workers.¹ Over 15 different cytotoxic drugs had been used besides asparaginase in the 190 children after relapse, but the response was poor even when the drugs had not been used previously. It seems that leukaemia cells after relapse are resistant not only to most previously used drugs, as pointed out by Drs Cornblett and Chessells, but also to a wide variety of other cytotoxic drugs. The usual rationale for changing therapy in ALL after relapse assumes that resistance occurs at the metabolic site of action, and thus drugs acting at a different metabolic locus in the cell cycle should produce a therapeutic response. The poor response to drugs other than asparaginase may be more in favour of resistance occurring because of reduced uptake of drugs by the leukaemia cells. On the other hand the action of asparaginase is extracellular and its effect on leukaemia cells is independent of drug uptake by lymphoblasts. Certainly new approaches such as bone marrow transplantation are justifiable in selected cases; but the prospect of transplant in all relapses is daunting and is neither indicated nor feasible at present. The alternatives are palliative therapy or using protocols which test hypotheses about relapse. With this in mind a protocol could be designed to circumvent therapeutic resistance at cell membrane level. Asparaginase, glutaminase, asparagine synthetase inhibitors, and high-dose methotrexate could be tried in appropriate combinations. Some parents and patients may prefer this option to either palliative therapy or bone marrow transplantation.

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¹ Kung, F H, *et al*, *Cancer*, 1978, **41**, 428.

Quality of cervical mucus and Huhner's test

SIR,—The opinion of Mr G T Kovacs and his colleagues (1 April, p 818) that "any post-coital analysis which shows any motile spermatozoa per high-power field should be considered as indicating a normal result" puts a new interpretation on Huhner's postcoital test. It has been thought for some time that the number of sperms indicating a "good count" has been placed much higher than is necessary.¹ However, it would seem from the authors' statement that "the quality and quantity of mucus did not correlate with sperm counts or motility" that it is unnecessary to take at least the quality of the mucus into account when assessing the results of the test.

Many authors have demonstrated the differing properties of the mucus during the course of the menstrual cycle which enable it to play an active role in the migration of sperm into it and hence into the cervix after intercourse, this role depending on the fibrillar structure and its molecular alignment.² Moghissi³ found that sperm penetration occurs at approximately five or six days before ovulation and that penetrability increases gradually to a maximum at ovulation, with inhibition of penetration one or two days after ovulation. Dubois *et al*⁴ used a sensitive light-scattering technique to show variable migration rates of sperm into mucus.

Mr Kovacs and his colleagues state that all tests were performed during the ovulatory

phase of the cycle, but the methods they used to assess this phase⁵ would not enable it to be delineated precisely. The differing results for the two blood-stained specimens of mucus are therefore of interest. Without knowing the precise time of ovulation it is not certain whether these were specimens of premenstrual or of preovulatory mucus. Thus, while most of those mucus specimens which reflected enhanced numbers and higher percentage of motile spermatozoa were probably of type E of Odeblad,² in the absence of evidence to the contrary—for example, spinnbarkeit, fern test, or the woman's assessment of the quality of the mucus in accordance with the rules of the ovulation method¹—it is very possible that some of the specimens were of type G of Odeblad.

Huhner's test cannot be correctly interpreted unless the current state of the woman in regard to the cervical mucus is taken into account.

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¹ Billings, E L, Billings, J J, and Catarinich, M, in *Atlas of the Ovulation Method*, 3rd edn. Melbourne, Advocate Press, 1977.

² Odeblad, E, in *Cervical Mucus in Human Reproduction*, World Health Organisation Colloquium, Geneva, 1972, p 58. Copenhagen, Scriptor, 1973.

³ Moghissi, K S, in *Cervical Mucus in Human Reproduction*, World Health Organisation Colloquium, Geneva, 1972, p 128. Copenhagen, Scriptor, 1973.

⁴ Dubois, M, *et al*, *Nature*, 1974, **252**, 711.

⁵ Kovacs, G T, *British Medical Journal*, 1978, **1**, 1421.

Diflunisal (Dolobid) overdose

SIR,—A 47-year-old woman with chronic low backache took 116 diflunisal tablets, each containing 250 mg, in quick succession over 40 min on account of persisting pain. She also took pseudoephedrine hydrochloride for a cold. She felt giddy an hour later, having difficulty in maintaining balance, and eventually sank to her knees.

Three hours later she was admitted to the casualty department, where she was observed to be drowsy with blurred vision. Blood pressure was 130/90 mm Hg. Gastric lavage revealed food particles but no tablets. The patient deteriorated, becoming stuporose and then deeply unconscious over 10 h, unresponsive to painful stimuli. Forced diuresis was given but produced little clinical effect. Spontaneous recovery occurred and by 24 h consciousness had been regained.

Diflunisal is a new long-acting analgesic with a plasma half life of about 10 h. The recommended dose is two tablets a day. The compound, a salicylic acid derivative, is quickly absorbed, undergoes hepatic conjugation and is largely excreted in urine as the glucuronide metabolite. In considerable overdose depression of the central nervous system occurs, but the uneventful recovery in this case suggests that the drug is relatively non-toxic.

