and short answer to the overwhelming needs of patients whose medical symptoms of depression have their roots in alienation, loneliness, or unhappiness in their lives." Unfortunately, as the "former psychiatric patient" rightly emphasises (19 November, p 1351), these treatments are often not "a quick and short answer" in many cases; one wishes this could be so. But when this expatriate refers to "frustration if dissatisfied with psychiatry" Dr Lieberman's point should be noted, that often the life circumstances that he mentions have to be taken into account. These presumably include poor housing or financial circumstances, unemployment, interpersonal conflicts, physical illness, limited intelligence or personality attributes, and many of the other ills that can beset us. The term "unhappiness" is often more appropriate than the clinical description "depression". However, surely the significant qualifying factor is that many of these human problems may only to a limited extent be amenable to help by psychiatrists, in spite of liaison with knowledgeable family doctors, social workers, psychologists, disablement resettlement officers, community doctors and nurses, and housing managers, and the help of marriage guidance councils, clerics, MIND, the Samaritans, day care, home helps, and other agency colleagues.

Let us be practical and acknowledge, as undeniably obtains and is accepted in other medical specialties (with their often less successful cure or improvement rates), that we should not present or infer psychiatry as the panacea for each and every distressing condition. Most of us are only too aware, even when reactive factors are minimal, that reference to, say, an 85% success-response rate does leave an oppressively sad residuum of 15%; they and we have to struggle on. If we are realistic and maintain our integrity by effort and sympathy while thus honestly acknowledging our limitations, then perhaps the credibility gap will narrow and it will be regretfully accepted that we cannot cure even every "pure" psychiatric illness and that we can but do our best with our current techniques. Then, I hope, fewer patients will be "frustrated and dissatisfied." Perhaps we should amend our memos and hospital signs to read "Department of Psychiatry—Limited."

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Perforation of chronic duodenal ulcer during treatment with cimetidine

SIR,—It is likely that an attitude of critical scepticism towards new drugs, maintained by a profession consisting of scientifically inclined practitioners, is to the ultimate advantage of their patients. Such an attitude has become apparent in recent reports of problems encountered among patients taking the H_2 -receptor antagonists cimetidine and metiamide.

We would expect the drug to be most effective in early uncomplicated duodenal ulceration, and adverse reports of four cases have appeared from those engaged in treating such lesions (Dr W A Wallace and others, 1 October, p 865, and Dr B D Keighley, 15 October, p 1022). On the other hand several contributors have recently described problems associated with the use of H_2 antagonists in oesophageal ulceration (Drs M J Gill and

J B Saunders, 29 October, p 1149), erosive gastritis, haemorrhage from gastrojejunal fistula, and gastric ulceration with pancreatitis.¹ To imply criticisms of the drug when it apparently fails in such cases is surely unrealistic.

We wish, however, to draw attention to a more serious indictment of cimetidine. We believe this to be the first report of a patient presenting with perforation of a chronic duodenal ulcer while using cimetidine under medical supervision. After diagnosis of duodenal ulceration with bleeding in January 1977 a 72-year-old man was given a course of cimetidine 1 g daily. His symptoms abated and endoscopy in February 1977 indicated healing of his ulcer. Apart from a six-week break in treatment during July and August, during which his symptoms recurred, the drug was taken continuously and regularly until the present admission. In early October urgent admission was required for epigastric pain which appeared two hours after the nightly dose of cimetidine. At laparotomy a large chronic ulcer on the superior wall of the first part of the duodenum was found to have perforated. Obviously complete relief of symptoms does not necessarily indicate healing of the ulcer, a fact which must be borne in mind by practitioners using these drugs.

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¹ Dudley, H A F, *et al*, *Lancet*, 1977, **1**, 481.

Antidepressants—yes or no?

SIR,—Dr J G Edwards (19 November, p 1327) questions the effectiveness of viloxazine in the treatment of depressive illness compared with placebo. His trial has many implications which suggest that the use of antidepressants needs reviewing. In his study there were more patients on placebo than on viloxazine and more women on placebo than men. Although it is not stated, it looks as though an important proportion of the women on placebo might be under 40 years of age. Raskin *et al*¹ have shown that women under 40 respond better to placebo than to antidepressants. It ought to be added that although some depressed patients might appear to do well on placebo, others will not respond to active antidepressants. "It is therefore important to identify as early as possible, those primary depressives who will not respond to anti-depressant drugs."² They may need other treatment such as electric convulsion therapy (ECT).

