International Relations in Medicine

SIR,—The Royal Society of Medicine last year established an International Relations Office, one of whose principal aims is to provide members of the Society with information likely to be of help to them when visiting other countries.

The International Relations Office now has a list of doctors in many European medical centres who speak English, and who on that account alone would be prepared to help members of the Royal Society of Medicine when they go there. The response to requests for help in this way has been most encouraging. I should therefore be most grateful if readers of this letter would let me have the names and addresses of doctors in European medical centres known to them, whom I might invite to join in this particular form of international co-operation in medicine.

The natural corollary of this is that the Royal Society of Medicine hopes to be able to return the same courtesy to foreign doctors visiting Britain; and, similarly, I should be most grateful if British doctors able to speak other languages would let me know whether they would be prepared to help the occasional foreign visitor who finds difficulty in speaking English when he comes to Britain.

I should, of course, be pleased to provide further details of the work now under way in the International Relations Office of the Royal Society of Medicine.—I am, etc.,

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Stature in Cystinuria

SIR,—The literature contains data demonstrating that patients with the congenital metabolic disorder cystinuria are below average height or that the state of their nutrition is very poor. Colliss *et al.*¹ showed that the mean stature of their series of 44 patients in England was 2.5 cm. less than of the normal population.

In a series of these patients whom we had occasion to study during the past 10 years in Czechoslovakia,² we determined stature in relation to age. We examined 41 male and 36 female patients over the age of 20, in

significance of the deviations of the differences by Student's *t* test. The mean stature of the cystinuric patient was then calculated from the standard deviation and the weighted mean of the stature of the normal population. The results are given in the Table.

It can be concluded that, unlike the series of Colliss *et al.*, our series does not show that adult cystinurics in Czechoslovakia have a lower stature than the normal population. On the contrary, the stature of both male and female patients was somewhat higher than in the normal population, although the

Sex	Normal		Cystinuria		Differ.	<i>t</i>	Significance
	No.	Height	No.	Height			
Males ..	4,343	168.90 cm.	41	171.04 cm.	+2.14	1.77	P < 0.10
Females ..	4,752	157.41 cm.	36	157.79 cm.	+0.38	0.42	Not signif.

whom cystinuria was conclusively demonstrated by biochemical methods. Their stature was compared with the values for a normal Czechoslovak population (4,343 men and 4,752 women) examined by Reisenauer and Svobodová³ between 1949 and 1952. We compared the stature of our patients with the mean statures in the corresponding age groups of the normal population, determining the

differences were not statistically significant.—I am, etc.,

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VLADIMÍR KRÍŽEK.

REFERENCES

- 1 Collis, J. E., Levi, A. J., and Milne, M. D., *Brit. med. J.*, 1963, **1**, 590.
- 2 Krížek, V., *Med. Klin.*, 1967, **62**, 1230.
- 3 Reisenauer, R., and Svobodová, H., *Cas. Lék. čes.*, 1961, **100**, 481.

Lithium—A Special Clinic?

SIR,—Lithium (usually as the carbonate) started to be used in psychiatry for the treatment of manic-depressive illness in 1949, when in general medicine it had already fallen into disuse as a salt substitute for cardiac patients, because its toxicity had led to several deaths.^{1,2} Consequently many psychiatrists are reluctant to use lithium. Its use was reviewed by Schou³ with the conclusion that "lithium therapy seems to offer advantages over other available therapies," but stressing that lithium is toxic and patients should be supervised clinically and biochemically. Baastrup⁴ suggested that lithium has a prophylactic action in manic-depressive illness and reports since have supported this view. Recently it has been reported that there may be a subgroup of patients who are lithium responders.⁵ It is clear that lithium must not be given in a haphazard manner. It has been said that the criteria for selection of patients and prophylaxis are not rigorous

enough, that there has been no controlled double blind trial, and that stringent demands for safety and efficacy should be met before a new drug is widely used,⁶ but an adequate trial in manic-depressive psychosis would be difficult. In 1961 Wingard⁷ concluded that there were no therapeutic uses for lithium, but since then the opinion has gained ground that it is beneficial to a proportion of patients with severe disease. An answer could be its use under carefully controlled clinical and chemical supervision in a special clinic. This might help us to learn more about prescribing lithium and the type of patient responding to it.

A general hospital outpatient clinic has been developed for patients with manic-depressive illness maintained on lithium carbonate. Patients usually have had a long history with many attacks and are often our former inpatients, but cases are also referred from elsewhere in the region. All patients are

studied psychologically and biochemically (for example, total body water and electrolytes) during a period of illness and after recovery, and assessed physically to ensure fitness for treatment. The procedures are explained to the patient and his relatives to ensure their co-operation and to acquaint them of the toxic effects and how to avoid them. Patients are asked to attend every one to four weeks, according to their clinical and biochemical state. At each visit lithium is prescribed according to that day's serum lithium result, and this level and the dose soon remain constant over many months. This may be the reason patients tend to remain well and free from toxic effects, but it may be the regular attention which is therapeutic—if so, the clinic is still justified. Attendances are usually supervised by the local mental welfare officers, who are enthusiastic about the results. They may have known the patients for many years and may have coped with many difficult admissions. They feel their patients are now well, often working, and showing a quality of improvement not seen with other treatments.

