Misuse of Drugs Regulations 1973

SIR,—So far there seems to have been little comment on the introduction of the Misuse of Drugs Regulations 1973. From the general practitioner's point of view there has been cause for concern on several grounds.

(1) The lack of specific information initially supplied to doctors—the Plymouth Executive Council had fewer than 20 copies of the regulations available.

(2) The incorrect information circulated to pharmacists by their representatives and the invention of additional criteria for returning prescriptions to the prescriber—the chemists do not seem to have copies of the statutory instruments even now. In this area prescriptions have been returned, or dispensing delayed, because the chemist did not like the form of the patient's address and in another case because a different pen was used for the address, despite the doctor confirming by phone that he had written both parts. (So much for the chemist as an expert on hand writing!) The most annoying aspect is the refusal of some pharmacists to accept dating by a rubber stamp when the regulations have obviously been framed specifically to allow this. Section 15(1) (a) states the doctor must date the script before it leaves his hands but subsection (b) states that the requirement of being in the doctor's own handwriting applies only to subsections (e) and (f). This is not a mere quibble as I use my date stamp to save time as I do not have to think of the date each time.

(3) With two surgeries I have to keep a dangerous drugs register on each premises for the drugs kept there, but there seems to be no provision for those I carry in my car, which are the only ones I normally administer. Will writing down the name of the recipient of two tablets of pethidine or one ampoule of DF118 administered at 2 a.m. really help to solve the drug problem? Few patients know what drug the doctor gives them in an emergency and if I really want to administer them to myself, even my amateur conjuring would be good enough to switch drugs in the patient's house.—I am, etc.,

STUART R. COVERLEY

Plymouth

Return to Work

SIR,—I was interested in your leading article on return to work (28 July, p. 186) and fully agree that this is one of the most important outcomes of medical care and should be the constant concern of doctors. That this is so for only a small number of doctors may be due to the lack of emphasis on rehabilitation during training. When showing students and practitioners round a rehabilitation centre one is frequently left with the feeling that the philosophy and practice of rehabilitation and resettlement are interesting, surprising, and totally unfamiliar to most of them. Hopefully this will change when the recommendations of the Tunbridge Report are put into practice and departments of rehabilitation with appropriate consultants become an integral part of major hospitals.

Return to work is, of course, a major preoccupation of medical and paramedical staff concerned with rehabilitation, and it is unfortunate that the break in departmental responsibility between medical re-

habilitation in hospital, outpatient department, and rehabilitation centre (the Department of Health) and industrial rehabilitation, retraining, and sheltered work (Department of Employment) occurs at a time when a patient is at his most vulnerable and anxious. He may have been given little guidance and is uncertain where to turn on leaving the sheltered medical environment. Communication at this stage is vital and may have to include not only the patient, his family, and general practitioner but also the employer and disablement resettlement officer. Far from the services of the Department of Employment being totally separate from medical rehabilitation, in a centre where many patients are severely disabled or elderly close co-operation with the disablement resettlement officer is an integral part of medical rehabilitation.

In our case this consists of a weekly visit from the disablement resettlement officer with free access to remedial departments to observe patients' activities in the workshop and gymnasium and an office for private interviews with patients and staff as necessary. In addition to medical information, including physical and mental problems, prognosis, and possible restrictions, we aim to provide the disablement resettlement officer with up-to-date information on attitudes, work tolerance, and skills, which are fully assessed by the occupational therapists and remedial gymnasts during the course of treatment. Contact with the disablement resettlement officer is made as soon as there is a suspicion that re-employment may not be entirely straightforward, and is often initiated by the social workers. The patient's reaction is usually one of relief that his future is being considered, previously unvoiced anxieties can be discussed, and a positive and realistic attitude towards life and work with a disability inculcated. Discussion may need to continue during the patient's stay, and should lead to a definite plan being made and notified to all concerned before the patient's discharge. It is obvious that this aim is more likely to be achieved by the joint efforts of the remedial team and officials of the Department of Employment.

