much to reduce the need for severe mechanical traumatization, while it is the fact that ether and, to a smaller degree, the other relaxing inhalational anaesthetics are potent agents in predisposing towards ileus from the second cause. Here again the use of curare by permitting the administration of reduced quantities of inhalational intestinal depressants should lessen the chances of development of post-operative ileus. The effect of curare itself on the gut was at first claimed in the U.S.A. to be parasympathomimetic. Workers in this country, possibly because of the greater purity of the product used, have been unable to confirm this; but as far as I know nobody has yet considered it to have the reverse action, and until some experimental evidence is produced that it does have any such adverse effect I see no reason why such a disadvantage should be imputed to it.—I am, etc.,

Preston, Lancs.

A. J. GRAY.

Curare or Magnesium Sulphate?

SIR,—The danger of curare lies in the fact that relaxation of the muscles may be too extensive; it also appears that the action may continue and increase after the operation. It is surprising, therefore, that use is not made of a drug which gives relaxation to the same extent; and though it has the same possible danger of respiratory failure this can be countered immediately; so also can its effect be annulled when the operation is over. I refer of course to injections of magnesium sulphate (0.5 to 1 ml. of 25% solution). Its action is countered immediately by calcium salts, though I am not sure of the appropriate dose. In practice, then, it should be absolutely safe.—I am, etc.,

Kingston-on-Thames.

W. F. COOPER.

Penicillin Pastilles

SIR,—Dr. G. I. C. Ingram (Jan. 4, p. 31) discusses the possible causes of stomatitis following the use of penicillin pastilles. In the final paragraph of his letter he suggests that the base in which the penicillin is included may be of importance in the causation of this stomatitis.

In the original work by Long and myself on the use of penicillin pastilles in oral inflammatory conditions we made use of penicillin in a simple gelatin base to which only "nipagin" had been added as a preservative. The results that we published both in this *Journal*¹ and in the *British Dental Journal*² were obtained with this type of pastille, and we found that when fresh they were most effective. In over 1,000 patients who were treated with these pastilles we occasionally saw some discoloration of the tongue, but the stomatitis which occurs so frequently with the modern commercial pastilles did not apparently occur. The disadvantage of these gelatin pastilles was, of course, that owing to the comparatively high water content they did not remain stable for long periods and had to be made up frequently in fresh batches. We regard the base, however, as of considerable importance.

In a further publication on the spread of drugs in the oral cavity³ we showed that with a gelatin base the spread backwards along the mucous membrane appeared to be very much more efficient than when a solid and non-glutinous base was employed. For this reason again, therefore, we advocated the use of gelatin as a base for the penicillin.

We have been most disappointed with the modern commercial lozenges. It is true that their keeping qualities are good, but in our experience they are not normally as effective as our original gelatin base type. We do not know the composition of the modern commercial types, but we feel that the frequent disappointment which arises from their failure to achieve successful results, and the very numerous cases of stomatitis following their use that we have seen, would appear to be due to the base employed. We would strongly advise those who have the requisite facilities whenever possible to get their own pastilles freshly made up in a pure gelatin base according to the method that we originally described.—I am, etc.,

London, W.1.

ALEXANDER MACGREGOR.

REFERENCES

- 1 MacGregor, A. B., and Long, D. A. (1944). *British Medical Journal*, 2, 686.
- 2 ——— (1945). *Brit. dent. J.*, 78, 33.
- 3 ——— (1945). *Lancet*, 2, 299.

Use of Penicillin Pastilles

SIR,—Having some experience of the manufacture of troch. penicillin, B.P., may I be permitted to reply to Dr. G. I. C. Ingram's letter (Jan. 4, p. 31). Penicillin is rapidly destroyed in aqueous solution, and for this reason the B.P. requires the lozenge to be prepared dry by compression.

Stomatitis after oral penicillin may be due either to the penicillin or the sucrose base. This sucrose base involves a number of technical problems if the resultant lozenge is to be smooth and is to dissolve easily in the mouth, but, having solved these problems and having used this method of preparation for a number of years and for a number of different lozenges, no instance of stomatitis from their use has come to our notice. In conclusion, may we have our terminology correct? Lozenges are prepared with a sugar base, pastilles with a gum or gelatin base.—I am, etc.,

Ashton-under-Lyne, Lancs.

