graduates in such a team have every opportunity for job satisfaction and an efficient use of their long period of training.—I am, etc.,

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Rupture of Uterus during Prostaglandin-induced Abortion

SIR,—Dr. I. Z. MacKenzie and his colleagues (21 December, p. 683), in their detailed analysis of the morbidity of prostaglandin-induced abortion, state that they have been unable to find any report of uterine rupture as a complication of pharmacologically-induced abortion. I wish to record the histories of two patients both of whom sustained rupture of the uterus during the middle trimester and in both of whom prostaglandin E_2 was used as an oxytocic.

Case 1. A woman aged 29 years was admitted with 15 weeks' amenorrhoea in her third pregnancy and slight vaginal bleeding for two weeks. The fetus was dead. In spite of a high-concentration oxytocin infusion and dilatation of the cervix under general anaesthesia on the seventh day of admission abortion did not follow. Four days later intravenous prostaglandin E_2 was infused (7.5 mg over 25 hours). The cervix dilated slightly but a left adnexal mass became palpable. The fetus and placenta were evacuated under general anaesthesia and the uterus packed. When the pack was removed 24 hours later severe haemorrhage followed. At laparotomy a complete rupture of the lower uterine segment was discovered. Subtotal hysterectomy and ligation of the left internal iliac artery proved necessary and 3.3 l of blood was transfused. An abdominal drain was required and the bladder drained continuously. Fortunately the patient recovered uneventfully with the help of antibiotics.

Case 2. A woman aged 35 years was admitted with 24 weeks' amenorrhoea in her sixth pregnancy, slight uterine bleeding, and colicky abdominal pain. The fetus was dead. Apart from three normal deliveries she had had a spontaneous middle trimester abortion and evacuation of the uterus after an incomplete abortion at the twelfth week. Despite a high-concentration oxytocin infusion the cervix dilated very slowly. Forty-eight hours after admission the membranes ruptured and offensive fluid drained. Prostaglandin E_2 was infused intravenously over the next five hours. The concentration used was that recommended by the makers, 5 mg/l, and the dose no more than 10 µg/min. The cervix did not dilate. Moderately severe pain and tenderness developed in the right iliac fossa. At laparotomy a large right broad-ligament haematoma was evacuated, subtotal hysterectomy performed, and 1.1 l of blood was transfused as well as dextran 70. The abdomen was closed with drainage and a self-retaining catheter inserted. Mild pelvic peritonitis responded to penicillin and kanamycin. Though she recovered well and was discharged on the twelfth day she was readmitted on the 21st day with a pulmonary infarction which was treated successfully with intravenous heparin and later with warfarin.

Both of these patients had fetal death in utero and were managed with oxytocin as well as prostaglandin E_2 and undoubtedly differ in many ways from a patient terminated in the middle trimester who has a live fetus. It may well be that uterine infection and multiparity predisposed to rupture, yet there was no evidence of old scarring found in the excised uteri. In both these patients the uterine rupture was associated with very considerable morbidity from anaemia, infection, and in one patient from pulmonary infarction. Rupture of the uterus in the middle trimester is very uncommon and the fact that prostaglandin E_2 was used in both these cases may be coincidental, but it would seem reasonable to list rupture of the uterus as a complication of prostaglandin-induced termination if only under exceptional circumstances.

I am grateful to my colleague Mr. J. C. Newbold for permission to record the details of the first patient.

—I am, etc.,

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Epidemiology of Cowpox

SIR,—Though your report from the Epidemiology Research Laboratory on cowpox (4 January, p. 46) deals principally with infection without direct contact with cows it also raises some other interesting points about cowpox virus.

Your contributors correctly assess the extent of human infection. However, I am not certain that bovine infection is as rare as they and others^{1,2} indicate. Nor is it certain that the incidence is declining as has recently been suggested.³ Eight human cases since 1967 compares well with 10 cases from 1944-50 studied by Downie,⁴ who suggested that infection was as common as in Jenner's time. Cases are investigated only when either human infection occurs or when many cattle are involved; in a recent outbreak 75% of the herd was infected before veterinary advice was sought.³

Downie⁴ suggests that cowpox virus is maintained via trivial infection in cows which would probably go unnoticed. The virus would not survive for long in the soil and there is no evidence that other animal hosts are involved. I have recently compared the biological characteristics of 10 British cowpox virus isolates. The results (to be published) indicate that at least five different virus strains are currently in circulation. For example, viruses isolated in 1937, 1965, and 1971 were indistinguishable from each other whereas three viruses separately isolated in 1969 and 1971 were quite distinct. A substantial total incidence of bovine infection is required to maintain these separate strains.