As regards the question of subsidies, and in spite of all the very real disadvantages associated with such a scheme, these would undoubtedly be helpful in encouraging a previously highly-paid disabled worker, with heavy financial commitments covered by unemployment and subsidiary benefit payments, to consider training or employment at lower rates of pay. In the long run this would not only benefit the patient's morale by shortening his period of unemployment but might prove economically advantageous.—I am, etc.,

ANNEMARIE D. TUPPER

Wolfson Medical Rehabilitation Centre,
Atkinson Morley's Hospital,
London S.W.20

Osteoporosis and Long-term Corticosteroid Therapy

SIR,—Drs. D. J. Hosking and M. J. Chamberlain (21 July, p. 125) report no evidence of osteoporosis developing in five patients

having corticosteroids over periods up to three years. This finding is reminiscent of our attempt,¹ by other means, to study steroid osteoporosis; steroid-treated patients with rheumatoid arthritis did not have osteoporosis significantly more often than those not so treated.

Osteoporosis being a well-recognized feature of Cushing's syndrome, both sets of results are perhaps unexpected and require explanation. Drs. Hosking and Chamberlain comment that in their patients age and improvement in the disease being treated might have been factors which outweighed the steroid effect. Our patients all had rheumatoid arthritis, itself probably associated with osteoporosis,² so that the added effect of steroids was difficult to detect. Thus, not surprisingly, the risks of osteoporosis with steroid treatment are heavily influenced by the disease for which the treatment is being given.

There is probably at least one other factor. In 1963, in a study of 70 women having 10 mg of prednisone daily for rheumatoid arthritis, Dr. H. Scarborough and I found that 34 developed steroid purpura (unpublished observations). The time of onset of the purpura was very variable; about a third of the patients developed it early, within 36 months of starting treatment. This was not because they were older or had more severe rheumatoid disease. Dr. Picton Thomas measured free and bound "cortisol" in the plasma and also 17-hydroxysteroids; there were no significant differences. We were driven to the conclusion that some patients are more "susceptible" to steroids than others. This view was supported by the finding that easily recognizable features of Cushing's syndrome had appeared in 77% of patients with purpura but in only 22% without purpura. If the same considerations hold for steroid osteoporosis it might well be difficult to detect a susceptible minority.

Osteoporosis is often quoted as a major hazard of steroid treatment. In fact, it is difficult to be sure just how often steroids are solely responsible for it and it is seldom, except perhaps in children, a really troublesome complication. There are much greater dangers—infection and gastrointestinal catastrophes—besides which osteoporosis is a minor risk.—I am, etc.,

BRIAN MCCONKEY

Dudley Road Hospital,
Birmingham

¹ McConkey, B., Fraser, G. M., and Bligh, A. S., *Quarterly Journal of Medicine*, 1962, 31, 419.

² Dent, C. E., and Watson, L., *Postgraduate Medical Journal*, 1966, 42, 581.

Coeliac Disease in the West of Ireland

SIR,—Dr. E. J. Moynahan (26 May, p. 484) makes the interesting suggestion that the high incidence of coeliac disease in the West of Ireland may be attributed to lack of exposure of the Irish to wheat until after the famine of the 1840s, with consequent persistence in the population of the genetic factors associated with coeliac disease. Some support is available for this theory in that the cereal consumed in greatest amount by the Irish for several millennia was probably oats, either as oatmeal porridge or bread.¹ However, wheat of different varieties, notably Emmmer and Einkhorn, is said to have been cultivated all over Europe since neolithic times² and there

is ample evidence from contemporary accounts that wheat has been consumed regularly in Ireland since early historic times,¹ although until the middle of the 19th century it was probably eaten regularly only by the more affluent. Specific finds of wheat are few; two that we have been helped to trace are those made by Hartnett³ in a bronze age grave in County Wicklow and by Walshe⁴ in a burial cairn in County Wicklow. Dr. Moynahan's remark that "bread wheats were not cultivated in the West of Ireland" is probably incorrect, but it does seem likely that wheat was not the staple cereal of the majority of the population.