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Social problems of schizophrenics

SIR,—With reference to your leading article (8 July, p 76), in which you refer to the study of schizophrenia in the community carried out in Salford by myself and my colleagues,¹ you

might be interested to know that the problems of social withdrawal and consequent social isolation experienced by the more neurotically handicapped patients in our sample was explored by us in some depth.²

I fully agree that your very apt quotation from Thoreau ("Most men lead lives of quiet desperation") describes the lives of many of these patients, but it would be regrettable if the minimisation of these very profound personal/social problems (whether labelled "neurotic" or explained away as an inevitable cerebral defect (Dr G J Lodge, 22 July, p 280)) should gain these people any sort of "dismissive attitude."

To be more optimistic, I would hope that the acknowledgment and recognition of the seriousness of these problems might create a climate for the rethinking and reconstitution of more appropriate rehabilitation programmes and consequently help the mentally ill living in the community to avoid a chronic backward type of existence in the homes of our cities.

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¹ Cheadle, A J, Freeman, H L, and Korner, J R, *British Journal of Psychiatry*, 1978, **132**, 221.

² Korner, J R, Freeman, M C, and Cheadle, A J, *International Journal of Mental Health*, 1978, **6**, 45.

Relative activity of atenolol and metoprolol

SIR,—I would welcome the opportunity to reply to the comments made by Professor J H Barber (29 July, p 357) on my letter about the relative activities of atenolol and metoprolol (8 July, p 128).

Firstly, evidence is available from the recent study by Dr T Reybrouck and others (27 May, p 1386), in which hypertensive patients were given metoprolol for four weeks (300 mg once a day—higher than the doses used by Professor Barber), which is at variance with his own and more like my results obtained in volunteers. In this study after the four-week treatment the decrease over placebo in the mean heart rate increase on exercise was 60 beats/min 2 h after a dose and 28 beats/min 22 h afterwards—that is, a much lesser degree of beta-blockade at 22 h than at 2 h. The difference between the various sets of results is probably consequent upon different trial designs.

Professor Barber describes his study as "a well-designed general practice study." From the little detail given of the study the portion dealing with exercise testing falls short of the requirements to allow any conclusion about the relative potency of atenolol and metoprolol in patients on chronic therapy. In the first instance the study is a between-patient study (six only in each group) and further the level of exercise chosen (75 W for each patient—136 W in the trial of Dr Reybrouck and his colleagues) is indeed low (even perhaps lower than the kind of exercise taken by the patients in their daily lives) and such that the heart rates achieved by the patients if they had not been taking therapy could be achieved by "vagal withdrawal" with minimal sympathetic nerve stimulation. This is given support by the small increases in heart rate after taking the beta-blocker which would give actual exercise heart rates in the region of 90 beats/min—at least 10-20 beats below the intrinsic heart rate.¹ Consequently it is not surprising

that the results look the same at 3 and 23 h after giving the beta-blockers because these drugs only block β -adrenoceptors. The trial design does not make it possible to know the heart rates achieved by the level of exercise before therapy commenced, there is a lack of control values with patients on placebo, and the standard dose of atenolol (100 mg/day) has not been compared with that of metoprolol.

Thirdly, evidence is available from studies using atenolol in volunteers² and in patients³ that the attenuation of the heart rate response to exercise after acute and chronic administration is similar.

Lastly, I agree with Professor Barber's view that one should be wary in extrapolating results about the relative potencies of atenolol and metoprolol from volunteer studies to patients on therapy, but not for his reasons (based on his trial design). One needs to be careful because of the relevance of the measure used to determine the relative potencies (that is, the attenuation of the heart rate response to exercise) to their potencies as agents in therapy, a point not considered by Professor Barber. A good case can be made that the increase is relevant to therapy of angina pectoris by beta-blockers,⁴ but it may be dubious in other cardiovascular diseases which require therapy with beta-blockers.

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¹ Carruthers, S G, et al, *British Journal of Clinical Pharmacology*, 1976, 3, 991.

² Brown, H C, et al, *Clinical Pharmacology and Therapeutics*, 1976, 20, 524.

³ Wolfson, A T J, et al, *Proceedings of the Royal Society of Medicine*, 1977, 70, suppl 5, p 36.

⁴ Robinson, B F, *Postgraduate Medical Journal*, 1971, 47, suppl 2, p 41.

Lost pedestal?

SIR,—I have just finished my paediatric medical outpatients. Of a total of 18 patients, including six new ones, seven patients, including one new referral, failed to attend. Is this indicative that the pedestal on which the doctor certainly was, and certainly ought to be, has been eventually and sadly knocked from underneath him?

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Lord Mayor Treloar Hospital, Alton

SIR,—In the interests of accuracy and clarification it is necessary for us to reply to a letter from 11 orthopaedic surgeons (5 August, p 436) concerning the future of the orthopaedic centre at Lord Mayor Treloar Hospital, Alton.

