test characteristics for delivery before 34 weeks (they are unlikely to be better) the prior odds would now be only 1:100 and the posterior odds approximately 4:100 (say 4%). The identification of women with a 20% risk of delivering before 37 weeks and 4% risk of delivering before 34 weeks is less impressive than a 94% chance of preterm delivery. Since 17·5% of women not delivering prematurely will have had a positive test much anxiety will be caused if such testing becomes routine.

We would not wish to suggest that this test is not an exciting development. It seems to perform better than cervical assessment, which until now has been the best single predictor of preterm labour. However, any test is only likely to be useful if there is an effective intervention that can follow a positive result. No such intervention has been shown to reduce perinatal mortality in properly conducted randomised trials, although tocolysis does prolong pregnancy and reduce the respiratory distress syndrome in women who are already having contractions. In such high risk groups fibronectin measurement may direct treatment to women actually likely to deliver prematurely.

Many people will argue that there should be a randomised trial of the fibronectin test. We disagree. Tests for preterm labour cannot in themselves improve outcome. Only the interventions which follow the test result can do this. These interventions might follow any risk factor such as an early pregnancy risk score, uterine activity monitoring, cervical microbiological culture, or assessment of cervical dilatation. Women identified to be at high risk of premature labour by one or more of these tests should logically be entered in trials of the relevant intervention, not trials of the test. The first step is proper evaluation of test sensitivity and specificity in a larger series of patients. Results must be concealed from clinicians to avoid the treatment paradox that true positive results which are followed by an effective intervention will seem to be false positives. If the fibronectin test continued to perform well in such studies it could be used to identify a high risk group for trials of possible treatments.

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Bovine insulin

EDITOR,—None of the contributors to the "human insulin and hypoglycaemia debate" mentioned bovine insulin.[1] In our fascination with the scientific minutiae of hypoglycaemic unawareness we seem to have forgotten that some of the worst problems occurred when middle aged or elderly people were unnecessarily switched, on a unit for unit basis, to human insulin from the once daily, long acting bovine insulin that had suited them for years.[2]

In a 1988 paper 22 diabetic patients with true sulphonylurea failure (mean age 64·5 (range 50-88) years) were randomly allocated to once daily long acting bovine lente insulin (Neulente, Nordisk/Wellcome) or once daily human insulin zinc suspension (Humulin Zn, Eli Lilly).[3] The only striking difference between the two groups was that after six months' treatment the patients receiving Neulente had had only four episodes of hypoglycaemia, whereas those receiving Humulin Zn had had 46, 36 of which occurred between 3 am and 6 am. Humulin Zn is now described as an intermediate acting insulin, although studies in normal volunteers had shown that its action was equivalent to a lente insulin, with the nadir of blood glucose concentration occurring 20 hours after injection.[4]

When acting as a referee for the 1988 study[3] I commented how strange it was that by the time the paper was published the insulin which "worked" would have been withdrawn. The fact is that there is no satisfactory long acting human insulin that can be used either for once daily treatment of older patients or as the basis of a basal bolus regimen for younger patients. The problem is compounded by the fact that human Ultratard is described as a long acting insulin when in fact its 50% disappearance time is 12-18 hours versus 35-53 hours for the now withdrawn bovine equivalent.[5] One clinical study concluded that the onset of action of human Ultralente is two to four hours, with a broad and variable peak between six and 12 hours after injection,[6] so it does not produce the constant basal insulin concentrations that the architects of the basal bolus concept originally envisaged.[7]

My experience is that attempts to treat older patients with a once daily injection of any human insulin formulation are often frustrated by nocturnal hypoglycaemia and morning hyperglycaemia, leading to one version of brittle diabetes in the elderly.[8] Once daily bovine lente (Hypurin Lente) or protamine zinc insulin (Hypurin PZI) works well in these patients and is also sometimes a good choice as a basal insulin for younger people who are plagued by nocturnal hypoglycaemia on a four times daily regimen in which the human intermediate acting insulin last thing at night does not last long enough.

Why has bovine insulin apparently been consigned to the scrap heap?

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Practising intubation on cadavers

EDITOR,—Alison Tonks gives a misleading interpretation of the BMA's policy on training in intubation techniques and how that policy stance was reached.

The issue was initially raised at the September 1991 meeting of the BMA Ethics Committee, and after a long debate covering the philosophical, spiritual, legal, and ethical considerations it was agreed that the practice was ethical but that protocols should be established with regard to who should be taught and how training should be performed to maximise its usefulness while ensuring that the body was treated with due respect.