Finally, your report describes a human infection considerably more severe than smallpox vaccination. Such severity in unvaccinated individuals has been noted previously;⁴ even infection of well-vaccinated individuals can be more severe than vaccination. From a survey of the literature (to be published) I calculate the serious complication rate (death or encephalitis) in human cowpox as 3%, far higher than the 15 per million for smallpox vaccination.⁵

Whether the incidence and severity of human cowpox infection will increase with the cessation of smallpox vaccination is a question to which the answer will be awaited with interest.—I am, etc.,

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1 Miller, W. C., and West, G. P., *Black's Veterinary Dictionary*, 9th edn. London, Black, 1970.

2 Lauder, I. M., et al., *Veterinary Record*, 1971, 89, 571.

3 Gibbs, E. P. J., Johnson, R. H., and Collings, D. F., *Veterinary Record*, 1973, 92, 56.

4 Downie, A. W., *British Medical Journal*, 1951, 2, 251.

5 Dick, G., *Progress in Medical Virology*, 1966, 8, 1.

Problem of the Dangerous Offender

SIR,—I remain unreassured on reading in your pages (14 December, p. 640) Dr. P. D. Scott's thesis, much of which he propounded

on 8 November to the Thames Valley Division of the Royal College of Psychiatrists.

(1) "The law," he writes, "is already so flexible that most objectives can be achieved without new legislation. . . . It would perhaps help if approved parts of the prison system could be designated as hospitals . . . so that hospital orders could be effected . . . in prison. . . ." This is precisely what could not happen without controversial new legislation. A hospital order under section 60 of the Mental Health Act 1959 is not for any necessary length of time and could not therefore be made to coincide with the term of a sentence. For this reason, among others, I cannot envisage the linking of Broadmoor and the other special hospitals with the prison service.

(2) I consider the Department of Health and Social Security's mere 18 months in the semisecure unit,¹ mentioned by Dr. Scott, to be unrealistic. Reform of severely distorted personalities may take many years, far longer than prisons can hold them most times, and requires an approach of progressive resocialization into the community. But if hospitals where prisoners could be locked up indefinitely came to be contained in prisons where terms of sentence were otherwise all finite, what devices would not prisoners use to avoid the loathed and stigmatized "loony bins where you stay for ever"?

(3) If, as he advocated at Broadmoor, Dr. Scott's policy were to set up hospital units in the larger long-stay prisons it would sabotage that principle of progressive resocialization into the community that would stimulate the strongest drive to reform. Broadmoor and Grendon Underwood are already so isolated as to find difficulty in establishing links with their residents' communities, much less establish an adequate system of half-way housing. The same difficulty will be great enough from a regional "medium security" non-prison unit; by pushing these units into such isolated major prisons as Dartmoor or the huge metropolitan prisons it will become overmastering.

I am all for the best possible link-up of the psychiatric part (which is only one part, after all) of the prison medical service with N.H.S. psychiatry. I am of the opinion that many mentally abnormal offenders, and indeed non-offenders, need long-term and closely supervised care. But now that thought is being directed away from the custodial disposal of offenders towards, for example, compulsory community service, should we not try to think out better ideas than Dr. Scott's for the slow but methodical rehabilitation into society of the dangerously mentally abnormal?—I am, etc.,

SEYMOUR SPENCER

Oxford

¹ Department of Health and Social Security, *Security in N.H.S. Psychiatric Hospitals*, E.C.D. 168/73. London, D.H.S.S., 1973.