An unpublished study of ours, also using the Hamilton and Global clinical scales, with 98 depressed inpatients found no significant differences between amitriptyline, mianserin, and placebo in effectiveness; nor did it show any particular subgroup doing well on antidepressants either on the clinical scales noted or on psychological measures such as the Cattell Clinical Analysis Questionnaire. Similarly, Dr Edwards's trial does not show if any clinical age group does better on antidepressants than on placebo. For these reasons and others previously stated³ there is a need to examine closely antidepressant trials and not to close discussion about the effectiveness of antidepressants. For example, Rogers and Clay⁴ found that imipramine was of undoubted value

for treating acute endogenous depression. Maxwell,⁵ looking at the same paper, also felt (as did we) that there was further need for trials that included a placebo in establishing the place of antidepressants.

It is interesting that in the same issue of the *BMJ* Dr Lieberman (p 1355) rightly points out that medication is used as if it would provide a quick and short answer to patients whose symptoms have their roots in unhappiness and various environmental factors. In other words, is it only a small proportion of depressed patients who are suffering from endogenous depression? Perhaps relief from symptoms is less dependent on the actions of antidepressants or placebo and more on "natural causes," as suggested, again in the same issue, by a "former psychiatric patient" (p 1351), while Mr A J Cooper (p 1358) notes the "Catch 22" situation in which L-tryptophan is an antidepressant when prescribed in tablet form but is classed as a food and not as a drug when prescribed as a powder.

If to these reservations are added other controversies concerning the nature of depression and its treatment (for example, ECT) it seems clear to us that this is one of the most important problems requiring clarification, particularly for the treatment of individual patients. After 40 years the use of ECT is being more and more frequently questioned. It is to be hoped that 40 more years do not go by before we can clearly say yes or no about the effectiveness of antidepressants.

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¹ Raskin, A, *et al*, *Archives of General Psychiatry*, 1970, **23**, 164.

² Davidson, R T, *et al*, *British Journal of Psychiatry*, 1977, **131**, 403.

³ Kerry, R J, and Orme, J E, *British Journal of Psychiatry*, 1976, **128**, 510.

⁴ Rogers, S C, and Clay, P M, *British Journal of Psychiatry*, 1975, **127**, 599.

⁵ Maxwell, C, *British Journal of Psychiatry*, 1976, **128**, 510.

Further experience with primary excision of brain abscess

SIR,—Mr J S Garfield and Mr A J Keogh, (19 November, p 1349) restate yet again the time-honoured arguments in favour of conventional burrhole drainage for brain abscess. This method has, we believe, been discredited by paper after paper in which poor results have been reported; the bibliography of our article (29 October, p 1119) contains many of these.

It is perfectly obvious that the computerised tomographic scan is clearly superior to all other forms of investigation in this disease, and the method is used wherever and whenever it is available. In our hands it has provided an excellent guide for immediate primary excision, demonstrating clearly multiple loculi and daughter abscesses which are simple to excise but notoriously difficult to tap or drain.

The policy in this centre for management of brain abscess is now immediate excision and we should like to take the opportunity to report a further eight consecutive cases so treated with excellent results, no deaths, and no morbidity. Thus, although our original series was small, our conclusions have been amply born out by further experience. Three were deeply unconscious patients (two

of them unresponsive to pain; grade 4) who had abscesses which were both massive and multilocular. (The accompanying illustration shows EMI scans of one of these cases; the brain oedema and mass effect are obvious.) The response of these patients to immediate excision, with simultaneous reduction of tentorial hernia, was rapid, with complete recovery.

EMI scans of massive and multilocular right frontal abscess before and after excision.

Deep abscesses in the thalamus, pons, or medulla cannot be excised, but are very rare; multiple abscesses certainly can be excised, as in one of the cases reported in our original article.

Finally, we are not alone in our views about primary excision of cerebral abscess. French neurosurgeons at the Bristol meeting of the Society of British Neurological Surgeons in April 1977 pointed out that they had reached this conclusion some years ago.¹

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¹ Taylor, J C, and Choudhury, A R, *Journal of Neurology, Neurosurgery and Psychiatry*, 1977, **40**, 1026.

Radiation of the young brain

SIR,—No mention was made in your leading article entitled "Does radiation of the young brain affect growth hormone?" (27 August, p 536) of the important observations regarding the moderate impairment of growth and development which occurred in persons in Hiroshima who were exposed during intra-uterine life or early childhood to a single dose of mixed neutron-gamma radiation from the atomic bomb.¹⁻³ In Nagasaki, where the

atomic bomb radiation was almost pure gamma in type, growth alterations in exposed infants and children were not significantly different from those in the non-exposed. It was observed in Hiroshima that the earlier the age at time of exposure, the greater the impairment of growth. Air dose radiation measurements for those with growth reduction were mostly in the range of 50-150 rads for the children exposed in utero and 100-300 rads for those who were exposed during the first 5-10 years of life. Pituitary gland and hypothalamus dose estimates for the bomb survivors would have been only a fraction of those for the same tissues in children who receive therapeutic craniospinal radiation. It is unlikely that the radiation doses to the pituitary glands and hypothalamic areas of the Hiroshima exposed were large enough to have produced enough direct tissue damage to have resulted in permanent impairment of glandular function. The possibility of increased glandular tissue sensitivity during early development, such as occurs with the thyroid, resulting in a growth defect due to reduction in growth hormone or primary or secondary hypothyroidism cannot be excluded however.⁴

