, an unpleasant taste in the mouth, and a constant feeling of tiredness. Surely all one can really conclude from this report is that women with pain report many symptoms. To conclude that dyspareunia is a further manifestation of the irritable bowel syndrome is not justified.

Finally, there is another explanation for chronic pelvic pain in women of childbearing age; 80% of such women have been shown to have dilated pelvic veins and pelvic congestion.² This study was based on the firm evidence of pelvic phlebograms comparing normal subjects with patients with pelvic pain. A further study of the symptoms of these patients showed that their pain was aggravated by long periods of standing, during and after sexual intercourse, and in the premenstrual period (unpublished findings).

We believe that labelling patients as having disease on the basis of a questionnaire alone is likely to result in a misleading diagnosis. The conclusion on such scant evidence that the irritable bowel syndrome is the major cause of pain in women with normal findings at laparoscopy simply further muddies the waters of this difficult subject.

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1 Beard RW, Reginald PW, Pearce S. Pelvic pain in women. *Br Med J* 1986;293:1160-2.

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Pinch skin grafting or porcine dermis in venous ulcers

SIR,—Mr K R Poskitt and colleagues (14 March, p 674) are to be congratulated on their study of pinch skin grafting as there are very few randomised clinical trials on the management of venous ulcers. In particular, they show what can be achieved with experienced team care and relate some useful facts on healing rates.

The finding, however, that human skin is a better dressing for most ulcers than pig skin is hardly surprising. Nevertheless, before we all rush to use pinch grafts there are three points that are not clearly brought out in the discussion. Firstly, there seems to be a very wide variation in the healing rates in the pinch graft group, which suggests that not all pinch grafts take equally well on the same ulcer. Secondly, nearly a third of the patients in the pinch graft group required further grafts at around three to five weeks, yet there is nothing to show for this in the results. Thirdly, successful pinch grafts might be expected to maintain a high healing rate for the very reasons proposed by the authors—namely, length of epithelial margins and production of epithelial growth factors—yet the percentage reduction in ulcer size

differed only in the first two weeks and thereafter was similar to that in the pig skin group.

Infection is known to impair wound healing, and I would suggest that the bacteria present on the ulcer may have contributed to poor healing in some of the patients with pinch grafts. Chronic ulcers are rarely sterile, and *Pseudomonas* has been known for over 30 years to impair the healing of skin grafts¹ and has been linked to the failure of pinch grafts.² A retrospective study of partial thickness skin grafts for chronic leg ulcers at Northwick Park Hospital found that not only *Pseudomonas* but also *Staphylococcus aureus* significantly impaired the healing of grafts, their relative prevalence in ulcers being 60% and 17%, respectively (E L Gilliland, C Doré, N Nathwani, J D Lewis, fourth European American symposium on venous diseases, Washington, DC, 1978).

Pinch skin grafts may not be lifted by discharge from the ulcer but in my experience neither are properly prepared and applied partial thickness skin grafts; the skin applied is destroyed by bacteria or the enzymes produced by these bacteria. To suggest that pinch grafts may be applied "on granulating tissue within an ulcer that has been less than perfectly prepared" is bound to lead to a significant failure rate. Ulcer swabs are an important aspect of ulcer care and should always be taken before applying any form of skin graft.

If venous ulcer management is to be transformed from nineteenth century empiricism to a twenty first century science we need more trials like that of Mr Poskitt and coworkers—in particular, to compare non-biological dressings and the different forms of compression that have been advocated.

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Guidelines on halothane

SIR,—I am grateful to the chairman and former chairman of the Committee on Safety of Medicines (25 April, p 1100) for clarifying the final paragraph of my letter (28 March, p 836). During editing a paragraph heading was removed from my letter, which was intended to ensure that "no change" from previous advice referred only to post-operative fever, advice which conforms with the existing data sheets.

We agree, of course, that the substituting of a minimum interval of three months for 28 days between re-exposure to halothane, unless there are overriding clinical circumstances, does indeed considerably strengthen the advice given by the committee.

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Clinical Algorithms: Infertility

SIR,—Mrs T R Varma's algorithm on infertility (4 April, p 887) emphasises the importance of careful management and counselling of both partners. As sperm problems are the most common defined cause of a couple's infertility¹ the husband should be seen by a specialist with an interest in andrology (usually a urologist, endocrinologist, or gynaecologist) rather than simply being referred when varicocele or obstructive azoospermia are considered to require surgical intervention. Such a specialist is often available to a joint infertility clinic and has the delicate task of accurately

assessing the man before recommending treatment and can counsel from experience to minimise the inevitable denting of the male ego. Hence before referral for psychosexual counselling is considered it is important that aspermia, whether due to impotence or ejaculatory dysfunction, is investigated properly because specific treatments are available (intracavernosal papaverine, autonomic drugs).