Secure Hospital Units

SIR,—We wish to support Mr. M. R. Bury and Dr. J. A. O. Russell (24 August, p. 519) in their criticism of the proposal to establish regional security units for mentally abnormal persons. We agree with them that neither the circular H.S.C. (I.S.) 61 nor the reports of the Butler Committee¹ or the Department of Health and Social Security's

working party² make it clear what sort of people it is intended to detain in these places or what objectives will be attained by doing so.

The proposed units are not to be used for long-stay care (Butler Report, para. 17; D.H.S.S. Report, para. 44). But a major problem with discharge from special hospitals now is the reluctance of staff in ordinary hospitals to take these patients (Butler Report, para. 5). No reasons are given why discharge from a regional security unit should be any easier. Faith is placed in the possibilities for "therapy" in the proposed units (Butler Report, para. 9; D.H.S.S. Report, paras. 23, 28, 29(3), and 50) but its nature is not discussed. The Butler Committee is justifiably concerned about overcrowding in special hospitals, but if this is due to the number of people there who have "dangerous, violent, or criminal propensities" (para. 4) it is not made clear how overcrowding is going to be relieved by the provision of units which are not to house people who would be an immediate danger to the public (para. 12). This can be achieved only if we succeed in convincing many people that many of those now in special hospitals are less dangerous than they have hitherto thought them to be. Otherwise the security at regional units cannot be less strict (D.H.S.S. Report, para. 8) than at special hospitals.

The working party states (paras. 28 and 29) that "the meaning of security is no longer well understood," but neither report clarifies the important issues involved. They mention the difficulties experienced by staff in ordinary psychiatric hospitals when dealing with clients whose behaviour presents problems of management on the ward (Butler Report, para. 9; D.H.S.S. Report, paras. 7, 19, 20, and 22). Admissions to regional security units will clearly be from among patients whose behaviour is disruptive. However, no indication is given of any help likely to be provided to staff in existing psychiatric hospitals to develop rich and sophisticated rehabilitation programmes which could decrease the frequency of disruptive behaviour and avoid the need for restraint. Without such help it seems likely that transfers from ordinary hospital to security units could soon fill the new places created and merely regionalize the problems now faced in the State security units. We are concerned that alternative ways of providing resources for training patients referred to security units should be developed before new units are created.

We have every sympathy with the points made by Dr. D. Tidmarsh (2 November, p. 286) but we cannot see how, in the absence of a clearly stated admission policy and goals of treatment, the proposed regional units can be prevented from becoming as badly blocked as the existing special hospitals.—We are, etc.,

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World Medical Association

SIR,—Understandably in the present financial climate the question is being asked whether the B.M.A. can afford to continue its membership of the W.M.A. I believe the B.M.A. can and must because never before has there been such a need for those who believe in professional freedom to stand together—not only in Britain but throughout the world. We may be struggling against Government interference in Britain but the position of our colleagues in many other countries is far more precarious, especially in developing countries where Governments, for compelling reasons, often have to assume dictatorial powers. The "honour and dignity" of the profession can be sustained only when there is a free and strong medical association. If this is essential on a national level it is just as essential on an international level. International agencies, the U.N., I.L.O., U.N.E.S.C.O., and of course W.H.O. in particular, are involved in matters which often have a direct impact on the way medicine is practised. It is therefore essential for the voice of the profession to be heard at this level. Just as the B.M.A. is the voice of the medical profession vis-à-vis the Government in Britain, so is it equally important that a similar authoritative body should exist at international level.

The B.M.A. was one of the founder members of the W.M.A. and has been a highly respected and staunch supporter ever since. Its subscription to the W.M.A. costs two Swiss francs per U.K. member, roughly 30p each, a very small contribution to make to a very important task.

May I take this opportunity to remind B.M.A. members that they are entitled to join the W.M.A. personally as associate members? Not only does this help to support the work of the W.M.A., but such membership can be useful to those who do much international travel. Associate members are also entitled to take part in the annual assembly. The subscription rate is at present £6 per annum, including subscription to the *World Medical Journal*. Anyone interested should contact the B.M.A.—I am, etc.,

H. A. CONSTABLE

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Effective Dosage of Tricyclic Antidepressants

SIR,—Continuing the debate on the clinical significance of tricyclic antidepressant plasma concentrations and the optimum "therapeutic range," to which Drs. A. J. Coppen and S. A. Montgomery refer (11 January, p. 91), we feel that further detailed comment may not be out of place.