Growth impairment following radiation exposure during infancy and childhood is probably related to many factors, of which the quality, intensity, duration, and location of the radiation, age at time of exposure, and a great many other host factors play impairment roles. Structural changes may be due to primary or secondary reduction in the production of growth or thyroid hormones, direct damage to bone and other structural tissues, nutritional inadequacies, or various combinations of these factors.

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- ¹ Wood, J W, et al, *American Journal of Public Health*, 1967, **57**, 1374.
- ² Belsky, J L, and Blot, W J, *American Journal of Public Health*, 1975, **65**, 489.
- ³ Blot, W J, *Journal of Radiation Research*, 1975, **16**, suppl, p 97.
- ⁴ Conard, R A, *Brookhaven National Laboratory—Report 50424*, 1975.

Thyroid disease and asthma

SIR,—A recent leading article (5 November, p 1173) described an association between severity of asthma and hyperthyroidism such that the asthma appeared to improve with adjustment to the euthyroid state. Similarly asthma was said to improve if the patient became hypothyroid. These findings prompted us to analyse the data of the Oxford Record Linkage Study to ascertain whether patients who were hyperthyroid were at increased risk of developing asthma and conversely whether hypothyroid patients were at reduced risk of doing so.

The data analysed for this purpose consisted of details of all hospital discharges and deaths occurring to a defined population over a five-year period. The data were linked together into person-orientated longitudinal records^{1 2} and analysed using our standard package,³ which computes the expected number of persons to have any association between diseases after taking account, inter alia, of the variation of each disease with sex, age, and time period. Corrections are introduced for loss of the cohort through death and migration out of the area.

Of 890 persons on the files with a diagnosis of hyperthyroidism but no record at that time of asthma, only one was subsequently admitted with asthma. The expected number of persons to have this association was 0.9. In contrast, there were 316 persons with a diagnosis of hypothyroidism, two of whom were subsequently admitted with asthma (both after an interval of four months). The expected number of persons with this combination was 0.27 ($P=0.03$).

Analysing the files from the opposite viewpoint, there were 1360 persons with admissions for asthma but no record of thyroid disorders. Of these, one subsequently developed hypothyroidism (expected = 0.29, $P=0.25$) and four developed hyperthyroidism (expected = 0.87, $P=0.01$).

The numbers of cases in these analyses are small, but nevertheless a significant association with asthma after treatment for hypothyroidism may indicate that treatment of this state increases the likelihood of development of asthma. Conversely, the association between asthma and subsequent hyperthyroidism might suggest that the treatment of the asthma contributed to the development of thyrotoxicosis. We hope to extend the analysis to a large cohort covering a longer time period in the near future.

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¹ Acheson, E D, *Medical Record Linkage*. London, Oxford University Press, 1967.

² Baldwin, J A, *Proceedings of the Royal Society, Series B*, 1973, **184**, 403.

³ Baldwin, J A, Simmonds, H, and Fedrick, J, submitted for publication.

Oral contraceptives, smoking, and venous thromboembolism

SIR,—It may be premature to conclude from the data presented by Professor D H Lawson and others (17 September, p 729) that differences in fibrinolytic activity between smokers and non-smokers play no part in venous thrombosis in women on oral contraceptives. Their study arose from our suggestion¹ that the increase in "coagulability" in women on oral contraceptives may be compensated for by an increase in fibrinolytic activity in non-smokers but only to a limited extent in smokers.

Our reservations partly arise from the design of their study, which precludes satisfactory consideration of the role of modifying as well as initiating factors; both of these should be considered when assessing a process such as venous thrombosis in which changes occurring after the first development of a thrombus are obviously crucial in terms of clinical outcome. The women in their study had (a) survived and (b) been admitted to hospital and thus cannot be said to represent the full clinical spectrum of thromboembolism. It is possible that those women with only minor episodes and who may not be admitted to hospital are those with particularly active fibrinolytic responses and that this activity is partly due to the fact that they do not smoke. Conversely, women who die before they reach hospital may be those with poor fibrinolytic responses determined in part by the fact that they do smoke. If the balance between coagulation and fibrinolytic activity does not play much part in determining the onset of a venous thrombus it may nevertheless be con-