One example which casts doubt on the scientific validity of the guidelines is the comment "Benzodiazepines are not suitable for use in combination products." This extreme and unjustifiable pronouncement effectively abolishes all future research in this field (and who knows what clinical benefits may await present or future benzodiazepines coupled with some other known or unknown compound?), and in respect of current products it casts a judgment without allowing debate.

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Kidney biopsy

SIR,—The very clear description of the technique of renal biopsy (23 February, p 547) worries me because the authors imply that the procedure could be used in many hospitals. There are two reasons why this should not be so.

Firstly, to maintain competence in the procedure one needs to perform at least two biopsies each month. General medical wards are unlikely to provide sufficient patients for a single member of a firm to achieve or maintain expertise in kidney biopsy. Secondly, it is unfair to ask a pathologist to make a reasonable diagnosis unless he is reporting on at least 30 renal biopsies annually. In addition, light microscopy alone even in the best hands is inadequate for diagnosis. Immunofluorescent or immunoperoxidase studies and electron microscopy are essential for full morphological analysis. These techniques are only possible with the help of highly trained and skilled technical staff. Kidney biopsy is therefore a team procedure and every hospital cannot have such teams.

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SIR,—It is a great pity that recent contributions on needle biopsy of the kidney (23 February, p 547) and liver (15 March, p 776) should recommend a procedure at variance with that proposed by the manufacturers of the Tru-Cut needle. The instructions supplied with the needles were amended to improve safety, and operators should consult and comply with them.

The disposable Tru-Cut needle was introduced and became popular without formal comparison with the reusable Menghini needle. It is very much more expensive, and certainly for liver biopsy confers no advantage.[1]

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[1] Bateson MC, Hopwood D, Duguid HLD, Bouchier IAD. *J Clin Path* 1980;**33**:131-3.

SIR,—I noted your correction (8 March, p 700) to the table of contraindications to kidney biopsy (23 February, p 547); however, I feel that some of the haematological data still require comment.

A prothrombin time of greater than or equal to 16 seconds may be a contraindication, although a safer limit would be "not greater than 2-3 seconds longer than the time for control plasma" (which is from a pool of normal plasma samples and which may give times as short as 11 seconds, depending on the thromboplastin used in the test). Recording the result of the test plasma as a ratio of the control value is a recommended method.[1]

The expression of the platelet count $\times 10^{10}$/l [added in the subediting—ED, *BMJ*] is unfortunate when the conventional factor is $\times 10^{9}$/l,[2 3] the contraindication then becoming a platelet count under 100×10^{9}/l. One useful simple screening test in renal disease is the bleeding time,[4] which helps to detect abnormal platelet function (the major factor contributing to the haemostatic defect of uraemia). Abnormalities of platelet retention (in glass bead filters) and platelet factor 3 availability (decrease often associated with abnormal platelet aggregation) have been found in a variable percentage of uraemic patients by most investigators.[5] In general, however, these defects are observed in patients with clinically noteworthy bleeding and usually disappear after peritoneal dialysis or haemodialysis.[6]

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Vitamin D supplements in Asian women

SIR,—Dr O G Brooke and others (15 March, p 751) report a better calcium status in babies born to Asian women whose diets were supplemented by calciferol 1000 IU/day during pregnancy. The recommendation is therefore to give calciferol to pregnant Asian women. Before such a recommendation is adopted on a wide scale further information must be provided. If allocation to the trial were on a random basis, why at the end of the trial were there 67 women in the control group and 59 in the treatment group? Patients were excluded from the trial for reasons such as preterm deliveries and congenital malformation. Was there a higher incidence in these complications in babies born to mothers receiving the calciferol supplement, and if so can an explanation be provided?

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*** We sent a copy of this letter to the author, whose reply is printed below.—ED, *BMJ*.

SIR,—We thank Dr Bissenden for his interest and respond to his questions as follows:

(1) In all, 135 women entered the trial. They were allocated at random by the hospital pharmacy on the basis of their hospital numbers, and there were initially 63 in the treatment group and 72 in the control group. Simple statistical analysis shows that there is a 5% chance that the size of one of the groups could be less than 56 or greater than 79. Our group sizes were thus well within these limits.

