

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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- 1 Southwest Oncology Study Group, *Archives of Internal Medicine*, 1975, 135, 147.
- 2 Osserman, E. F., and Lawlor, D. P., *Journal of Experimental Medicine*, 1966, 124, 921.
- 3 Edwards, G. A., and Zawadzki, Z. A., *American Journal of Medicine*, 1967, 43, 194.
- 4 Rosner, F., and Grunwald, H., *American Journal of Medicine*, 1975, 57, 927.
- 5 Hartwich, G., Götz, H., and Horstmann, H. J., *Blut*, 1970, 21, 137.
- 6 Forbes, I. J., *Medical Journal of Australia*, 1972, 1, 918.
- 7 Petersen, H. S., *Scandinavian Journal of Haematology*, 1973, 10, 5.
- 8 Kyle, R. A., Pierre, R. V., and Bayrd, E. D., *New England Journal of Medicine*, 1970, 283, 1121.
- 9 Staven, P., and Harboe, M., *Scandinavian Journal of Haematology*, 1971, 8, 375.
- 10 Shimkin, M. B., et al., *Journal of the National Cancer Institute*, 1966, 36, 915.
- 11 Osserman, E. F., *British Medical Journal*, 1971, 2, 237.
- 12 Kyle, R. A., Pierre, R. V., and Bayrd, E. D., *Archives of Internal Medicine*, 1975, 135, 185.
- 13 Holland, J. F., *New England Journal of Medicine*, 1970, 283, 1165.

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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- 1 Felix, R. H., Ive, F. A., and Dahl, M. G. C., *British Medical Journal*, 1974, 4, 321.
- 2 Cumberbatch, J. B., St.C., *British Medical Journal*, 1974, 4, 528.

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

measure the acid refluxing into the oesophagus is to monitor the intra-oesophageal pH by continuous recording." Such a method is, however, impracticable except in a few patients being studied in a research programme; it is not a routine procedure which can be used readily in a busy radiological department during an upper gastrointestinal examination session.

Various manoeuvres have been devised or employed for the demonstration of a hiatus hernia and/or gastro-oesophageal reflux, but because of the complexity of some of these they are not used except by enthusiasts of a particular technique. None are likely to be used by busy radiologists unless they are simple, and indeed even the head-down (or Trendelenburg) position has been abandoned by some.

I am indebted to Dr. W. R. Eyer of the Henry Ford Hospital, Detroit, (editor of *Radiology*) for drawing my attention to the simple expedient of observing whether reflux occurs when a patient drinks water from a disposable cup via a drinking straw in about a 10-15-degree head-down position and turned to the right 20-30 degrees—a method used previously by de Carvalho and termed by him "test du siphonage."¹ This is simple, takes up very little time, and is not at all unpleasant to the patient, who will almost without exception readily drink a cup of water after having had his barium sulphate. For 10 years I have used this method and commended it to registrars in training. I have always found that the results obtained by this method closely follow symptoms described by the patients. Many who, for example, complain of sore throats and oesophagitis have gross reflux up the throat demonstrated in this way, whereas other manoeuvres show only minor reflux. The same is true for patients with upper oesophageal webs. Hiatus hernias are also readily studied, but as pointed out by many authors these are not necessarily present with reflux or vice versa. These two conditions are also clearly distinguished in de Carvalho's paper. The only essential preliminary point is that the oesophagus should be empty of barium before the water is swallowed. Monitoring of swallowing is readily observed, either by watching (on the T.V. monitor) air bubbles passing down the oesophagus with the water or by looking at the cup. If the water test is carried out as the last part of the stomach and duodenal examination there is no problem arising from dilution of the barium suspension in the stomach, and if a follow-through is to be done the water is helpful in facilitating the transit of barium through the small intestine.—I am, etc.,

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¹ de Carvalho, M. M., *Archives des maladies de l'appareil digestif et des maladies de la nutrition*, 1951, 40, 280.

Epigastric Pain in Duodenal Ulcer

SIR,—In the original Bernstein test pouring 0.1 N hydrochloric acid blindly down a nasogastric tube occasionally produced epigastric as well as retrosternal pain.¹ This observation, combined with the fact that blowing up a balloon in the lower oesophagus could produce abdominal pain,² was the basis

for my developing the lower oesophageal acid perfusion test for epigastric pain. In the first study³ the possibility that epigastric pain could arise from the oesophagus was confirmed, but it was not a completely reliable test. A second study,⁴ however, showed that if attention was paid to the severity of the symptoms the test was always positive. Nocturnal waking was used as an indication of severity and if the patient had been awoken any time during the previous four weeks he always had a positive epigastric pain reproduction test.