With regard to dermatitis herpetiformis, we agree with Dr. Moynahan that this condition is rarely associated with coeliac disease in our experience, which amounts to one definite case among 40 adults and none among 190 children. However, the number of adult cases of coeliac disease studied is not large enough for our findings to be significant.

We agree with Drs. P. Asquith and W. T. Cooke (26 May, p. 484) that a study of HLA antigens in coeliac and normal populations would be worthwhile, and this is in progress. With regard to the suggestion that the combination of the foreign proteins of cow's milk and wheat may have a synergistic deleterious effect, we can only say that we have not yet encountered a child with coeliac disease in whom we could demonstrate milk protein allergy. Apart from the early weeks of treatment, when occasional mild lactose intolerance has occurred, all our patients have made satisfactory progress on cow's milk.

The suggestion of Drs. Asquith and Cooke that wheat cereals should be withheld until after 6 months of age from HLA8-antigen-positive siblings of coeliacs has merit. It would probably be justifiable to carry out a controlled trial of early and late feeding of wheat to such infants; however, apart from being dependent on the goodwill and co-operation of parents, it would need to extend over many years to have validity. We have been alarmed for many years by the early and heavy exposure of infants to wheat cereals and have endeavoured both privately and publicly to discourage this. An earlier onset of coeliac disease is certainly a result of early wheat feeding, and of 190 children with the disease, 11 presented before 6 months, 55 before 12 months, and 96 under 2 years. In addition to the encouragement of breast feeding, we believe that all infants should be maintained on milk alone for several months, if possible, that rice should be the principal cereal used when hunger demands it, and that wheat should not be introduced until about six months of age.

We wish to thank the following for providing information on cereals in Ireland: Professor M. Duignan, Dr. M. Mitchell, and Dr. E. Rynne, of University College, Galway, and Dr. J. Raftery of the National Museum of Ireland.

—We are, etc.,

M. MYLOTTE
B. EGAN-MITCHELL
C. F. MCCARTHY
B. MCNICHOLL

Departments of Gastroenterology and Paediatrics,
Regional Hospital and University College,
Galway

- ¹ Lucas, A. T., G. Werin, 1960, 3, pt. 2 p. 8.
- ² Jessen, K. and Helbeck, H., *Kongelige Danske Videnskabernes Selskabs Skrifter*, 1944, 3, pt. 2, 1.
- ³ Hartnett, P. J., *Proceedings Royal Irish Academy*, 1957, 58, (Sect. C), 197.
- ⁴ Walshe, P. T., *Proceedings of the Royal Irish Academy*, 1941, 46, (Sect. C), 221.

New Urinary Steroid in Hypertension

SIR,—We would like to report that during routine analysis of aldosterone in urine a new steroid was detected and thereafter isolated in patients with hypertension. Because this steroid occurs in measurable amounts only in patients with hypertension it has been given the name "hypersterone." The compound is obviously not identical with any steroid which has previously been suggested to be involved in hypertensive disease in man or animals.¹ The complete structure of hypersterone is not yet known, but we wish to present some characteristic data (see table).

A small amount of hypersterone was oxidized with periodic acid and submitted to combined gas chromatographic-mass spectrometric analysis and the oxidized compound was found to have a molecular weight of 360. This could correspond, for example, to an underivatized compound with a structure of aldosterone but with two additional hydroxyl groups. But there are also some other possible structures. The base peak was at m/e 345 and the fragments in the higher mass region were typical of a lactone derivative. However, in the lower mass region the spectrum was uncharacteristic, perhaps owing to the very small amount available for analysis or to thermal decomposition (very long retention time) or both. Because of the very labile nature of the compound a mass spectrum of the non-oxidized steroid has not yet been obtained. The infrared spectra of hypersterone and the oxidized derivative showed a stronger hydroxyl band than those which were obtained for 5 β -dihydroaldosterone- γ -etiolactone and 18-hydroxycorticosterone- γ -etiolactone. The steroid showed a strong absorption of ultraviolet light, suggesting a Δ^4 -3-oxo- configuration.

