extreme reluctance, to the conclusion that, in the present circumstances, I could not regard the passage of some appropriate measure through Parliament as justifying an end to organized resistance to the elimination of facilities for independent practice from the hospitals of the N.H.S. in contexts where no alternative exists. Practical co-operation by Government in relating the rundown of facilities to the provision of alternatives, with the acceptance of a small residue of facilities where no alternative outside the N.H.S. can be provided, would of course be quite another matter. As we have undoubtedly seen a hardening of the Secretary of State in the recent past so, I trust, we shall see a hardening of attitudes in the profession. I cannot believe that we would be right to allow our natural reluctance to resist parliamentary authority to persuade us to leave a shackled profession behind for succeeding generations.

As some of your readers may know my connexion with the Central Committee for Hospital Medical Services and its sub-committees I hasten to assure you that the views expressed here are entirely personal and, I fear, without significant support among the leadership of the profession.—I am, etc.,

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Maintenance Therapy in Myeloma: Risk versus Benefit

SIR,—The Southwest Oncology Study Group has recently published the results of a study designed to compare the effectiveness of three regimens (no treatment, melphalan plus prednisone, or BCNU plus prednisone) in maintaining remissions in multiple myeloma patients. In brief, they found no differences in the frequency of relapse, the duration of remission, or in the survival time among the three groups of patients, though the frequency of pneumonia and herpes zoster was higher in patients receiving chemotherapy. They concluded that continued melphalan-prednisone or BCNU-prednisone chemotherapy after the first year is of no major value to responding patients with multiple myeloma.¹

The finding is particularly timely because of one possible adverse effect of long-term melphalan treatment which has only recently come to light. In 1967, about four years after the introduction of melphalan into general use for treating multiple myeloma, reports of acute myeloid leukaemia developing in multiple myeloma patients following irradiation and chemotherapy began to appear.^{2,3} Since then numerous reports have linked an apparent increased incidence of acute leukaemia in multiple myeloma patients to melphalan treatment, irradiation, or a combination of the two; the most recent review of this subject documented a total of 46 cases in which multiple myeloma terminated as acute myeloid leukaemia.⁴ Forty-three of the 46 patients had been treated with melphalan and about one-half had also received irradiation. Patients treated with melphalan received the drug over periods of 14-102 months and developed acute myeloid leukaemia 34-147 months later.⁴

Acute leukaemia has also developed in a number of patients treated with melphalan for other diseases, such as macro-

globulinemia,⁵⁻⁷ amyloidosis,⁸ and cold agglutinin disease.⁹ These case reports do not with certainty incriminate melphalan as a leukaemogen in man, nor does the finding that melphalan is carcinogenic in mice.¹⁰ Even if multiple myeloma patients treated with melphalan are at higher risk of developing acute leukaemia than is the general population, the consensus among clinicians appears to be that the increases in survival time and in the quality of life of melphalan-treated patients far outweigh the risk of drug-induced acute leukaemia.^{4,11-13} However, since no benefit appears to derive from melphalan maintenance therapy of myeloma patients in remission, perhaps the clinician should attempt to reduce this possible risk by shortening the duration of melphalan maintenance therapy or by abandoning it altogether.—We are, etc.,

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Ocular Reactions to Beta-blockers

SIR,—A syndrome of skin rash with ophthalmic signs and symptoms has recently been noted with the use of practolol.¹ Other beta-blocking drugs may also cause this syndrome and a similar skin rash has recently been described in a patient taking oxprenolol.²

We have observed a patient in whom the ophthalmic manifestations of this syndrome occurred when taking oxprenolol. She was receiving clonidine, bendrofluzide, frusemide, digoxin, and oxprenolol. Her treatment had been unchanged for 16 months. She had taken oxprenolol for 18 months, in a dose of 10 mg twice daily for the initial two months and subsequently in a dose of 20 mg twice daily. She first noted red eyes approximately 15 months after the treatment started. She did not initially comment on this until they became sufficiently troublesome, approximately three months after they were first noticed. At this time there were no other relevant symptoms. Her eyes were examined and showed conjunctival oedema, more marked on the left side, and congestion of the conjunctival vessels. Both corneae showed punctate epithelial opacities in the exposure area, but again more marked on the left side. The visual acuity was unimpaired and the eyes were otherwise normal apart from hypertensive changes in the fundi.

The oxprenolol had initially been given to reduce exertional tachycardia and therefore it was withdrawn slowly over a period of one month. Her cardiovascular symptoms did not return, but there was some improvement in her eyes with a reduction in dose and her symptoms had completely dis-

appeared within one week of total withdrawal. At this time her eyes showed a considerable improvement. There were still some residual epithelial opacities, but the conjunctival changes had largely disappeared.

It seems probable that this syndrome, already described with practolol, may also occur with other members of this group of drugs. It is obviously important to anybody who uses these for a prolonged period and should encourage doctors to use the drugs with the longest history of safe use whenever these are appropriate. Propranolol has not yet been shown to cause this effect, though the possibility that this drug may cause the skin manifestations of the syndrome has recently been raised by Dr. P. L. Padfield and others (15 March, p. 626).—We are etc.,

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SIR,—Following the recent reports of an association between practolol and dry eyes or keratoconjunctivitis sicca I wish to report a similar case associated with oxprenolol administration.

The patient was a 72-year-old man. He developed anginal symptoms in August 1974 and ischaemic heart disease was confirmed by E.C.G. Oxprenolol 40 mg three times daily quickly relieved his symptoms and at subsequent monthly visits he reported that he felt much better. No other medication was being taken.

In March of this year, however, he spontaneously volunteered that his eyes felt dry and gritty. Examination revealed little at first but two weeks later his eyes were so dry that it was necessary to prescribe hypromellose drops to alleviate the irritation. I reduced the dose of oxprenolol to 20 mg three times daily and then tapered it off, with immediate relief of the eye symptoms but return of the anginal symptoms. In order to confirm that the oxprenolol was involved I then cautiously reintroduced it, with a return of the eye symptoms.

As I am not aware of other reports of this side effect with oxprenolol I beg to bring this to the attention of your readers in order that they may watch their patients more carefully for the possibility of dry eyes. I have reported this finding to the Committee on Safety of Medicines.—I am, etc.,

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Diagnosis of "Reflux Oesophagitis"

SIR,—There has been considerable correspondence in various journals in recent years about the value of the "acid barium swallow" in the diagnosis of reflux oesophagitis. Dr. G. W. Stevenson (15 February, p. 395) maintained that this test is preferable to the acid perfusion test. On the other hand Drs. M. Yunus and J. R. Bennett (26 April, p. 192) point out that "acid perfusion tests detect oesophageal pain," while "acid swallows demonstrate an oesophagus which responds to acid stimulation with a motor response, but this tells one neither that it causes symptoms nor that the patient suffers from gastro-oesophageal reflux." Drs. Yunus and Bennett also state that "the best way to