and a small outbreak was recorded in Bristol in 1961.² A week ago two cases were seen in Bristol, and within the last ten days at least 20 cases have occurred in a small area of Buckinghamshire. A very similar outbreak has occurred in Swindon involving about the same numbers.

Recent observations suggest that some patients in these outbreaks may only suffer from mouth ulcers, and this fact and the mildness of the condition may not cause it to be recognized immediately. It seems, however, that the disease may well be occurring in many different parts of the country, and it would be of interest to hear of further outbreaks that have occurred.—We are, etc.,

Swindon, Wilts. K. D. CROW.
Bristol. R. WARIN.
Amersham, Bucks. D. S. WILKINSON.

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- ¹ Alsop, J., Flewett, T. H., and Foster, J. R., *Brit. med. J.*, 1960, 2, 1708.
- ² Flewett, T. H., Warin, R., and Clarke, S. K. R., *J. clin. Path.*, 1963, 16, 53.

* This disease was the subject of an annotation in the *Journal* of May 25, 1963 (p. 1363).—Ed., *B.M.J.*

Persistence of Barbiturates

SIR,—Your leading article "Persistence of Barbiturates" (September 21, p. 695) gives an erroneous impression. The patients described by J. M. Hinton,¹ whom you cite, were psychiatric cases. In spite of some being less severe clinically than others Hinton by means of an 8×8 Latin square determined, to quote his words, that "there was no follow-on effect from night to night." He used amylobarbitone sodium, butobarbitone, and quinalbarbitone sodium. He found there was no significant difference between these, in onset or duration of hypnotic action. Although phenobarbitone is cumulative,^{2,3} it seems clear from Hinton's work that your statement that "there is little or no evidence to justify the use of a sedative night after night for the treatment of insomnia" is not supported by the worker to whom you yourself refer.—I am, etc.,

G. de M. RUDOLF.

Mount Pleasant Nursing Home,
Clevedon, Somerset.

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- ¹ Hinton, J. M., *Brit. J. Pharmacol.*, 1961, 16, 82.
- ² Butler, T. C., Mahaffee, C., and Waddell, W. J., *J. Pharmacol. exp. Ther.*, 1954, 111, 425.
- ³ Hinton, J. M., *Brit. J. Pharmacol.*, 1963, 20, 319.

Antihistamines and the Ovum

SIR,—My attention has been drawn to a letter which appeared in the March 30 issue (p. 887) under the title "Antihistamines and the Ovum," written by Dr. B. E. Finch.

The role of histamine in nidation, specifically in the induction of decidualization, has been explored mainly in the rat, and to a lesser extent in the monkey, guinea-pig, and rabbit. The administration of antihistamine drugs to rats by systemic routes does not result in the

suppression of decidualization, since the absorption and distribution of these drugs is such that extremely little (if any?) reaches the endometrium. The suppression of decidualization by antihistamines is achieved only by topical application.

There is no evidence of which I am aware that the ordinary clinical use of antihistamines influences nidation in a deleterious way. If an antihistamine with a predominant absorption by the uterus could be designed, it might possibly be a fertility control agent—but such a drug would have to be synthesized first and then tested.—I am, etc.,

M. C. SHELESNYAK.

Weizmann Institute of Science,
Endocrine and Reproduction Physiology,
Rehovot, Israel.

Sutureless Skin Closure

SIR,—I write in support of the claims made for sutureless skin closure by Mr. N. G. Rothnie and Mr. G. W. Taylor, and by Mr. P. J. B. Murray, in their excellent articles (October 26, pp. 1027 and 1030). I have used this principle for the past two years in about 100 cases and I can confirm their views on the advantages of this method.

These articles both give the impression that the main factor in success is the use of a special surgical tape. I have used only conventional adhesive strapping

(Dalmas' "dumb-bell" and Johnson and Johnson's "butterfly" dressings) and I think the results are just as good. The accompanying photograph of the upper abdomen was taken on the ninth post-operative day after vagotomy and pyloroplasty. With all due respect I submit that the type of strapping is of minor importance, provided that it sticks well and air-spaces are left between the strips.—I am, etc.,

London W.1.

GEORGE QVIST.

Sutures and the Burst Abdomen

SIR,—In his analysis of the burst abdomen Dr. J. R. Hampton (October 26, p. 1032) states that there is no evidence that the type of suture material used is of any importance. This is an altogether unjustifiable conclusion from the evidence he adduces. Apart from one case in which silk was used there were equal numbers of wounds sutured with nylon and catgut. Since both these materials have a low knot-strength this factor may be the main cause of wound dehiscence. A striking omission in the analysis is the

lack of any details as to the state of the suture materials at the time of secondary repair. The only information on this vital point was that concerning seven patients whose wounds separated in the first three days. Two were said to have knot failure and in two the suture material broke, but no indication was given as to the type of suture material used.

Wound-bursting is by no means confined to the abdomen, but its effects in this region are dramatic and compelling. In orthopaedic wounds in which the deep layers are repaired with catgut the patient may complain of sudden pain several days after operation due to giving way of deep sutures. The bulge on the outer side of the knee following repair of meniscectomy wound with catgut is a familiar sight.

