prednisolone twice daily. At no time did he receive any sulphonamide preparation. While on this dosage of prednisolone he received, in October 1973, an injection of 1 ml of Admune subcutaneously, which he had had in the previous year. Within 10 days he began to suffer from myalgia, which affected all muscle groups, and arthralgia. His weight began to fall and this was associated with general malaise and anorexia. Clinical examination was unhelpful apart from a maintained pyrexia of 38-39°C and generalized muscle wasting.

Investigations showed a haemoglobin of 11·0 g/100 ml; E.S.R. 33 mm in 1 hr; serum electrolytes and urea normal; W.B.C. 22,000/mm³ with 6,300 eosinophils/mm³; serum creatinine phosphokinase 17 mU/ml; antinuclear factor negative; L.E. cells not seen. Both latex and Rose-Waaler tests were weakly positive. Urine contained protein 10 mg/100 ml, but no blood at any time. His blood urea then rose to 74 mg/100 ml and alkaline phosphatase to 22 King-Armstrong units. Serum asparate aminotransferase was 44 IU/l. and serum hydroxybutyric acid dehydrogenase 36 IU/l. Protein electrophoresis showed a low albumin level with increased α_2-globulin. An electromyograph showed small motor units consistent with myopathy. Muscle biopsy was performed and this showed necrotizing arteritis. Tests for antinuclear factor then became positive but serum complement was 132 mg/100 ml (normal 82-150 mg/100 ml).

He was started on 40 mg of prednisolone daily and made good symptomatic improvement. His temperature came down to normal, as did his blood urea, liver enzymes, eosinophil count, and E.S.R. However, his muscles became more wasted and despite the addition of azathioprine and anabolic steroids he continued to deteriorate. His weight had in fact fallen from 11 stone (70 kg) before his illness to 6 stone (38 kg). In the last two days of his life he developed macroscopic haematuria and ultimately died of bronchopneumonia. Necropsy revealed extensive polyarteritis of his muscles. His heart showed areas of microinfarctions and both his kidneys showed severe glomerulonephritis with epithelial crescents.

We think that the time relationship of the onset of his illness to the immunization makes Admune the likely cause of this acute fulminating collagen reaction.—We are, etc.,

C. F. P. WHARTON
R. PIETRONI

Orpington Hospital,
Orpington, Kent

Dangerous Patients

SIR,—Your leading article (23 March, p. 527) is welcome in drawing attention to the difficulties in making recommendations regarding dangerous patients in the light of current attitudes in mental hospitals towards mentally disordered offenders. However, there are further issues raised which you have failed to follow through in your argument.

You have indeed protested time and again about the shortage of beds in secure hospitals. However, in jumping to the next conclusion that the requirements for admission to a special hospital should be widened both you and the Royal College of Psychiatrists are rejecting the responsibility of mental hospitals to provide secure accommodation for at least a percentage of patients. It hardly solves the problem by shifting all responsibility to special hospitals and then expecting them to carry the opprobrium and also "like Janus of ancient mythology, to look in two directions at the same time: forward towards a therapeutic community . . . and backwards towards the security of a prison."

It is to be hoped that the community will come to recognize the consequences of the "open door" policy when pursued to its limit and begin to question whether the problem is solved by exchanging mental hospital beds for special hospital and prison beds.—I am, etc.,

N. F. HILLS

Department of Corrections,
West Perth,
Western Australia

SIR,—The harbouring in the general psychiatric hospital of potentially dangerous patients may not be quite so intractable under present legislation as your leading article (23 March, p. 527) implies.

In the event of such a patient becoming also uncooperative, it is open to the hospital to secure the almost immediate help of either my colleague, Dr. Patrick McGrath, or one of his Broadmoor Hospital colleagues. As the result of telephoned information an immediate bed could be secured for the patient's transfer to Broadmoor under the provisions of section 63(3) of the Mental Health Act (which takes up for section 60 detainees the provision of section 41(1a) of the Act). Alternatively a Broadmoor consultant could visit rapidly the detaining hospital and give an opinion on disposal, with transfer into security if deemed appropriate.

