At present methods of classifying and quantifying disability vary so much from centre to centre that it is difficult if not impossible to draw valid conclusions from any comparison between differing methods of rehabilitation. The methods used in rehabilitation also tend to be based more on ill-defined concepts of the virtue of exercise and example rather than validated methods of dealing with specific problems. It is extremely difficult to quantify rehabilitation methods in the same way as the dose of a drug is quantified. The response to these methods also varies from individual to individual, and certainly may contain a large placebo effect. It seems then that as a scientific discipline rehabilitation has hardly established its terms of reference and has not yet defined its units of measurement.

There have been a few notable studies in this field. The work of Copp in Manchester,¹ Ferguson and MacPhail in Glasgow,² and the multicentre trials of the British Association of Physical Medicine and Rheumatology spring to mind, but surely before implementing the recommendations of the Tunbridge report³ it is essential that basic studies should be carried out first by expanded academic departments of rehabilitation medicine, preferably organized on a regional basis, so that the degree and nature of the problems throughout Britain can be adequately defined and subsequently dealt with.—I am, etc.,

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Periodicity of Serum Prolactin Concentration

SIR,—Using a sensitive, precise, and specific radioimmunoassay for thyroid stimulating hormone (TSH) and a continuous blood sampling technique we have recently demonstrated the existence of a circadian rhythm of TSH concentration in peripheral blood in man.^{1,2} Our findings have confirmed the extensive observations of Nicoloff³ who obtained indirect evidence for fluctuations in thyrotrophic activity over the 24-hour period by using thyroïdal iodine release measurements.

When synthetic thyrotrophin releasing hormone (TRH) was shown to be a potent stimulator of prolactin release as well as of TSH,⁴ the obvious question was raised whether these two pituitary hormones had a common hypothalamic releasing hormone under physiological conditions. We therefore note with considerable interest the report by Dr. J. Nokin and his colleagues (2 September, p. 561) of a circadian rhythm of serum prolactin concentrations in men and non-pregnant women, with peak levels occurring between 1 a.m. and 5 a.m. This pattern bears a striking resemblance to the circadian rhythm of plasma thyrotrophin previously reported by our group.¹ It strongly favours a common releasing hormone for prolactin and TSH and supports the suggestion of Bowers⁵ that TRH should be renamed PTRH (prolactin-thyrotrophin releasing hormone).

Three additional points deserve comment. Firstly, the question of the physiological role of the prolactin inhibitory hormone has been highlighted by these findings. Secondly, in our studies of seven men and four women the basic circadian pattern of TSH has been similar in the two sexes. Finally, it is now becoming increasingly apparent that the plasma concentrations of several hormones—for example, cortisol⁶ and luteinizing hormone⁷ fluctuate widely over very short time intervals, suggesting episodic secretion. Consequently, intermittent blood sampling techniques fail to characterize adequately the total 24-hour pattern of circulating hormone concentrations, especially if sampling is infrequent, such as the four-hourly intervals employed by Dr. Nokin and colleagues. Our own recent evidence derived from blood samples collected continuously and integrated over 20- or 40-minute periods for 12 hours overnight in four healthy adults (two men and two non-pregnant women) and for 48 hours in one healthy male demonstrates that additional short-term variations of thyrotrophin levels occur superimposed on the circadian rhythm. The magnitude and pattern of these variations is such that periodic secretion of thyrotrophin seems the most likely explanation. Clearly, the simultaneous measurement of TSH and prolactin using very short sampling times or a continuous sampling technique or both are necessary to define more precisely the relationship between their daily secretory patterns and the physiological role of their possible common releasing hormone.—We are, etc.,

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Propranolol and Cluster Headache

SIR,—A report of favourable results in treating severe cluster headache in a 30-year-old man with propranolol may be of interest.

The patient had suffered for 10 years from recurring attacks of right-sided, throbbing headache lasting about 1-2 hours. During the two months before hospitalization the attacks had increased in frequency, occurring many times daily, and the patient had been almost unable to sleep. The attacks always began on the right side of the neck and spread up to the right side of the head, with maximum intensity in and around the eye. Often the pain was felt in the right shoulder and upper chest. During an attack the right eye wept, there was some photophobia, and the right temporal artery was swollen and tender. The attacks were never accompanied by visual disturbances but sometimes by nausea and vomiting. There was no family history of headache. Clinical examination and laboratory tests were normal. Many treat-

ments had been given, including ergot and dihydroergot preparations, prochlorperazine, corticosteroids, various kinds of analgesics, and carbamazepine, without any discernible effects.

During the first week of hospitalization the patient continued to have many attacks despite various analgesics. Treatment with propranolol was begun in the second week with a dose of 60 mg/day for two days and then 80 mg/day for another three days. After one day's medication the patient became completely symptomless and remained so for one week after stopping propranolol. Then mild symptoms returned, which ceased promptly after instituting propranolol 60 mg/day.

The type of headache described fits well with the criteria of so-called cluster or histamine headache.¹ Recently promising results from treating migraine with propranolol have been reported,² but so far as I know there are no reports of the effects of propranolol on cluster headache. The mechanism is open to discussion, but one might assume that the inhibitory effect of propranolol on histamine activity, demonstrated in relation to gastric acid secretion,³ might also be the mechanism of its effect on cluster headache. The favourable result in this one case seems to warrant further trials.—I am, etc.,

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Occupational Exposure to Nalidixic Acid

SIR,—A case of severe haemolytic anaemia in a breast-fed baby whose mother had been treated for pyelonephritis with nalidixic acid has been reported.¹ After recovery the infant's erythrocyte glucose-6-phosphate dehydrogenase (G-6-PD) was found to be normal. Another case of acute haemolytic anaemia in a baby after 48 hours' treatment with nalidixic acid has also been reported.² This baby has pronounced erythrocyte G-6-PD deficiency. We report here a case of haemolytic crisis in a man aged 20 who was exposed to nalidixic acid in his work in the pharmaceutical industry. He had no previous history of illness of any importance.

On 17 and 18 January 1972 the man's work consisted in pouring nalidixic acid dust into a large container with a small shovel three to four times a day. His working area had no extractor-fan ventilation and the process raised a very fine dust clearly visible to the naked eye. In the evening of 18 January he began to suffer from acute asthenia, anorexia, hyperpyrexia, and his urine became dark. He did not return to work but the symptoms improved during the next three days. When seen by us on 21 January his general condition was fairly good, the sclerae were jaundiced, and there was slight enlargement of the spleen. Investigation showed Hb 12 g/100ml; R.B.C. 3,800,000/mm³; leucocytes were within normal limits; a blood smear showed slight anisocytosis, no poikilocytes, no target cells, and no nucleated red cells. P.C.V. 34%, reticulocytes 25%. The urine was strongly hyperchromatic and contained much urobilin but no biliary pigments. Total serum bilirubin was 1.50 mg/100 ml and the indirect 1 mg/100 ml; serum transaminase and alkaline phosphatase were normal. Haemoglobin electrophoresis was normal and the HbA₂ was within normal limits. The fetal Hb was normal, and the direct