The establishment of a protocol was delegated to a joint working party of the BMA and the Royal College of Nursing which had already been convened to discuss resuscitation policy. At the first meeting of this working party it became clear that many nurses were uncertain of the ethical basis of this training and that the medical profession was itself divided over whether this type of training was useful. The working party therefore decided to send a questionnaire to all interested parties to establish how widespread the practice was and whether it was thought to be useful, and the results of this survey confirmed a sharp divide within the medical profession—namely, that accident and emergency staff thought it extremely valuable while anaesthetists considered it unnecessary. At this stage there was a meeting of the British Association of Accident and Emergency Trainees in Liverpool, where it was unanimously agreed that this type of training was an extremely useful way of training junior staff in essential intubation techniques.

The survey results were discussed at a further meeting of the joint working party and it was decided to outline the principles that should be included in establishing protocols but to advise the British Association of Accident and Emergency Medicine and the Association of Anaesthetists to try and establish joint guidance. This stance was subsequently supported by the BMA Ethics Committee and by BMA Council.

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1 Tonks A. Intubation practice on cadavers should stop. *BMJ* 1992;**305**:332. (8 August.)

EDITOR,—The BMA and Royal College of Nursing have issued a statement about tracheal intubation of patients who have just died, which is often done for teaching purposes.[1] The statement suggests that this should be done only in accident departments on patients who have died after sustaining major head and neck trauma as these patients may be difficult to intubate and the technique cannot be learnt elsewhere. The statement concludes that most doctors and nurses who need to be proficient in intubation techniques can obtain sufficient experience through practising on manikins and in the anaesthetic room.

No mention is made of the problems associated with learning to intubate newborn babies, the largest group of patients who may need emergency resuscitation. It does not seem from the statement that any paediatricians were consulted. In large units experienced staff accompany new trainees to deliveries, but this may not always be feasible. Manikins of newborn babies, although a useful training aid, do not show anatomy clearly and are not realistic. For this reason we believe that supplementing the teaching of trainees by intubation of stillborn infants is appropriate. This can be done sensitively and privately but is not easily discussed with the parents at such an emotional time. In our unit it is always supervised.

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Drug resistant tuberculosis

EDITOR,—The report of the discovery that the deletion of a single gene is the cause of isoniazid resistance in *Mycobacterium tuberculosis* contains some misleading comments.

New procedures (such as the Bactec radiometric

method) allow reporting of sensitivity tests for mycobacteria to be available to users within days rather than weeks. It is no longer the case that it is necessary to wait the 8-10 weeks described in the report.

Isoniazid resistance is only one of the resistances that are worrying in *M tuberculosis*. The multiresistant strains that have been described recently are also resistant to other agents. The mechanisms for these are not well understood but may be due to factors other than gene deletion.

The mere detection of resistance to a single drug dose does not help in terms of predicting other sensitivity patterns or the interaction of combinations of antimycobacterial agents. It will remain essential for strains of *M tuberculosis* and other mycobacteria to be sent to reference laboratories for identification and susceptibility testing, not only to guide the management of individual patients but equally importantly to provide the epidemiological information that will enable us to monitor national patterns of drug resistance in *M tuberculosis*.

Thus, while representing an advance in our understanding, the description of this gene deletion will not offer any immediate and clear benefits to those concerned with the diagnosis and treatment of mycobacterial diseases.

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1 Connor S. Gene deletion behind drug resistant tuberculosis. *BMJ* 1992;**305**:441. (22 August.)

Drug management of ulcerative colitis

EDITOR,—Michael A Kamm and Asha Senapati provided an extensive review of drug management in ulcerative colitis.[1] We feel that one point is worthy of comment.

The authors erroneously state that mesalazine is 5-aminosalicylic acid coated with Eudragit-S. In fact mesalazine is the British approved name for 5-aminosalicylic acid and is available in many different formulations including enteric coated tablets, sustained released tablets, rectal suppositories, and enemas.

There is little doubt that mesalazine preparations may rarely be associated with renal adverse effects,[2] but the suggestion that "this may be related to the release and absorption of large amounts of unacetylated 5-aminosalicylic acid in the terminal ileum" is unfounded. Several authors have suggested that such events are probably due to hypersensitivity and are therefore independent of dose.[3,4] Indeed, the mean serum concentrations of 5-aminosalicylic acid with different preparations are of the same order of magnitude.[5-8] For example, Dew *et al* quote a mean serum concentration of (<0·1 to 0·1 μg/ml for sulphasalazine compared with 0·1 μg/ml with Asacol.[8]

Renal adverse effects have been seen in patients receiving many different preparations containing 5-aminosalicylic acid including oral and rectal mesalazine[2,9,10] and oral sulphasalazine.[4,10] This suggests that renal adverse effects are independent of the mechanism by which 5-aminosalicylic acid is released in the gut.[5] There is also no available evidence to confirm the suggestion that unacetylated 5-aminosalicylic acid is more or less likely to cause renal effects than its acetylated metabolite.