This orthopaedic centre was developed in 1970 to meet a shortage of facilities throughout Hampshire and adjacent parts of Wessex. It was set up on an interim basis pending the development of adequate local services nearer to the patients' homes. This policy was clearly established by the former regional hospital board, which set in hand plans for locating full orthopaedic services within each district hospital. As part of these plans a large orthopaedic unit is being developed in the new teaching hospital at Southampton—the main user of orthopaedic facilities at Lord Mayor Treloar Hospital, 31 miles distant.

By 1982-3 district hospital facilities for

orthopaedics will have been satisfactorily developed in line with the region's policy, and it is then that the health authorities intend to transfer services from the Lord Mayor Treloar Hospital.

The Hampshire Area Health Authority has set up a special panel of its members to ensure that the Lord Mayor Treloar Hospital maintains effective orthopaedic services until the carefully planned arrangements have been implemented. This panel will also supervise arrangements for the transfer of work from Alton. Personnel policies to safeguard the interests of staff have been adopted by the authority.

The area authority's reaffirmation of the policy that the orthopaedic services at Lord Mayor Treloar Hospital should eventually transfer to district hospitals was in no way a hasty one. It was the culmination of years of consultation, planning, and expenditure to make this possible.

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General practice records

SIR,—Dr J Tudor Hart (15 July, p 207) calls for some fresh endeavour to overcome the present stalemate in our efforts to introduce A4 records into general practice. He suggests a conference of interested parties. Such a conference was held recently under the auspices of the King's Fund in London with Sir Francis Avery Jones as its chairman. I am uncomfortably aware that we owe Dr Tudor Hart a sincere apology for not making sure that he was present. The least I can do to make amends is to give a brief account of a conference that gave those attending some real hope that a solution might be possible.

Perhaps the most important outcome of the conference was the recognition that, at least at the present time, the general introduction of A4 records for all patients was not a practical objective because of its cost. On the other hand it is abundantly clear that A4 filing is essential for that important minority of patients with voluminous notes (10-15% of a doctor's list). The other essential requirement is for a simple and adequate method for the storage of important background information. This is needed for all patients and can be achieved using cards of existing size and appropriate design.

At the conference I proposed the following compromise solution as the way ahead for A4 records in general practice. Existing cards (FP7 and 8) would continue to be used for the doctor's own clinical recording. Appropriately designed cards of the same size would be used with them for the recording of important background information. A4 files would be used so as to allow letters and reports to be filed without folding. They could be used for all patients in the practice or only for those with thick notes. When records are transferred to another doctor the existing record envelope would be used. The A4 file would be kept in the practice and reconstructed for another patient.

A compromise system of this sort has several advantages when considering the introduction of A4 records into general

practice at the present time. Firstly, it can be introduced gradually as individual practices find themselves able to achieve a partial or complete conversion. Secondly, the system does nothing to increase the difficulties of those doctors who continue to use existing record envelopes, since no additional A4 insert sheets are produced. Further, the difficulty and cost involved in the transfer of A4 records from doctor to doctor through the family practitioner committee is avoided.

A flexible and gradual introduction of A4 records made possible by this system will not present the Department of Health and Social Security with the need to find large funds over a short period to finance a general conversion to a total A4 record system. It would seem perfectly possible for the DHSS to supply both the background data cards, once the design of these has been agreed with the profession, and A4 files to any doctor wishing to use them for some or all of his patients. Furthermore, this system can still form the basis of a total conversion to A4 records (including the use of A4 insert sheets) at some future date if that proves to be the wish of the profession.

I would submit that we do not need another conference: we need action. The profession must stop crying for the moon in the shape of A4 records and new surgeries for all, while the DHSS must face up to the comparatively modest cost of supplying suitable background data cards and A4 files in the quantities needed. It is now over 10 years since the Wantage trial demonstrated the practicality of using A4 files together with existing records in general practice. Since that time the whole effort to reform our records appears to have become bogged down over the question of the financial consequences of a total conversion to A4. We would do better to accept what we have a chance of getting.

It is imperative that we do something now to improve the quality of our records. We are about to introduce mandatory training for general practice. To miseducate a whole new generation of doctors in the appalling standards of note-keeping current in British general practice would surely be unforgivable.

At the conference Sir Francis Avery Jones referred to the long-standing interest of the King's Fund in medical records. The fund is taking up the problem of how to increase the number of general practices using a record system capable of accommodating A4-size documents and it hopes to build up a body of knowledge about the practical consequences of a total or partial changeover.

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Negotiating rights for junior hospital doctors

SIR,—Dr J N Johnson's reply (5 August, p 436) to my letter (22 July, p 282) shows his maturing skill as a politician. He attacks me for alleging that preplanned filibustering prevented debate on Motion 104 at the Hospital Junior Staff Conference and the remainder of his letter is a polished explanation of why such allegations are unjust.

His skill lies in the fact that I made no such allegations—I would as soon involve myself in a Paisley v Vatican debate on the doctrine of Papal infallibility as an argument about the reasons for Motion 104's demise. Such debates