My Broadmoor colleagues prefer the extra grip afforded by an indefinite time restriction order under section 65 of the Act; but I do not believe they would consider it a sine qua non. It is, however, open to the general psychiatric consultant to insist on this. He can thus refuse inpatient admission under section 60 from magistrates' courts but require that, if psychiatric disposal is thought suitable by the bench, the patient be remanded to crown court for the addition of the indefinite restriction order.—I am, etc.,

SEYMOUR SPENCER

Oxford

Epilepsy and Driving

SIR,—The *British National Formulary* has rightly become a respected publication, but unfortunately there is an error on page 82 of the 1974-76 edition which is causing confusion to doctors when advising their patients about epilepsy and driving.

The passage in the *B.N.F.* reads:

"Under recent regulations in the U.K. an epileptic may be eligible for a driving licence but, if controlled by drugs, he must not alter the regimen unless he is prepared to give up his licence for three years; if he subsequently has a fit during daytime he must wait a further three years, even if medication is resumed, before applying for a licence."

In fact the relevant regulation[1] is as follows:

"An applicant for a licence suffering from epilepsy shall satisfy the conditions that—(*a*) he shall have been free from any epileptic attack whilst awake for at least three years from the date when the licence is to have effect; (*b*) in the case of an applicant who has had such attacks whilst asleep during that period he shall have been subject to such attacks [while asleep but not whilst awake] since before the beginning of that period; (*c*) the driving of a vehicle by him in pursuance of the licence is not likely to be a source of danger to the public."—We are, etc.,

T. A. BETTS
M. ESPIR
F. B. GIBBERD
R. H. E. GRANT
P. M. JEAVONS
A. RICHENS
C. W. M. WHITTY

British Epilepsy Association,
London W.C.1

1 *The Motor Vehicles (Driving Licenses) Regulations 1970*, 22(2). London, H.M.S.O., 1970

British Academy of Psychopharmacology

SIR,—Further to the letter from the steering committee (2 March, p. 391) the inaugural meeting of the British Academy of Psychopharmacology was held on 22 April and the academy formally constituted.

As a result of the steering committee's letter we received 129 letters supporting the formation of the academy and one letter against its formation. The inaugural meeting was attended by 45 interested individuals, many of whom had travelled considerable distances to attend the meeting. Letters of congratulation and support were received from the presidents of the International, American, German, and Turkish Colleges of Psychopharmacology.

Professor Max Hamilton was elected first president of the academy, and Dr. Alec Coppen president-elect. Other officers and a council of 10 members were also elected. It was decided that one of the main objects of the academy would be to provide a means of integrating the many disciplines involved in psychopharmacological research, though there would be some emphasis on clinical psychopharmacology. To this end applications for membership will be considered from interested individuals, and any of your readers who may like further details are invited to write to me.— Iam, etc.,

DAVID WHEATLEY
Honorary Secretary,
British Academy of Psychopharmacology

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Withdrawal Symptoms after Stopping Phenelzine?

SIR,—In the past month two of my patients have suffered similar symptoms related to the withdrawal of phenelzine.

The first is a man in his thirties with a rather long-standing neurotic depression who has benefited from phenelzine without making a full recovery. Because of residual symptoms I decided to give him a course of electric convulsion therapy and I thought it wise to stop the drug meanwhile. However, within a day of doing so he was suffering from a severe frontal headache which lasted for several days and, more significantly perhaps, shivering and a feeling of intense cold which lasted well over a week. He said he felt just like Frank Sinatra

looked in the drug addiction film "The Man with the Golden Arm."

Then at my outpatient clinic another patient suffering from neurotic depression told me how very ill she felt after stopping her regimen of phenelzine and haloperidol to go on to lorazepam. The lorazepam made her excessively drowsy and she stopped it after a day or so but then she felt depressed and irritable and also described this feeling of cold and shivering.