Although the use of lithium for the treatment and prophylaxis of manic-depressive illness is open to controversy, evidence suggests it is effective. Critics reasonably feel that it is not always prescribed with due regard to the rigid clinical and chemical control that is desirable. The establishment of a clinic may overcome some of these criticisms while allowing the lithium responders to continue their treatment safely. A special clinic allows more to be learned about the type of patient who does well on lithium. Eventually we may discover how effective lithium really is in manic-depressive illness. As the service is economical compared with the human and financial cost of the illness, it may be useful to try such a clinic in other areas.—I am, etc.,

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REFERENCES

- 1 Corcoran, A. C., Taylor, R. D., and Page, I. H., *J. Amer. med. Ass.*, 1949, **139**, 685.
- 2 Hanlon, L. W., Romaine, M., Gilroy, F. J., and Deitrick, J. E., *J. Amer. med. Ass.*, 1949, **139**, 688.
- 3 Schou, M., *Psychopharmacologia*, 1959, **1**, 65.
- 4 Baastrup, P. C., *Compr. Psychiat.*, 1964, **5**, 396.
- 5 Kerry, R. J., and Owen, G., *Amer. J. Psychiat.*, 1968, **124**, 1702.
- 6 Blackwell, B., and Shepherd, M., *Lancet*, 1968, **1**, 968.
- 7 Wingard, C., *J. Amer. med. Ass.*, 1961, **175**, 340.

Mood and the "Pill"

SIR,—I agree with Dr. Ellen C. G. Grant and Dr. J. Pryse-Davies (28 September, p. 777) that there is a significant incidence of depression and diminished libido in women on oral contraceptives, even taking into account that some women may already be depressed and/or have marital difficulties before embarking on the pill. Lumping together depression and diminished libido, which in my experience not infrequently occurred independently of each other, my figure of 17.7% in a 5-year follow-up of 1,000 women at Croydon compares very favourably with Dr. Grant's overall incidence of 16% in what is essentially a subjective clinical assessment.

I am very impressed by Dr. Grant's account of the fluctuations of endometrial monoamine oxidase in response to the various oestrogen/

progesterone combinations. But so far as the combined preparations are concerned, my findings fail to confirm her hypothesis that depression and loss of libido is dose-specific. With the seven different products in use in the Croydon clinic from 1962 to 1967, the incidence varied from 12.4 to 23.8% over an average of 21.9 cycles, compared with Dr. Grant's range of from 10 to 34% over an average of 14.9 cycles with the same preparations. For the strongly progestogenic tablets with ethinyl-oestradiol the incidence was 17.2% compared with Dr. Grant's 28%, and with mestranol 16.7% (Dr. Grant 17%), and for the intermediate combined tablets with ethinyl-oestradiol 23.8% (Dr. Grant 20%) and with mestranol 18.8% (Dr. Grant 16%).

As in the case of headache, a change from one preparation to another with a different oestrogen/progesterone combination only occasionally resulted in sustained relief, and I had one patient who developed a psychotic depression on Volidan (megestrol acetate, ethinyl-oestradiol), who later found that her identical twin sister had had a similar reaction on a different compound. That the response is specific there seems little doubt, but, as with the development of migraine, is the specificity as much in the patient as in the pill?—I am, etc.,

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JOY WEST.

SIR,—Drs. Ellen C. G. Grant and J. Pryse-Davies (28 September, p. 777) show that the highest incidence of depression together with a concomitant rise in endometrial monoamine oxidase occurs with the use of those oral contraceptives with high progestogenic content. I have been using injection of progesterone in premenstrual tension with depression, obtaining excellent results over a number of years. This is equally effective in both reactive and endogenous types of depression in which there is an exacerbation during the intermenstrual phase and when monoamine oxidase inhibitor drugs are not in use. This would appear to contradict the conclusions reached.—I am, etc.,

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E.C.G. Changes in Amitriptyline Poisoning

SIR,—The paper by Dr. R. J. Barnes and colleagues (27 July, p. 222) and the letter from Dr. R. G. Brackenridge (10 August, p. 377) prompt me to report another case of amitriptyline poisoning in which E.C.G. abnormalities were recorded.

