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 multi-resistant 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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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.^{5,6} 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.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 manage-

ment 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 paper² 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.^{3,7}

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 colleagues¹ 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

believe total withdrawal of the capsule formulation is possible by the end of the year.

We will be passing our results to the Advisory Council on the Misuse of Drugs and support the argument that the continued availability of temazepam tablets and elixir will provide adequate formulations for all patients.

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1 Fox R, Beeching NJ, Morrison C, Ruben S, Garvey T. Misuse of temazepam. *BMJ* 1992;305:253. (25 July.)

Predicting mortality from cervical cancer

EDITOR,—Cervical screening may be predictive, but it has never been shown to be protective in the ordinary meaning of the word. It is unfortunate that Gerrit J van Oortmarssen and colleagues use the word "protection" in their paper¹ because, although they define the term "relative protection" as meaning "the ratio of the risks in unscreened and screened women," readers have consciously to resist the implication that the screening process somehow confers protection. It does not, or at least has not been proved to do so.

More alarming still is the authors' statement that the International Agency for Research on Cancer's working group on screening frequencies "assumed that all women participate in screening." Could it really have assumed this? If so could its conclusions be flawed? How soundly based is current practice? There has not yet been a prospective, randomised controlled trial of screening or subsequent interventions. The need is as pressing as ever.² Perhaps the authors could tell us what would be required.

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1 Van Oortmarssen GJ, Habbema JDF, van Ballegooijen M. Predicting mortality from cervical cancer after negative smear test results. *BMJ* 1992;305:449-51. (22 August.)
2 McCormick J. Cervical smears: a questionable practice. *Lancet* 1989;ii:207-9.

EDITOR,—The report of Gerrit J van Oortmarssen and colleagues¹ shows that the potential effects of screening strategies need to be evaluated carefully. The authors suggest that five yearly screening from age 35 could have a similar impact on mortality from cervical cancer to that of more intensive and potential expensive strategies. This is based on as yet unattainable ideals: that all women enter the screening programme and are screened at the recommended intervals and that the sensitivity of the screening test remains constant across the vast array of potential smear takers.

Although mortality is a major end point for evaluating screening policies, this measure takes no account of the profound consequences to patients of the morbidity, both treatment related and psychological, of a diagnosis of cancer. On these grounds, reducing disease incidence—that is, prevention rather than cure—remains a vital component of screening. The need to address potential negative health effects of additional diagnostic and therapeutic procedures induced by screening is important and clearly needs critical evaluation, but it is premature to suggest that the magnitude of the problem merits allowing a proportion of women to develop invasive malignancy as long as no excess mortality results.

We agree that asymptomatic presentation due to

abnormal cytology carries a better prognosis than presentation due to disease related symptoms, almost certainly because asymptomatic disease is more likely to be small volume and early stage. Our observations in stage I disease confirm this impression, with superior disease free survival in those presenting with abnormal cytology than in those presenting with symptoms² because of the correlation between symptoms and disease volume. Recent cancer registry data from our region suggest a trend toward presentation with early stage disease. Although this observation may not result from screening activity, detecting early invasion will considerably reduce mortality and treatment related morbidity and is a further cogent argument against reducing the frequency of screening.

With the current screening strategy in the United Kingdom no major reduction in deaths from cervical cancer has occurred. The most important high risk group is non-attenders, and every effort should be made to get uniform coverage of the target population. A move towards less frequent screening, no matter how tempting on economic grounds, should be avoided until the ideal of screening the whole female population has been achieved and until any adverse sequelae of diagnostic and therapeutic procedures induced by screening have been more thoroughly evaluated.

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1 Van Oortmarssen GJ, Habbema JDF, van Ballegooijen M. Predicting mortality from cervical cancer after negative smear test results. *BMJ* 1992;305:449-51. (22 August.)
2 Buxton EJ, Saunders N, Blackledge GRP, Kelly K, Redman CWE, Monaghan J, et al. The potential for adjuvant therapy in early stage cervical cancer. *Cancer Chem Pharmacol* 1990;26:17-21.

AUTHORS' REPLY,—In our paper we addressed the appropriate interval between successive Papanicolaou smear tests and the way that this problem was dealt with by the International Agency for Research on Cancer (IARC) working group on cervical cancer screening. For this reason we followed the concepts and the terminology in the IARC's paper in which the relative protection against invasive cancer was the principal outcome.¹ But we agree with C M Anderson that we should have avoided using the word "protection."

Both Anderson and C J Buxton and colleagues emphasise the impracticability of realising 100% attendance. The IARC group assumed 100% attendance in order to calculate the impact of regular participation. This is the correct approach when the aim is to inform individual women about the benefits of screening. On a public health level non-participation is important. In our calculations of cost effectiveness we assumed 65% attendance, as observed in the Netherlands. We also analysed non-participation and its association with increased risk of cervical cancer in more detail to assess both the public health consequences and the economic consequences of low coverage.² The results of this analysis underscore Buxton and colleagues' remark regarding the need for attaining full coverage in the United Kingdom. It seemed that considerable resources may be used to increase participation; this increased participation would yield a greater reduction in mortality than would using these resources to increase the frequency of screening. Indeed, similar arguments can be used to show the importance of a high quality of the screening test. In other words, frequent screening of women who are eager to participate will not greatly improve the performance of the screening programme and will not solve the problem of low coverage and uneven quality.

With regard to the need for a randomised trial,

we think that the empirical evidence of the effectiveness of screening—for example, the studies by the IARC group and by others³—precludes a trial in which the control group is not screened at all. On the other hand, frequent screening is also unethical because of the adverse health effects for a considerable proportion of the women screened.⁴ Therefore, a trial in which two screening intervals—for example, three years and seven years—are compared would in our opinion be both ethically justifiable and informative for practical decision making.

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Quality of life of cancer patients

EDITOR,—Maurice L Slevin states that doctors may feel that emotional support of terminally ill patients is more appropriately delegated to nurses, psychologists, or social workers.¹ He fails to mention the supportive role of the general practitioner in caring for the physical, psychological, and emotional problems of such patients and their families, and the importance of this role in enhancing the patient's quality of life.

During a six month period, 65% of dying patients in this practice died either at home or in the local community hospital, looked after by their general practitioner and appropriate members of the primary health care team. A minority of these died suddenly, but most of the others spent their last few weeks at home. The general practitioners have a vital role in assessing and supporting the quality of life of such patients, particularly as they are in the privileged position of having an overview of the patient, the family, and the social circumstances, to which hospital doctors seldom have access.

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1 Slevin ML. Quality of life: philosophical question or clinical reality? *BMJ* 1992;305:446-9. (22 August.)

Oesophageal achalasia mistaken for anorexia nervosa

EDITOR,—Discussing diagnostic confusion between anorexia nervosa and achalasia of the oesophagus, K M Pagliaro states that because "most patients with dysphagia have a physical obstruction endoscopy should be the first choice [of investigation]"—presumably preceding barium swallow.¹

Achalasia may indeed be misdiagnosed as anorexia nervosa by the unwary because the regurgitation of food masquerades as self induced vomiting, but it should not be forgotten that the