This last symptom is quite reminiscent of the "cold turkey" reaction to the withdrawal of narcotics from the habituated, and the reaction followed so swiftly the discontinuation of the drug that I wonder if it might not represent a genuine physical response to deprival of the drug rather than a purely psychological one or the return of the depression. The medical adviser to the manufacturers tells me that no such withdrawal symptoms have previously been reported but I wonder if any of your readers can record similar experiences?—I am, etc.,

BRICE PITT

The London Hospital
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Malaria in the United Kingdom

SIR,—In your epidemiological report (5 January, p. 43) you mention 84 cases of malaria in immigrants to the U.K. in 1972. The adult populations of countries where malaria is endemic are generally considered to be immune to malaria in the sense that they do not suffer overt attacks of the disease.

It would be valuable to know if there is any record of the proportion of immigrants in whom malaria was considered to be the cause of their illness rather than simply a concomitant finding, the number of adults, and whether any factors were found, such as acute infections or steroid therapy, which might have been responsible for a temporary lowering of resistance to malaria.—I am, etc.,

ANTHONY BRYCESON

Department of Medicine,
Ahmadu Bello University,
Zaria, Nigeria

Intensive Care: Allocation of Resources

SIR,—Your issue of 23 March (p. 567) contains an article by Dr. K. Astvad and others on the effect on mortality from cardiac infarction of the establishment of an (intensive) coronary care unit. *Health Trends* for February 1974 includes a report by Dr. Eva Alberman on stillbirths and neonatal mortality in England and Wales by birth weight during 1953-71.

The first article suggests that intensive care makes little difference to the overall mortality of patients with coronary heart disease; the second makes it clear that provision of adequate neonatal care, including intensive care, in maternity hospitals makes a great deal of difference to mortality in newborn infants, as it has also done to morbidity.[2 3]

The moral as regards allocation of resources is obvious, but it is not obvious that it has been drawn, nor that it will be while the British Paediatric Association remains a poor relative of the royal colleges with no direct representation, for instance, on the Central Health Services Council and similar bodies.—I am, etc.,

J. A. DAVIS

University Department of Child Health,
St. Mary's Hospital,
Manchester

1 Alberman, E., *Health Trends*, 1974, **6**, 14.
2 Stewart, A., in *Perinatal Medicine*, ed. H. Bossart, J. M. Cruz, A. Huber, L. S. Prod'hom, and J. Sistek, p. 181. Bern, Huber, 1973. *Lancet*, 1972, **1**, 437.

Thromboembolism and Oral Contraceptives

SIR,—Your leading article (9 February, p. 213) suggests a difference in the possibly thrombogenic effect of unnatural oestrogenic compounds and natural oestrogens.

A normal content of fibrinolytic activators in the vessel walls is important for counteracting thrombosis.[1] In an earlier investigation we found that ethinyloestradiol in a large dose (250 μg daily for 10 days) depressed the fibrinolytic activity in the venous vessel wall in post menopausal women about to be operated upon for uterine prolapse.[2] We now have given 17-beta-oestradiol to a similar group of 16 women in a biologically equivalent dose (10 mg daily for 10 days). Biopsy specimens of superficial veins were obtained before and during the last day of treatment and were examined histochemically for their content of fibrinolytic activators. In contrast with the findings during treatment with ethinyloestradiol, no significant depression of the fibrinolytic activity was found, which is in accordance with your editorial suggestions.—We are, etc.,

B. ÅSTEDT
S. JEPPSSON

Coagulation Laboratory,
Allmänna, Sjukhuset,
Malmo, Sweden

1 Isacson, S., and Nilsson, I. M., *Acta Chirurgica Scandinavica*, 1972, **138**, 313.
2 Åstedt, B., *Acta Obstetricia et Gynecologica Scandinavica*, 1971, **50**, 279.