A 34-year-old European housewife was admitted to hospital nine hours after swallowing 2,450 mg. (44.2 mg./kg.) of the drug. She was deeply comatose, with flaccid paralysis and dilated pupils unresponsive to light. The E.C.G. showed regular rhythm at 110 beats/min., with widening of QRS (to 0.16 sec.) in leads III, aVL, and aVF, sagging depression of ST segment not suggestive of ischaemia in leads I, III, aVL, aVF, and V2-4, and T-wave flattening in all leads, without recognizable U or P waves. She regained consciousness after eight hours, without chemotherapeutic interference, as recommended by Steel *et al.*,¹ but remained confused for a further 24 hours. At no time was she hypotensive, and serum electrolytes were normal. The E.C.G. pattern did not return to normal until the seventh day.

An abnormal E.C.G. in a comatose patient may well be a pointer to amitriptyline or imipramine ingestion, though as Dr. G. R. Burston (24 August, p. 500) points out similar changes occur in poisoning by other agents, but its real value would appear to be the caution it indicates in the management of such cases.—I am, etc.,

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REFERENCE

- ¹ Steel, C. M., O'Duffy, J., and Brown, S. S., *Brit. med. J.*, 1967, **3**, 663.

Recovery from Subacute Encephalitis

SIR,—I found your leading article (21 September, p. 693) "Recovery from Subacute Encephalitis" most interesting, particularly the suggestion that so-called subacute sclerosing panencephalitis may be due to measles virus (27 April, p. 189) and that recovery may occur.¹ It is perhaps worth adding that the characteristic clinical picture of progressive spasticity and dementia of this type of subacute encephalitis described by your article is not the only type of subacute encephalitis known.^{2,3} Patients with a presumptive subacute virus encephalitis who recovered, and where the clinical features were of lengthy retrograde amnesia with parietic Lange patterns in the cerebrospinal fluid, were described as long ago as 1960,² and I reported two cases³ where there was presumptive evidence that herpes zoster and perhaps respiratory syncytial virus may have been the causal agents. In these, subacute encephalitis was associated with a clinical picture of minimal general intellectual deficit, a pronounced Korsakoff dysmnnesia,⁴ abnormal electroencephalogram signs principally in the temporal regions, a mildly parietic Lange curve, and profound retrograde amnesia, with eventual recovery.

Admittedly, the inevitable difficulties of identifying the causative virus in patients who recover made the grounds for incriminating these particular viruses relatively slender, but the clinical picture in both my patients was almost identical with those described by previous workers,¹ and quite different from the kind of subacute encephalitis which your article seems to imply is the only type occurring. Certainly this seems also the impression one gains from most textbooks. It seems that the term "subacute virus encephalitis" should perhaps embrace a whole variety of subtypes, and it is interesting to speculate that the condition may perhaps be commoner in a mild form than is generally recognized, and that more than one of the common viruses may be responsible. If this were so, recovery may not be as exceptional as has hitherto been supposed.—I am, etc.,

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REFERENCES

- ¹ Cobb, W. A., and Morgan-Hughes, J. A., *J. Neurol. Neurosurg. Psychiat.*, 1968, **31**, 115.
² Rose, F. C., Symonds, C. P., *Brain*, 1960, **83**, 195.
³ Brierley, J. B., Corsellis, J. A. N., Hierons, R., and Nevin, S., *Brain*, 1960, **83**, 357.
⁴ Hall, P., *Lancet*, 1963, **1**, 752.
⁵ Hall, P., *Lancet*, 1965, **2**, 1077.
⁶ Korsakoff, S. S., 1889, translated by M. Victor, P. I. Yakovlev, in *Neurology*, 1955, **5**, 1396.

Synthetic Isoquinoline in Acute Respiratory Disease

SIR,—Your leading article "Chemoprophylaxis of Influenza" (20 July, p. 137) referred to the efficacy of the isoquinoline derivative U.K. 2371 (Pfizer Ltd.) in preventing infection with myxoviruses.¹ The therapeutic efficacy of a related compound, 1-(4-chlorophenoxymethyl) 3, 4 dihydroisoquinoline hydrochloride (U.K. 2054, Pfizer Ltd.) in children up to 5 years of age with acute lower respiratory infection was tested by us in a double blind trial designed to encompass the usual early winter epidemic of respiratory syncytial virus infection in Glasgow.² Possible effects on both clinical illness and viral excretion were sought. Compound U.K. 2054 or placebo was given for seven days, and all patients were given ampicillin with or without cloxacillin. A clinical score was assigned to lower respiratory signs daily.

Comparison of daily median clinical scores (Fig. 1) showed no reduction in illness in the treated group compared with controls. Children with virologically proved respiratory syncytial infection were analysed separately; no difference in clinical response was found. Moreover, the duration of infectivity indicated by serial isolation of respiratory syncytial virus from throat swabs was not altered by the drug (Fig. 2).

FIG. 1.—Comparison of daily median clinical scores in treated and control groups. FIG. 2.—RS virus isolations on admission (D 0) and on subsequent three days (D+1, D+2, D+3).

The seriousness of respiratory syncytial virus infection of young children is well recognized, and its treatment and control present difficulty. There is doubt about the efficacy of antibiotic treatment³ and also about the feasibility of a protective vaccine