Although the very small risk of renal adverse effects with the 5-aminosalicylic acid products should not be ignored, current evidence supports the suggestion that they are likely to be a "class effect" of 5-aminosalicylic acid and that dose, duration, and release mechanism may not have an important role in the development of such events. The proven efficacy of mesalazine in the management of ulcerative colitis far outweighs the small risk of idiosyncratic renal adverse events in those patients with no known renal impairment.

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AUTHOR'S REPLY,—I welcome Dr Barrow's correspondence and additional information regarding the nephrotoxicity of 5-aminosalicylic acid drugs.

Although the mechanism may be one of hypersensitivity in some cases, it is not proved to be so in all. The fact that serum levels are similar for the different preparations of 5-aminosalicylic acid does not preclude the rare circumstance in which an individual absorbs an excessive amount of the drug in a short period of time. Now, however, the exact mechanism by which 5-aminosalicylic acid causes nephrotoxicity must be regarded as inconclusive.

I accept that nephrotoxicity has been reported in association with a variety of 5-aminosalicylic acid preparations. I would completely agree that these drugs offer enormous benefit with only a very small risk. In practical terms these drugs can and should be prescribed for patients with ulcerative colitis.

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Selective serotonin reuptake inhibitors

EDITOR,—In the debate in the correspondence on selective serotonin reuptake inhibitors,[1-4] T Walley's summarisation of the key points made in our paper[5] does not accurately reflect the substance of the argument which we outlined. We simply attempted to highlight the potential benefits which more widespread use of "non-tricyclic" antidepressant drugs would bring. It seems that Walley would dispute the efficacy and safety of "less established" drugs including the selective serotonin reuptake inhibitors. We are not aware of any convincing evidence that the older tricyclic drugs are more effective than the newer agents, but there can hardly be doubt that the older drugs are much more toxic both at therapeutic levels and in overdose.[6,7]

The issue of a possible legal challenge following death by suicide is an interesting one. There exists no published evidence that tricyclic drugs are more beneficial in preventing suicide, and they are frequently the agent of fatal self harm.[8] A direct comparison of the influence of different categories of antidepressant drug on the epidemiology of suicide has not yet been made. We are currently collecting data which will provide some indication of the relative contribution of these drugs to all categories of suicide, not just the atypical group who die by overdose.

This is an important debate and we would urge all clinicians to look closely at the real cost-benefit analysis.[9] For depressed patients and their relatives the "newer" drugs (including the selective serotonin reuptake inhibitors) are a considerable advance in the treatment of depression.

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Misuse of temazepam

EDITOR,—We write to support R Fox and colleagues[1] in calling for a withdrawal of all capsule formulations of temazepam and to provide evidence that such a withdrawal can be achieved without affecting clinical care of patients.

In June 1991 the local medical committee, local pharmaceutical committee, and family health services authority covering the Sefton area agreed to recommend a voluntary switch from temazepam capsules to temazepam tablets to help combat the problems described by Fox *et al*.

A joint letter from the three organisations was sent to all general practitioners and community pharmacists. It explained the reasons for the proposed switch and sought cooperation from the practices, which were also asked generally to review their prescribing of all anxiolytic and hypnotic drugs. Mersey Regional Drug Information Service provided an information bulletin on the use of anxiolytic and hypnotic drugs. This was also circulated to all practitioners. Medical and Pharmaceutical Advisers from the family health services authority discussed the issue with practices on "improving prescribing" visits. We were also helped considerably by the fact that all hospitals in Merseyside had decided to switch to temazepam tablets during 1991.

During the quarter ending June 1991 in Sefton 3 750 000 mg of temazepam were prescribed in capsule form and 3 250 000 mg as tablets; in the quarter ending March 1992, 1 300 000 mg were prescribed in capsule form and 3 900 000 mg as tablets. Prescribing of elixir remained constant at 100 000 mg. During the same period prescribing of all other hypnotics and anxiolytics, including newer agents, fell by 8%.

Practices have reported very few problems and patients' acceptance of the change once an explanation has been given. Anecdotal evidence suggests that by June 1992 a further shift from capsules to tablets will have been achieved, and we now