Skin Reactions to Practolol

SIR,—Since the report by Rowland and Stevenson[1] in 1972 of a patient with exfoliative dermatitis who was taking practolol we have been concerned at the increasing number of patients we have seen who have developed a rash caused by this drug. Although a minority of patients presented with either an eczematous eruption or exfoliative dermatitis, the majority have presented with a distinctive psoriasiform eruption, further details of which will be the subject of a full communication.

We have been struck by the uniformity of this type of eruption, particularly in its distribution on the hands and bony prominences, the main features of which are scaling and thickening of the skin of the palms, soles, and sides of digits with atypical psoriasis-like plaques over the knees. The remainder of the rash is widely scattered over the body, being red and characterized by marginated scaling. In our opinion the clinical features produce an easily recognizable diagnostic picture.

These patients have been taking practolol for periods ranging from three weeks up to two years, with a mean duration of treatment of 10 months, before the onset of the rash. As this drug has now been available for over two years this latent period before the onset of the rash may be one explanation for the apparent increased frequency of the practolol-induced rashes that is our impression at present. We therefore consider it timely to draw the attention of the medical profession to this entity.—We are, etc.,

ROBIN FELIX

Department of Dermatology,
Royal Victoria Hospital,
Newcastle upon Tyne

F. A. IVE

Dryburn Hospital,
Durham

1 Rowland, M. G. M., and Stevenson, C. J., *Lancet*, 1972, **1**, 1130.

Drugs Affecting Oral Contraceptives

SIR,—Ever since oral contraceptives were introduced, their efficacy has almost been taken for granted. By both the doctor and the patient they have been regarded as being almost infallible. In the very rare cases where a pregnancy occurred the blame was first laid against the patient for having forgotten the pill and then only rather grudgingly against the pill. Recent publications have, however, started to accumulate to show that neither the patient nor the pill may be at fault. It may in fact be that the patient is taking other medicines and that these may be preventing the pill from producing the proper contraceptive effect. This effect appears to act mainly against the oestrogen content and may explain the strange finding that the average age of the patients who became pregnant while taking the pill was 35[1]. This was found to be occurring predominantly on sequential-type oral contraceptives.

The most marked effect on oral contraceptives would appear to come from the antibiotic rifampicin. This antibiotic is one of the recently introduced antituberculosis drugs and it has gained wide usage in many countries as it is very effective and easy to administer. Unfortunately, since it is given to ambulant patients many of these may also be taking oral contraceptives to prevent unwanted pregnancies during their treatment period. The first indication of this interaction came from Reimers *et al.*,[2] who found that of 88 patients with pulmonary tuberculosis who were taking oral contraceptives in addition to rifampicin, 75% suffered from cycle disturbances and five became pregnant, whereas in another group, who received streptomycin, only 4% showed any cycle irregularity and there were no pregnancies.

Though other workers[3] found no cycle disturbances or pill failure, it was felt by Reimers that rifampicin might influence the biogenesis and metabolism of the oestrogens and that this might lead to failure of action. Other antibiotics have also been shown to affect oestrogen metabolism, for ampicillin given to healthy mothers in the latter weeks of pregancy decreases the urinary oestriol levels by as much as 69% of the pretreatment level.[4] It was felt that ampicillin also could give rise to unexpected complications with oral contraceptives by affecting the enterohepatic circulation of the oestrogens. This type of work has been confirmed by other workers.[5]

The second most common therapeutic group to affect the mechanism of action of oral contraceptives are the barbiturates. This could have been expected, as it was reported in 1968 by Levin[8] that in animals chronic treatment with phenobarbitone could reduce the uterotropic effect of oestrogen and progestogens. Other workers[9] reported that barbiturates stimulate the metabolism, by enhancing the hydroxylation, of all steroids, and it was confirmed[10] in vitro and in vivo in animals that the conversion of mestranol to erthinyloestradiol could be increased as much as three times by pretreatment with barbiturates.