T. H. MANNERS KERFOOT.

A Method of Giving Penicillin

SIR,—Herewith we wish to offer you a summary of the preliminary report to the Society of Clinical Studies, Havana, Cuba, made at its session of Nov. 14, 1946, referring to a new slow-absorption method for penicillin injections. The method consists in mixing a penicillin solution with whole blood, using as a solvent of the drug a solution of neutral sodium citrate (2%) and procaine (2.7%) in triple-distilled water. We (Machado Espinosa and Ramirez Corria) have used the following technique:

(1) We take 5 ml. of the solvent and add to it the quantity of penicillin we wish to give in one injection—for instance, 500,000 or 600,000 units—shaking until the drug has been dissolved. (2) We then introduce the solution into a 10-ml. syringe, preferably into a safety syringe (Yale-Luer-Lock). (3) With the syringe thus prepared we make a venous puncture in the patient who is to receive the injection, or in another person, and we extract a volume of blood equal to that of the solvent—i.e., 5 ml. (4) We shake the mixture in the syringe vigorously for not less than two minutes. If so desired the mixture of solvent, penicillin, and blood may also be introduced into an empty penicillin flask and be shaken there instead of in the syringe for two minutes.

(5) We now administer the total amount of the mixture in one deep intramuscular injection with an appropriate needle, preferably in the gluteus region. (6) The injections must be given at the rate of one injection every 24 hours or according to the criterion of the physician. (7) The dose our experience has shown us to be optimal and which we recommend is one of 500,000 to 600,000 units for an adult weighing about 70 kg. For lower weights doses of 100,000 units for every 10 kg. of body weight should be given.

We have been using crystalline penicillin, which in experiments with human volunteers, after injection in the above-mentioned amounts, has proved to be present in the blood at an exceptionally high concentration for adequate bacteriostasis as long as 48 hours after one injection.—I am, etc.,

Havana, Cuba.

M. MACHADO ESPINOSA.

Behcet's Syndrome

SIR,—I was interested in Dr. E. W. Prosser Thomas's case (Jan. 4, p. 14) because thrombosis of the inferior vena cava occurred. Furthermore, a section of the curious erythema-nodosum-like lesion seen in these cases showed the pathology to be that of an acute inflammation and thrombosis of a vein. In one of the cases I reported in 1934 thrombosis of the deep veins of the thigh occurred. I do not think the ulcers of the genitals are always small and discrete. Some of the vulval ulcers are large, and repeated attacks cause considerable loss of vulval tissue. These genital ulcers also occur in the vagina and on the cervix, and can be of some size in these situations. Fortunately in the vast majority of cases the lesions are confined to the mouth, and aphthous ulcers in this site are of course exceedingly common. The syndrome can, however, be very widespread and suggests multiple perivascular lesions; because of this the syndrome falls into many specialized branches of medicine and its study suffers thereby. Some cases get no eye changes, but I believe that many of the cases get acute ulcers of the stomach and that this accounts for the dyspepsia so often occurring with the mouth ulcers. If I

remember rightly, gastroscopy has been reported as confirming this supposition.

In view of the utter uselessness of all treatment up till now any therapeutic measure would be welcome. The peculiar sensitivity of the skin would suggest a trial of "benadryl." This might be a valuable measure in those cases with eye lesions where any decrease of inflammation would mitigate the cumulative and recurrent damage to these organs.—I am, etc.,

Oxford.

G. WHITWELL.

Endocrine Receptors

SIR,—Mr. Aleck Bourne's admirable survey of the endocrines in gynaecology (Jan. 18, p. 79) deserves high praise, and he is right in drawing attention to that neglected aspect of hormonal physiology, the reacting tissues, though whether the hypothesis of the "endocrine receptor" is necessary or not is another matter. That the question has not escaped the attention of all endocrinologists may be illustrated, for example, by the emphasis which H. Zondek (*The Diseases of the Endocrine Glands*, London, 1944) has placed on the importance of variability in the responsiveness of reacting tissues in bringing about some of the results observed in certain endocrinopathies. Cases such as that of Mr. Aleck Bourne in which vaginal but not uterine responsiveness to oestrogens occurred are not so rare nor so exclusive as may be imagined; Zondek, for instance, describes a number of cases of undoubted Graves's disease which were accompanied by obesity, either generalized or localized, while the instances of localized gigantism and the very common occurrence of wide variations in the degree of development of different secondary sexual characters in individuals (males, perhaps, more than females) may also be cited as examples of localized hyper-reactivity or unresponsiveness of certain tissues to various hormones.

The variation in responsiveness of certain tissues to hormonal influences is, indeed, a matter of everyday occurrence in the case of the alteration of sensitivity of the uterus during pregnancy to the oxytocic fraction of the posterior pituitary, and it is difficult to see here how the postulation of a receptor substance, or its presence in altered amount, can help to explain the observed phenomena. By all means, then, let due and increasing attention be paid to the question of the responsiveness of tissues to hormonal action, but let us at the same time avoid, as far as possible, complicating the already complex by the postulation of nebulous substances whose existence may well be impossible to prove.—I am, etc.,

London, N.W.3.