If the duration of involuntary infertility is longer than three years the prognosis is poor.² Similarly, testicles are normally at least 4.5 cm long, 60% of testes 3-4 cm long showing impairment of spermatogenesis when biopsied (J P Pryor *et al*, paper presented at 5th European congress on sterility and fertility, 1978). Varicocele ligation is not usually carried out for high semen volume alone but more often for reduced sperm motility, a more important indicator of infertility. The inadequacies of conventional semen analysis techniques have been shown, however, by the use of the heterologous ovum penetration assay in defining sperm head dysfunction in cases of unexplained infertility where the semen is apparently normal.

There is always debate about the precise definition and importance of "low sperm count," "low motility," and "oligospermia," but artificial insemination by the husband is more likely to succeed when the semen volume is low (oligospermia) and in cases of ejaculatory dysfunction where sperm retrieval from the bladder or from artificial sperm reservoirs is carried out. The follicle stimulating hormone concentration is valuable in the assessment of severe oligospermia as well as azoospermia, the highest concentrations being found in patients with Klinefelter's syndrome. Hormonal problems are rarely found to be the cause of infertility in men, and hyperprolactinaemia has not been proved to cause semen abnormalities but may lead to impotence. It is more resourceful to investigate the possibility of hypogonadotrophic hypogonadism, a treatable cause of azoospermia as well as severe oligospermia.

The past decade has seen important advances in defining some of the disorders that cause male infertility but, sadly, few controlled treatment studies. If this matter is to be solved the husband should be regarded as a patient and not simply the provider of a semen sample for the treatment of his wife's infertility by whichever method is available.

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- 1 Hull MGR, Glazener CMA, Kelly NJ, *et al*. Population study of causes, treatment and outcome of infertility. *Br Med J* 1985;291:1693-7.
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SIR,—There are one or two points in Mrs T R Varma's algorithm on infertility (4 April, p 887) with which I feel I must take issue.

While I agree that in many patients the history may be unhelpful, there are still some cases in which the diagnosis may be made from the history alone. I was surprised that Mrs Varma did not mention the importance of a history of pelvic sepsis, such as appendicitis or acute salpingitis, both of which may lead to tubal problems. It is also important to inquire about hirsutism and to note its presence during the examination as this could indicate the polycystic ovary syndrome, which is an extremely important cause of failure to ovulate. Numerically, this is probably second only to weight related anovulation, and in this respect it is obviously important to inquire whether the patient has experienced any recent changes in weight. Also important is a history of smoking, which the

Oxford workers have shown to be of particular importance in subfertility.

I fail to see the relevance of asking the man whether he has any children from previous relationships as men, as well as women, may go on to develop secondary subfertility. In addition, I would dispute the relevance of temperature charts. Most infertility specialists believe that keeping temperature charts only makes the couple anxious; nowadays ovulation can be confirmed far more accurately with progesterone assays.

I would dispute the fact that the only thing necessary to do at the first visit is to give the patient a temperature chart and to obtain a semen sample. To wait three months before carrying out any further investigations is to lose valuable time. I believe that it is better to carry out all the investigations at the first visit so that by the time three months has elapsed the patient at least has a diagnosis.

I was surprised to read the recommendation of endometrial biopsy for the confirmation of ovulation. This has been shown to result in intrauterine adhesions¹ and an increased incidence of tubal blockage² as a result of infection. I would certainly agree that the value of postcoital tests is controversial, and their use has really been superseded by the cervical mucus sperm penetration test. I think that the doctor should perform this at an early stage rather than wait for a negative postcoital test because the cervical mucus factor is now considered to be important in subfertility.³

Finally, I would disagree with the view that it is not worth treating antisperm antibodies as Shulman *et al* have shown high dose steroids to be extremely successful in the treatment of this condition.⁴

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SIR,—Mrs T R Varma's algorithm on infertility (4 April, p 887) completely overlooks the importance of investigation of the uterus and its cavity, a major factor in infertility. It is hardly surprising, therefore, that Dr Varma finds that 20% of infertility is "unexplained."

Hysterosalpingography is a crucial, inexpensive investigation, which when done competently and gently is, in our experience, totally painless. Radiology can pinpoint congenital and other uterine deformities usually missed on laparoscopy, uterine polyps and submucosal myomas, uterine synechiae (surprisingly common in inflammatory disease), and partial patency disturbance of the uterotubal junction. Moreover, it gives unique information about tubal disease which is not gained at laparoscopy. It is extremely worrying that so many centres continue to perform the highly invasive procedure of in vitro fertilisation and embryo transfer without paying any attention to the cavity in which the embryo will implant.

With regard to age and infertility, Ms Christine P West (p 853) and Mrs Varma seem to be party to a conspiracy. Surely, emphasis should be given to urgent investigation in the older patient? Although your leader writer suggests that "age is not a major factor in infertility," statistics on reversal of sterilisation in previously parous women argue the