(2) Three women in the control group and two in the treatment group withdrew, either because they moved to other areas before delivery or because they decided not to continue with the trial. Other exclusions were as follows: in the control group there was one preterm delivery and one neonatal death due to intrapartum anoxia and meconium aspiration; in the treatment group one woman was excluded because she developed gestational diabetes; and one infant had spina bifida. There is thus no evidence of a higher incidence of complications in the treatment group.

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Polypharmacy in rheumatic diseases

SIR,—We were pleased to read in your leading article (8 March, p 666) "Polypharmacy in rheumatic diseases" that the plasma half lives of drugs tend to be longer in older patients. We wish more pharmaceutical companies took notice of this statement, and would like to emphasise the need to establish the pharmacokinetic profile of various drugs in the older population before launching the sales of these drugs. It is well established that the older population is the major consumer of drugs,[1 2] in particular the antirheumatic agents, and yet when one screens the literature one is appalled by the paucity of information regarding the biological handling of these drugs by elderly patients. In fact, most of these parameters seem to be measured only in young healthy volunteers. Is it reasonable to extrapolate the findings to the older population, when it is well known that as the individual ages the intestinal mucosal surface area decreases,[3] the blood supply to the gastrointestinal tract decreases,[4] the hepatic and renal clearances become impaired,[4] the binding of drugs to plasma protein seems altered,[5 6] and the number of receptor sites on the target organs may well also decrease?[7]

We feel that clinicians should insist on knowing the pharmacokinetic profile of the various drugs they prescribe to their elderly patients and we look forward to the time when this information will become an integral part of the work done on any drug *before* it is marketed.

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Trimethoprim resistance in Finland

SIR,—Mr P Huovinen and Professor P Toivanen reported (12 January, p 72) that in 1978, after five years' use of plain trimethoprim in the Turku area, the incidence of trimethoprim-resistant *Escherichia coli* isolated from urines was 11% and 23% in outpatients and inpatients respectively. By contrast, the inci-

dence was 1% and 3% in Copenhagen[1] during 1970-2, 1·4% in London[2] in 1977, and <1% in the Helsinki[3] area during the period 1972 to 1977, all studies comprising both outpatients and inpatients.

At the 11th International Congress of Chemotherapy, Boston, in October 1979, P Toivanen and K Dornbusch presented the results of a comparative study of urinary tract pathogens from Stockholm and Turku. In Sweden, where trimethoprim was not used alone, the incidence of resistance during 1977-8 was just under 1%, unchanged throughout the period; while in Turku it was 15% (continuing to increase during the period of study).

For the moment we are again monitoring the sensitivity patterns of urinary tract bacteria at a Copenhagen city hospital. In 1979 we found 3·2% trimethoprim-resistant *E coli* strains—that is, the incidence was unchanged over a period of 10 years in an area where plain trimethoprim has been on the market for one and a half years. Furthermore, we know of a comprehensive series from Aarhus in Denmark (J K Møller *et al*, personal communication) during 1976-7, in which a sulphonamide-trimethoprim combination, but not trimethoprim alone, has been used since 1972. Among *E coli* strains 2·5% were trimethoprim resistant.

In both reports the authors consider that their findings, together with the rare occurrence of side effects and the convenient dosage scheme, confirm the usefulness of plain trimethoprim for urinary tract infections. In our opinion, all these results demonstrate a coincidence between the use of plain trimethoprim and the development of an *E coli* population resistant to this drug and perhaps also other drugs used in urinary tract infections (sulphonamides, nitrofurantoin, and ampicillin).

The possibility of a causal correlation could justify restriction in the use of plain trimethoprim for long-term treatment until further knowledge has accumulated.

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Examination of abortuses

SIR,—May I support the recommendations put forward by Dr D I Rushton (15 March, p 767) that all maternal deaths should be adequately necropsied by a recognised panel of pathologists with specific experience in this field?

Such an arrangement is long overdue and I would suggest that the same regional pathology teams should also encompass one other specialised form of necropsy within their remit—namely, the examination of all abortions undertaken on medical grounds. Like maternal deaths, such abortuses are relatively few in number and many are subject to only cursory examination. Not only is it essential to verify the diagnosis for which therapeutic abortion has been performed (usually craniospinal dysraphia or chromosomal abnormality) in order to monitor the accuracy of prenatal diagnostic techniques, but the parents and the public have a right to an independent reassurance of the propriety of medical practice. Indeed, on these grounds there is a strong case for making all therapeutic abortions notifiable to the coroner in the way which has long been a routine for other deaths occurring in the hospital operating theatre.