Acid must be perfused through the manometry units so that it enters the lower oesophagus accurately. It is of no use passing a nasogastric tube blindly into the oesophagus after gastro-oesophageal sphincteric pressures have been measured.⁵ I emphasize these points again because the study by Dr. J. B. Dilawari and others (3 May, p. 254) has shown that epigastric pain could be produced by pouring acid down the oesophagus but they are unable to make this test reliable. If these workers are still interested in this subject they might like to come and visit the East End of London one day to learn about the small details that make the test reliable.—I am, etc.,

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¹ Bernstein, L. M., and Baker, L. A., *Gastroenterology*, 1958, 34, 760.

² Pollard, W. S., and Bloomfield, A. L., *Journal of Clinical Investigation*, 1931, 10, 435.

³ Earlam, R. J., *British Medical Journal*, 1970, 4, 714.

⁴ Earlam, R. J., *British Medical Journal*, 1972, 2, 683.

⁵ Earlam, R. J., *Clinical Tests of Oesophageal Function*. London, Crosby Lockwood Staples. In press.

Abortion (Amendment) Bill

SIR,—For a journal which is expected to be a voice for the medical profession, the *B.M.J.* goes too far in its condemnation of Mr. James White's Abortion (Amendment) Bill (17 May, p. 352). Let's face it, abortion is a very controversial subject. This applies to doctors as much as to the public at large.

There is a good cross-section of our profession whose views you choose to ignore. These members include gynaecologists and general practitioners disillusioned through their experience of abortion in practice. They do not dream of a Utopia where the Department of Health will provide abortion for social convenience. The basic fact is that abortion destroys life, and any justifiable grounds must therefore be restrictive. Their belief, in a society which abhors totalitarian attitudes, is that doctors should honour the oath of Hippocrates: "I will maintain the utmost respect for human life from the moment of conception."

You attach great importance to the dangers of interfering with a doctor's discretion. The rights of society to demand some control on the practice of abortion are well established through previous Acts in 1803, 1861, and 1929. Though this may not have been the intention of its sponsors, the 1967 Act effectively removed any such control. Since the almost non-existent risk to the life of a healthy woman in an abortion properly performed early on in pregnancy is likely to be less than the present very low, but not wholly negligible, risk in childbirth, it is easy

to see how the 1967 Act can be used to justify abortion on demand.

The introduction of an Abortion (Amendment) Bill was probably inevitable given that the shortcomings of the Lane Committee Report,¹ which you quote with apparent approval, have not been debated in Parliament. Even this report acknowledges that abortion "violates the sanctity of life or extinguishes the potentiality of a life" (para. 606). Yet it unanimously recommends that the 1967 Act should not be amended in a restrictive way. The view is that the end justifies the means, involving the taking of a life. This creates a dangerous precedent in modern law.

We shall agree that it is unlikely that all parties can be satisfied whatever the outcome of the present Bill. If the B.M.A. is to make a responsible contribution it must fully represent all shades of medical opinion. This is an opportunity for the *B.M.J.* to act as an open forum so that decisions can be reached following an informed exchange of views.—I am, etc.,

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¹ *Report of the Committee on the Working of the Abortion Act*. London, H.M.S.O., 1974.

SIR,—Your leading article (17 May, p. 352) is quite right—the Lane Report¹ did state that "most N.H.S. abortions and many in the private sector had been on grounds within the terms of the Act." Which is another way of saying that some N.H.S. abortions and many (? most) in the private sector were *not* done within the terms of the Act. That must surely indicate a disregard for the law which would never be tolerated in any other field and which the Abortion (Amendment) Bill is designed to put right.

You also say that this Bill represents "a serious threat to the professional freedom of doctors. In assessing an individual case the question would no longer be what was best for the patient. . . ." But there are always two patients involved in obstetrical cases, one of them being the baby; and however much precedence may be given to the interests of the mother, treatment should not be prescribed for her taking no account of its effects upon the child. With abortion, of course, the child is sacrificed, which is why any law protecting the interests of the child (that is to say, not permitting abortion simply on demand, which was *not* recommended by the Lane Committee) must necessarily place some limits upon the professional freedom of doctors.

Finally, on the question of the onus of proof. It may be true that placing this upon the accused person in cases involving non-compliance with the regulations is "a denial of the fundamental legal presumption of innocence until guilt has been proved." But it is not an "extraordinary provision," or at any rate not an unprecedented one, since section 4(1) of the present Abortion Act provides that "in any legal proceedings the burden of proof of conscientious objection shall rest on the person claiming to rely on it."—I am, etc.,

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¹ *Report of the Committee on the Working of the Abortion Act*. London, H.M.S.O., 1974.