nique between three and 15 years before without discovering a recurrence, and the method for inguinal hernias has also been enthusiastically described.²

I believe that if Mr. Tinckler uses a muscle-splitting incision (instead of a low midline one)—we found that in our survey the McEvedy (pararectal) approach suffered from the incidence of incisional weakness, and the Henry (midline) operation often gave poor access in addition—Mr. Gibbon might be able to accept that the preperitoneal prosthesis (which is not commonly needed when repairing inguinal hernias by this method in any case) is a logical solution. May I recommend a muscle-splitting preperitoneal approach for operations on inguinal and femoral hernias to others who have not yet used it? Its advantages are well listed where the other operations are also, of course, fully described.²—I am, etc.,

W. M. KEYNES.

The Radcliffe Infirmary,
Oxford.

REFERENCES

- 1 Keynes, W. M., and Withycombe, J., in *Hernia*, ed. L. M. Nyhus and H. N. Harkins, 1964, pp. 309–314. Lippincott, Philadelphia.
- 2 *Hernia*, 1964, ed. L. M. Nyhus and H. N. Harkins. Lippincott, Philadelphia.

Natural and "Induced" Sleep

SIR,—Dr. J. I. Evans and his colleagues (2 November, p. 291) have reported their findings that the administration of a barbiturate as a hypnotic depressed rapid eye movement (R.E.M.) sleep. The work of Kales *et al.*¹ was cited as having shown that methaqualone also depressed this phase of sleep.

Dr. J. P. Duffy, Mr. J. W. Osselton, and I have carried out a study comparing, in 14 volunteers, continuous E.E.G. recordings of a single night's natural sleep with similar recordings of Tuinal (1 capsule) and Mandrax (1 tablet) induced sleep. (Tuinal capsules contain 100 mg. quinalbarbitone sodium and 100 mg. amylobarbitone sodium; Mandrax tablets contain 250 mg. methaqualone and 25 mg. diphenhydramine.)

Our results show that in Tuinal-induced sleep there is a highly significant reduction in R.E.M. phase ($p < 0.01$) as compared with natural sleep, while there is no statistically significant difference in the occurrence of R.E.M. between natural sleep and Mandrax-induced sleep.

It is intended that a detailed report of our work will be published in due course.—I am, etc.,

K. DAVISON.

Newcastle General Hospital,
Newcastle upon Tyne.

REFERENCE

- 1 Kales, A., *et al.*, presented at A.P.S.S. Meeting, March 1968.

Perinatal Mortality Survey

SIR,—Professor Douglas Hubble has written a most interesting review of the second report of the British Perinatal Morality Survey (22 February, p. 495).

In the last paragraph he refers to all those engaged on "this massive inquiry" but makes no mention of midwives. Since the questionnaires on the 17,000 births occurring during the week of the survey were all com-

pleted by midwives it is obvious that their contribution to this great enterprise was of vital importance. The second Report will be of great interest to them as well as to obstetricians, paediatricians, social workers, and teachers.—I am, etc.,

AUDREY WOOD,
General Secretary,
Royal College of Midwives.
London W.1.

Corticosteroid Therapy and Growth

SIR,—Your leading article entitled "Corticosteroid Therapy and Growth" (15 February, p. 393) does not mention the possibility that some steroid preparations may be more growth-inhibiting than others. The change from betamethasone to prednisolone in equivalent doses in three patients under my care has resulted in an increase in the rate of growth, and I have wondered whether other clinicians have noticed anything similar.—I am, etc.,

IAN G. WICKES.

St. Andrew's Hospital,
Billericay, Essex.

Gastrointestinal Haemorrhage and Aspirin

SIR,—Dr. A. J. Quick (1 February, p. 315) states that "aspirin appears to act by preventing the vascular contraction after mechanical injury of the micro-circulation." The following case appears to support his statement.

A 5-year-old boy had acute tonsillitis with high fever and generalized aches and pains. Oral penicillin for the tonsillitis and a 150 mg.-aspirin tablet for the pain were prescribed. A few hours later he had a haematemesis, losing about a half-pint (500 ml.) of blood. It was assumed that he was sensitive to aspirin.