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Mebendazole and hydatid disease

SIR,—We have followed with great interest the correspondence on mebendazole and hydatid disease. Although there is some evidence from Dr Anthony Bryceson (15 March, p 796) and others that with enormous doses by mouth mebendazole can be found in the plasma in low concentrations, it is not reasonable to treat this disease, which requires significant blood levels and indeed cyst fluid levels, orally with a drug developed specifically to be poorly absorbed from the gastrointestinal tract. Mebendazole is an excellent broad-spectrum anthelmintic capable of dealing with a wide range of intestinal parasites; and in this situation, of course, systemic absorption is not required or desirable.

The clinical evidence available to date is not encouraging and confirms that in established hydatid disease no dosage regimen so far devised for giving mebendazole by mouth offers more than an outside chance of causing cysts to shrink and scolices to die. The product licence for mebendazole (Vermox) does not permit us to recommend any dose above 200 mg per day for three days; and hydatid disease is not an approved indication, which accounts for the high apparent cost of Mr D R Osbourne's "full course of mebendazole" (19 January, p 183).

It is not our intention to pursue further studies with mebendazole in hydatid disease—we intend to look instead for alternative compounds and routes of administration.

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Lumbar puncture

SIR,—The value of the otherwise excellent series "Procedures in Practice" is marred by the recent description of lumbar puncture by Drs C Clough and J M S Pearce (2 February, p 297). The article nicely brings us up to date on the indications and contraindications for the technique. The account is, however, too complacent in its acceptance of unwarranted complications.

It is not surprising that 25% of the authors' patients experience a postspinal headache (and in half of those it is described as severe) when an 18-gauge needle is used. Headache is related to needle gauge and, presumably, to the size of the hole in the dura.[1] A 25-gauge needle should be adequate for diagnostic aspiration of cerebrospinal fluid and a 22-gauge needle should suffice otherwise. Disposable needles of these sizes are readily available in anaesthesia departments and have the added virtue of being reliably sterile and sharp, unlike the repeatedly used needles favoured by physicians.

The rare postspinal headache following the use of smaller needles can now be effectively and safely treated by the use of an epidural blood patch.[2-4] In this technique 10 ml of the patient's blood is taken aseptically and instilled into the epidural space, where it forms a gelatinous plug to seal the cerebrospinal fluid leak.

The authors may be criticised also for failing to stress the importance of a no-touch technique and the value of the patient's sitting in an upright position, particularly if he or she is obese.

It is no wonder that so many patients dread a lumbar puncture, whether for diagnostic or for therapeutic purposes. The time has come for the quality of the technique used on the wards to match that used in the operating rooms.

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SIR,—May we reply to the points raised by your correspondents about our paper on lumbar puncture (2 February, p 297)? Firstly, we would emphasise that the paper was written primarily for junior doctors in training, many of whom do not share all the facilities of specialised neurological and neurosurgical units; this may modify a counsel of perfection. For example, although we agree with Dr D C Thrush (23 February, p 564) that Queckenstedt's test is not necessary, this is based on the assumption that in any case of suspected spinal cord compression myelography will be performed, making manometry unnecessary. There are, however, doubtful or borderline cases which in a neurological centre would end up with myelography, but which in a smaller hospital may be investigated by a general physician by lumbar puncture; in these circumstances (usually cases of "probable multiple sclerosis" where some diagnostic confirmation is sought) manometry and Queckenstedt's test may provide additional information which could be the first hint of spinal block and the need for more specialised investigation.

We are not unduly impressed with Dr A C Young's observations (15 March, p 796) that manometers cost the Salford authority £660 in a year: this must be infinitesimal in comparison with the multitude of waste which occurs daily in a hospital. Dr Young has a neurological unit and therefore manometry should seldom be necessary, but others are less well equipped.

We agree with Mr J R Gibbs (23 February, p 564) that the correct alignment of the patient is vital, but this was plainly described in our paper—as Dr W H H Calwell points out (p 565). Precise details vary, and a firm mattress with the patient placed right up to the edge proves as satisfactory as a trolley, though the latter is easier on the operator's back.

Dr C E Blogg accuses us of being too complacent in "accepting unwarranted complications"—a nice self-contradiction. The figure of 25% we cite for headache after lumbar puncture (only half of which were severe) is based on actual observations of unselected ward patients,[1] and is not dependent on an unproved—albeit reasonable speculation—that