One and a half hours later the right testicle was explored under local anaesthesia. At operation it was found to be very oedematous and congested, and rotated through 180°. There was no evidence of a haematoma. The cord was untwisted and the testicle anchored to the scrotal wall. The wound was drained. The patient made an uneventful recovery, apart from postoperative retention of urine, for which he had to be catheterized on one occasion. He was seen subsequently on 30 April 1965 at follow-up when he was found to have a normal-sized testicle.

This is an unusual occurrence following a common operation. It is surprising that this complication does not occur more often. This case also emphasizes the importance of early exploration of the testicle when torsion is suspected.

I am grateful to Mr. A. F. Williams for his encouragement and permission to report this case.

—I am, etc.,

Oldham Royal Infirmary, Oldham. N. M. Kazi.

Vaccination Against Leprosy

Sir,—I have recently returned from Uganda and have been able to go through the issues published since the original paper by Dr. I. Sutherland, Miss M. M. Stone, and myself (1 January, p. 7). I have been surprised to read letters under the heading of "Vaccination Against Leprosy" which had, in fact, nothing whatever to do with vaccination against leprosy. They were concerned with the value of the drug diaminodiphenyl sulphone, in general use since 1948. I think they were prompted by the penultimate sentence in your very fair leading article on 1 January (p. 1) dealing with the subject matter of the paper.

I can understand how the confusion has arisen, but it would have been less misleading if the letters had been headed "Diaminodiphenyl Sulphone in Leprosy" and had referred to the leader. I am writing now lest the error be repeated, and attention be attracted away from the actual work we reported on the vaccine trial.—I am, etc.,

Hale, Cheshire. J. A. Kinnear Brown.

Care of the Mentally Subnormal

Sir,—The demand for places in hospitals for the mentally subnormal generally exceeds the accommodation that is available, though the provision of community care is gradually increasing.

Most hospitals for the mentally subnormal have a large proportion of long-stay patients who are likely to remain in hospital for life. Consequently the number of vacancies arising in these hospitals tends to be small, waiting-lists are long, and there is delay in the admission of patients from other hospitals.

An intermittent hospital care scheme can help to achieve a greater turnover of patients and allow the beds in existence to serve more people. In principle the scheme offers a patient a certain period—for example, three months—in hospital followed by a similar period at home, then readmission to hospital followed by another period at home, and so on. While the patient is at home the bed becomes available for other cases.

This scheme has many advantages. It can be offered to patients who otherwise would be awaiting a place for long-term care. Families are often prepared to have a mentally handicapped person at home provided they can be certain of obtaining periodic relief, and this they are assured under this scheme. The patient's progress under hospital conditions can be compared with that in the community. The period in hospital constitutes a training and treatment phase which should enable the patient to be managed more easily outside hospital. This pattern of care keeps patients under review and it breaks away from the preoccupation with permanent hospital care. Should long-term care become necessary for some cases, as a result of the intermittent care scheme it is more readily obtainable.—I am, etc.,

D. A. Spencer.

Westwood Hospital, Bradford 6.

Patients and Tablets

Sir,—It is known that unsupervised patients can be very remiss in taking their tablets.[1] The available evidence suggests that about one-half of hospital out-patients admitted to a drug trial will seriously default[2–5]; such trials are built on very unsure foundations.[6]

This preliminary report from a Surrey general practice is at variance with these findings.

A group of patients has been admitted to a controlled trial of an antidepressant drug. The trial has been in progress for the last 10 months and is expected to continue for a further two years. Following admission, patients are started on one tablet three times a day. If at the end of the first week the response to treatment is indifferent, then the dose is increased to two tablets three times a day (high schedule); if the initial response is promising then the patient persists with one tablet three times a day (low schedule). The adherence of each patient to the dosage has been assessed both by tablet counting and tablet marking.

A method of tablet counting has been evolved which offers no opportunity for patients to gain insight into the fact that they are being observed. Precisely 65 tablets are dispensed and the patient is seen routinely at the end of the first, second, and third week. This number of tablets is critical and ensures that the supply should be exhausted at a predictable time for both schedules. In the case of the "high schedule" there should be two tablets left at the second consultation, and for the "low schedule" this will occur at the third consultation. At each attendance the patient is asked whether any more tablets are required; discreet questioning then defines the approximate number which are left. The patient's answer at this critical consultation reveals, therefore, the extent of his cooperation. It would be possible for a gross defaulter to fabricate a reply rather than admit possession of a full box; in such circumstances a vague non-committal answer might be anticipated. This would contrast with the precision of a patient who has only two or three tablets left. Care was taken not to introduce an artificial element by adopting an over-authoritative attitude.

Many drugs may be looked for and detected in the urine. If, however, a control group is included in a trial, it is desirable to add a marker to both the drug and placebo tablets, in order to ensure a uniform detection technique for both treatment groups. Such a marker should be readily identifiable in the urine, but the patient must remain unaware of its presence. It should have a rapid excretion time, be non-toxic and pharmacologically inert, and only rarely be favoured as a self-medicament. The choice lies between dyes such as phenol red[7] and alizerin red S.,[7] or fluorescing compounds such as fluorescein, quinine, or riboflavin.[8,9]

It was correctly anticipated that most of the patients admitted to this trial would be women of child-bearing age, and riboflavin was preferred on ethical grounds. As a result of preliminary experiments on a subject, a dose of 6 mg. of the vitamin was selected for addition to each tablet. The urinary fluorescence caused by the recent ingestion of this dose may be clearly differentiated from the faint milky green fluorescence of some normal urines. Studies of large numbers of routine specimens showed that false positives from vitamin self-medication were rare. All specimens were assessed under an ultraviolet lamp and compared with standards derived from a mixture of fluorescein and quinine solutions.

Of the 40 patients who have already been admitted to the trial, six have defaulted, one left the district whilst under treatment, three admitted stopping their tablets from side-effects, and in one the original diagnosis was judged incorrect. Thus 29 out of 40 patients have up to now completed the trial; 22 of these patients are available for assessment in regard to their adherence to instructions, information about the remaining seven is incomplete owing to oversights and my occasional absence from the practice. Of the 22 patients, 13 were on the "high schedule" and nine on the "low schedule."

Seventeen out of these 22 patients had five or less tablets left at the critical consultation, one had about six left, and in three the number was suspected as being in excess of nine. This is a decisive result; confirmatory evidence as to its correctness is contributed by the nine patients—all judged "obedient" by tablet counting—who had been randomly allotted tablets marked with riboflavin. These nine submitted a total of 20 specimens of urine. Fourteen of these specimens were strongly fluorescent, four were intermediate, and only two were compatible with the recent omission of a tablet.

The conclusion that most patients who completed this trial took their tablets as prescribed is inescapable. If it should be confirmed as a constant finding from other practices, then it would provide a cogent argument for shifting the locus of such trials away from hospitals and into general practice.

I am grateful to Geigy Ltd. for supplying the marked imipramine tablets.

—I am, etc.,

Camberley. A. M. W. Porter.

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Vitamin-E Deficiency

Sir,—We were interested to read your leader on vitamin-E deficiency in man (16 April, p. 935). During the past year we have studied this problem in a wide range of patients. As judged by plasma levels or