G. I. M. SWYER.

Endogenous Depression in General Practice

SIR,—The letter (Jan. 18, p. 111) by Dr. A. Lionel Rowson should not, I think, pass without comment. Has he ever worked in a mental hospital? If so, it is difficult to understand the language of his first two paragraphs, which is both diffuse and, I submit, inaccurate—certainly not helpful.

Dr. Rowson does not take count of the constructive side of the problem. Patients are as a rule sent to mental hospitals because their relatives and/or their doctor have not the necessary facilities for adequate treatment. Nowadays the average mental hospital is staffed by intelligent medical officers who are keen on the curative side of their work, and in addition run clinics for out-patients to which the general practitioner brings or sends his patient for consultation. Moreover, in the hospital itself much use is now being made of many modern methods of treatment. I would mention electro-convulsion therapy as an example. It is not quite clear what Dr. Rowson means by endogenous depression—i.e., whether manic-depressive psychosis or anxiety neurosis. E.C.T. cures a large number of the former, and the consultative clinic of the latter. But they are quite different conditions.

Everyone who has worked in the larger mental hospitals would welcome improvements such as smaller wards and more female staff for the chronic cases, but those patients with acute depression are nowadays customarily treated in the "admission" or "acute" wards, which are well equipped both for diagnosis and therapy. For those who can afford a moderate inclusive charge a private institution is often very suitable for

cases of anxiety neurosis. I have myself worked in both types. Additional facilities for the cure of depressed cases are to be found in occupation therapy and the services of a good hospital chaplain.—I am, etc.,

Cambridge.

A. KNYVETT GORDON.

Protein Requirements of Adults

SIR,—With reference to the leading article on the above subject (Jan. 4, p. 19) I should like to point out that all protein requirement values based on balances are quite unreliable. Everything being equal, the "requirement" varies in inverse ratio to the length of the period during which the subject has become used to a low protein intake. With a protein intake which even for three months may give a negative balance, if the experiment is continued long enough, an equilibrium is frequently obtained. It is quite impossible to say what the minimum protein requirement is. Moreover, it varies considerably from individual to individual, depending as it does on the function of the thyroid, etc. (*High Blood Pressure*, 1937).

In the treatment of high blood pressure we found it was desirable to obtain requirement values for each individual. But it is not generally realized that the availability of other substances, such as a large intake of inorganic bases, influences protein requirement (Harris, I., Ireland, J. T., and James, G. V., *J. Physiol.*, 1941, 99, 370). Apparently the substances which are available in large quantities are more readily utilized. This has the force of a physiological law (Harris, I. et al., *Studies in Hypertony and Prevention of Disease*, 1946). Requirement value of protein not only depends on the protein intake but on the availability of other substances. Balances are clearly no evidence at all of requirement. The minimum protein requirement is unknown, and it is difficult to discover what the optimum protein requirement is. It is equally possible to obtain an equilibrium on a 25-grammes-of-nitrogen intake and on a 5-grammes intake per day. The question arises, Which represents the optimum requirement? We do not know. The only way to find out the optimum requirement of protein and of many other substances is by prolonged clinical observation. A number of high blood pressure cases on low protein have been under my observation for some time, and at the Institute of Research for the Prevention of Disease a number of normal cases are kept on low protein diet, and from time to time their intake of nitrogen is checked by the determination of urinary nitrogen. Only in this way will it be ultimately possible to find out which is the optimum protein requirement. It would be very valuable if all workers interested in the subject would co-operate in this most valuable experiment, pooling resources; for it is necessary to have a very large number of cases under observation for a very long period before a definite conclusion can be arrived at.—I am, etc.,

Liverpool.

I. HARRIS.

Secondary Abdominal Pregnancy

SIR,—An account of a case of this rare condition may be of interest.

CASE REPORT

The patient was a Bantu woman aged about 25 or 30. She stated that her husband had had syphilis, untreated except by native medicine, and that of her three children the first was stillborn, the second died at the age of 5 months, and the third died at 2 years. The causes of death were unknown—presumably syphilis.

She was admitted here at full term on June 15, 1946, and anti-syphilitic treatment was begun. The abdomen was the size of a nine-months pregnancy and the child lying as a breech presentation. No abnormality was suspected at this time. On June 25 ol. ricini and an enema were given to try to induce labour, and this was repeated the next day and on July 4. On June 30 the child was found to be lying transversely; it was turned to a breech presentation and a binder applied. On July 2 the presentation was difficult to define; the limbs were felt near the umbilicus. For the next three days the woman had intermittently what appeared to be labour pains, but on vaginal examination there was no "show" and no dilatation of the cervix, which was noted to be firmer than usual for full-term pregnancy. The presenting part could not be clearly felt. On July 5 the "labour pains" began again, and the patient's general condition began to deteriorate. To our surprise she not only consented to operation but asked for it. The women here are often reluctant to undergo operation.