One month later he was admitted to hospital for tonsillectomy. His record was clearly marked that he was sensitive to aspirin. Nevertheless the routine post-tonsillectomy aspirin gargle was given. Twenty minutes later he bled severely from the tonsillar bed and nearly died.

The potentially dangerous local action of an aspirin gargle is worthy of note. It is suggested that its use for this purpose be discontinued.—I am, etc.,

London E.10.

J. SAPERIA.

Tetracycline and Nystatin

SIR,—In commenting on the letter by Dr. K. M. Citron and his colleagues (1 March, p. 575) in answer to some of my criticisms (28 December, p. 829) of their paper (16 November, p. 411), I shall confine myself to the principal issues. In their original report these authors define the aim of their large multicentre trial as (a) to assess the frequency of side-effects of tetracycline given in a dose of 2 g. daily, (b) to determine whether side-effects could be prevented or reduced by the addition of nystatin (no reference made to the relevance of its dose), and (c) to correlate these clinical findings with the results of examination of the stools for *Candida* species.

One of the main and, if correct, most important conclusions after evaluation of their data was that there is not any association between *Candida* and gastrointestinal symptoms normally attributed to "chemotherapy." The absence of

quantitative methods, the large-scale inclusion of patients already suffering from gastrointestinal manifestations following earlier antibiotic therapy, and the failure to use nystatin on its own in varying doses invalidate in my opinion this conclusion. In their letter Dr. Citron and his colleagues now admit a more modest aim of their trial—that is, to determine whether the use of nystatin (in the form of Mysteclin) reduced the incidence of side-effects of tetracycline given for 10 days in acute exacerbations of chronic bronchitis.

One cannot help but regret that the Clinical Trials Subcommittee of the British Tuberculosis Association confined itself to such a limited study and then saw fit to draw sweeping general conclusions on issues which had been investigated either inadequately or not at all.

Whether, or to what extent, the manufacturers' claims in relation to Mysteclin are justified can be assessed only in relation to the conditions of a particular clinical trial, but I was under the impression that the relatively small dose of nystatin in Mysteclin (250,000 units) was expected to prevent the increase of *Candida* in the alimentary tract during tetracycline treatment and the concomitant gastrointestinal upset. It seems to me unreasonable to expect such a small dose of nystatin also to cure already existing candidosis, not only of the bowel but also of the mouth, genital tract, perineum, and natal cleft. I have in fact seen in several hundred patients fewer side-effects from oral antibiotics, including not only tetracycline but also cloxacillin and lincocin, by giving simultaneously 500,000 units, or, in some cases, 1,000,000 units of nystatin t.d.s.

The need for brevity prevented me from explaining in my earlier letter what I meant by "clearing" patients of an "excess" of *Candida* before admitting them to the kind of trial under discussion. I tried to convey that it is almost impossible to "clear" the alimentary tract of *Candida*, but it is nearly always possible to diminish the *Candida* population to such an extent that only repeated stool cultures show a scanty presence of *Candida* and gastrointestinal symptoms completely or almost completely disappear. This can only be achieved by treating such patients with amphotericin B lozenges, six to be sucked daily for one week after dentures have been removed, with nystatin 500,000 or 1,000,000 units t.d.s. for at least three weeks, and female patients also with nystatin pessaries, 1 nightly for three weeks. Any ano-genital skin lesions have to be treated at the same time with topical nystatin.

I, and evidently also Professor H. I. Winner (18 January, p. 186) feel that only after such preparations are patients who still have gastrointestinal side-effects from previous antibiotic therapy suitable for a "clean" trial comparing tetracycline with a combination of tetracycline and nystatin.

The relationship between antibiotic therapy and candidosis has been critically reviewed by Dr. Mildred Seelig in two papers^{1,2} listing over 300 useful references, including contributions concerning most of the immunological techniques used in efforts to shed light on the complex field of widely varying host reactions to *Candida*.—I am, etc.,

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REFERENCES

- 1 Seelig, M. S., *Bact. Rev.*, 1966, 30, 442.
- 2 Seelig, M. S., *Amer. J. Med.*, 1966, 40, 887.