There are now quite a number of published studies in which the relationship between tricyclic antidepressant plasma concentrations and clinical response has been examined. The findings, however, are by no means in concordance for the simple reason that the design of these studies conforms to no single pattern. Generalizations from the results of one study are therefore fallacious.

Firstly, there is little clinical consistency in the type of patients investigated. Some workers have considered only patients with "severe endogenous" depression, others have considered cases of

"moderate" depression, and one study specifically included patients with personality or environmental problems. It would seem illogical, if not foolish, to expect any sort of clear relationship between drug plasma concentrations and therapeutic response among such a diagnostic diversity of patients.

Secondly, not all of the studies have been devoted to the same drugs, some having been concerned with nortriptyline, others with imipramine, and yet another with amitriptyline. Since there are important pharmacological differences between the tricyclic antidepressants it is not always valid to compare the findings of studies conducted on different drugs.^{1,2}

Thirdly, the analysis of tricyclic antidepressant plasma concentrations is difficult to perform and the same techniques have not always been followed throughout. Thus the plasma nortriptyline levels reported in one particular study are quite at variance with the accumulated data on the pharmacokinetics of this drug in man.³⁻⁶

Fourthly, we understand that endogenous depression is a complex and biochemically heterogeneous disease, probably with a deficiency of at least two important neurotransmitter amines.⁷⁻⁹ Thus all the patients clinically classified as "endogenous depressives" in various studies need not be expected therapeutically to respond universally to antidepressive medication.

For many reasons, therefore, we at least would hesitate to propound a "therapeutic range" of plasma levels for all tricyclic antidepressant drugs that might be used in a diversity of patients superficially diagnosed as suffering from "depression." From our experience over a number of years now in offering a service for the measurement of tricyclic antidepressant drugs in plasma we in this unit would agree with the views of Asberg² that in patients who do not respond to seemingly adequate doses of antidepressant drugs and in those who suffer from serious side effects the measurement of plasma levels is a way of increasing the efficacy of treatment. In addition, the regular monitoring of these levels may also prove useful in those patients receiving long-term medication for the prophylaxis of recurrent endogenous depression.¹⁰ Patients with properly diagnosed endogenous depression, carefully managed in this way, must be distinguished from that vast population of people prescribed antidepressant medication for mental "depression" of no clear-cut aetiology, for whom, we would admit, the performing of plasma level analyses is of doubtful value.—We are, etc.,

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- 1 Braithwaite, R. A., et al., *Lancet*, 1973, 1, 556.
- 2 Asberg, M., *Clinical Pharmacology and Therapeutics*, 1974, 16, 215.
- 3 Alexanderson, B., *European Journal of Clinical Pharmacology*, 1972, 4, 82.
- 4 Alexanderson, B., M.D. Thesis, 1972. University of Linköping, Sweden.
- 5 Alexanderson, B., *European Journal of Clinical Pharmacology*, 1973, 6, 44.
- 6 Braithwaite, R. A., Ph.D. Thesis, 1974. University of London.
- 7 Sjöqvist, F., *International Pharmacopsychiatry*, 1971, 6, 147.
- 8 Asberg, M., et al., *Clinical Pharmacology and Therapeutics*, 1973, 14, 277.
- 9 Van Praag, H. M., *Pharmacopsychiatrie Neuro-Psychopharmacologie*, 1974, 7, 88.
- 10 Kragh-Sørensen, P., et al., *Psychological Medicine*, 1974, 4, 174.

Fluorescent Drumsticks in Human Female Polymorphs

SIR,—The presence of a sex specific nuclear appendage, called "drumstick," was first reported in human polymorphonuclear leucocytes by Davidson and Smith.¹ In normal

1 Home Office and Department of Health and Social Security, *Interim Report of the Committee on Mentally Abnormal Offenders*, Cmd. 5698. London, H.M.S.O., 1974.

2 Department of Health and Social Security, *Revised Report of the Working Party on Security in N.H.S. Psychiatric Hospitals*. London, D.H.S.S., 1974.