The oxidized form of hypersterone could be determined quantitatively by gas chromatography, the sensitivity of detection being 2.5 μ g per 24-hour urine specimen depending on the amount of interfering substances. With this method it could be demonstrated that hypersterone cannot be detected in normal urine, that it is not formed during the isolation procedure, and that it is not formed from aldosterone added to urine. The amounts of hypersterone excreted in patients with essential hypertension are in the same range as normal values for aldosterone in urine. In patients with hyperaldosteronism the excretion of hypersterone is normally somewhat increased, but usually the amount

of hypersterone in urine seems to be unrelated to that of aldosterone. Because of the very small amounts of hypersterone present in urine and the lability of the underivatized compound the characterization of the new steroid is extremely difficult, and we are therefore reporting our results at this early stage before its exact structure has been definitely established. Because the compound can now be at least semiquantitatively determined in urine it should be possible to obtain some information as to its role in hypertensive disease.—We are, etc.,

HERMAN ADLERCREUTZ
RIITTA HEKALI
ÖRN WAHLROOS

Department of Clinical Chemistry,
University of Helsinki,
Meilahti Hospital,
Helsinki, Finland

- ¹ Melby, J. C., Dale, S. L., Grekin, R. J., Gaunt, R., and Wilson, T. E., *Recent Progress in Hormone Research*, 1972, 28, 287.

Glucagon and Growth Hormone

SIR,—In your leading article (27 January, p. 188) you conclude that stimulation with glucagon alone is an effective test for the ability to secrete growth hormone but, since it "takes longer to perform" and "is rather less reliable" than insulin-induced hypoglycaemia, glucagon stimulation should be regarded as a second-line test except in certain special situations. However, as you also note, with the insulin test serious hypoglycaemia may occur (we have seen this even in patients with a good growth hormone response) and medical supervision is required. These factors may induce a physician to perform glucagon stimulation first as a matter of safety and convenience. Perhaps more important, the reliability of glucagon stimulation can be improved when the patient is pretreated with propranolol two hours before the test is performed.¹ With this manoeuvre the physician on occasion may see a response of serum growth hormone when glucagon alone¹ or insulin hypoglycaemia² is ineffective.—We are, etc.,

CLARK T. SAWIN
MARVIN L. MITCHELL

Veterans Administration Hospital,
Boston, Massachusetts

- ¹ Mitchell, M. L., Suvunrunsi, P., and Sawin, C., *T., Journal of Clinical Endocrinology and Metabolism*, 1971, 32, 470.
- ² Tiwary, C. M., Rosenbloom, A. L., and Julius, R. L., *New England Journal of Medicine* 1973, 288, 218.

Immunosuppression by Halothane

SIR,—Recently, increasing attention has been paid to the risk of anaesthetic contamination (leading article, 24 March, p. 693) and

Characteristic of Hypersterone

	Thin-layer Chromatography		Paper Chromatography: Benzene: Cyclohexane: Methanol: Water, 9:1:6:4 v/v (Rf values)	Gas Chromatography (1% OV-22) (Retention times relative to cholestane (= 1.0))
	CHCl ₃ : Dioxane 96:4 v/v (Rf values)	CHCl ₃ : Acetone, 1:1 v/v (Rf values)		
Hypersterone	0.16	0.41	0.28	
Aldosterone	0.16	0.57	0.45	
18-Hydroxydeoxycorticosterone	0.19	0.62		8.6
Aldosterone- γ -lactone ..	0.60			8.1
Oxidized hypersterone ..	0.47			