For over 15 years I have used nothing but plain cotton for wound repairs, and during this time I can only recall one patient in whom a buried suture had to be removed. Cotton is the ideal suture material because it is non-irritant and has a very high knot-strength. I am convinced that if interrupted cotton were used in place of catgut and nylon wound-bursting would become extremely rare. There must be a few abdominal surgeons who use interrupted cotton. If so, perhaps they could give us their experience of burst abdomens.

Finally, it should be emphasized that cotton must not be confused with linen thread. If the surgeon asks for "thread" while operating he will almost invariably be offered linen thread, but this material has a bad reputation for sinus formation and has no advantages over cotton.—I am, etc.,

A. W. FOWLER.

Bridgend, Glamorganshire.

Fluothane and Jaundice

SIR,—In the past few months you have published a great deal about jaundice and fluothane; may I report a further case of this?

A female patient, aged 34, received two uneventful exposures to fluothane six weeks apart. One week after the second she developed dark urine, pale stools, itchy skin, and jaundice. She had a smooth, sharp-edged, slightly tender hepatomegaly; liver-function tests and transaminases showed hepato-cellular damage. Alkaline phosphatase remained normal. She had evening pyrexia for the next week and then developed anorexia with nausea and vomiting, leucopenia with relative eosinophilia, and a drop both in haemoglobin and in plasma proteins (especially albumin).

She responded dramatically to steroids and was physically and biochemically well in eight weeks. No cause was found for her jaundice. There was no evidence of co-existent liver, renal, or pancreatic pathology, which one would expect, since jaundice in these cases is normally associated with hypoxia during a single fluothane anaesthetic, and carries a bad prognosis.

The double exposures and time relationships, together with the good response to steroids, form a pattern suggestive of a "sensitivity reaction" similar to that which has been reported with other

drugs. However, although it is not possible to prove this the responsibility of fluothane for the jaundice seems convincing. While many drugs have been indicated as causes of liver damage, this patient received no other agent even suspected of hepato-toxicity. Intra-abdominal operation near the liver and antibiotics have also been blamed; however, this lady was in hospital for immediate and delayed suture of her ulnar nerve, and antibiotics were not administered later than seven weeks before the onset of jaundice.

I would like to thank Dr. P. B. Newcomb for his kind permission to report this case.—I am, etc.,

Hackney Hospital,
London E.9.

J. ROBINSON.

Chlorphentermine

SIR,—I must protest at the reference made to chlorphentermine ("lucofen") (October 5, p. 853) in regard to the inference that chlorphentermine, while having an appetite suppressant action, also produces central nervous stimulation and is not satisfactory. We too have noticed amphetamines in this respect.

Chlorphentermine has been widely prescribed in this country and abroad and there have been no reports of nervous stimulation. This is corroborated by a number of publications, of which the following examples are listed.¹⁻³—I am, etc.,

D. D. H. CRAIG.

William R. Warner & Co. Ltd.,
Eastleigh, Hants.

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- Mune, O., and Pallesen, A. E., *Ugeskr. Laeg.*, 1960, 122, 605.
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* * We have shown this letter to our expert contributor, who replies as follows: "Although absence of stimulating effects was noted in the reports on chlorphentermine ("lucofen") quoted above, claims for any superiority over amphetamine or dexamphetamine must await adequate comparative trials, as similar claims for other anorectic drugs have often subsequently been shown to depend on the use of less effective dosage. It must also be noted that evidence of habituation or addiction may only appear after several years of general experience with such drugs."—ED., *B.M.J.*

Amiphenazole and Bronchitis

SIR,—The persistent bludgeonings which we suffer at the hands of advertisers have mercifully blunted my sensibilities, so that I usually find it a painless matter to consign automatically to the waste-paper basket all but the small informative fraction of the advertising matter for pharmaceutical products which

comes through my letter-box. But I am moved to protest by an advertisement in the form of a news-sheet which caught my eye, with banner headlines on the first page, "Major Breakthrough in Chronic Bronchitis." Wondering whether I had missed something important in my own field of interest, I read on, to find that the drug to which it referred was none other than amiphenazole, under the trade name "daptazole." We have been familiar with the actions of this drug in chronic bronchitis for several years; as far as I am concerned, since my friend Dr. Tom Simpson drew my attention to it about five years ago. Publications by him and by Dr. G. M. Little were quoted in the advertisement. The observations of Dr. Simpson and Dr. W. Hawkins were recorded briefly in a letter in your columns¹; they concerned patients with ventilatory insufficiency and carbon-dioxide retention, in whom large doses of amiphenazole intravenously at hourly intervals were found to "stimulate the respiratory centre even when depressed by oxygen." It was also noted that effective doses made the patient cough, and caused nausea which helped to clear the sputum. Dr. Little's² work also concerned patients who were gravely ill with exacerbations of ventilatory insufficiency, and his moderate conclusion was a suggestion that amiphenazole might have a place in the treatment of carbon-dioxide retention. I hope that all who perused this document did so with an alert critical faculty and so perceived the extremely tenuous connexion between these quoted observations and the sweeping claims that "by prescribing this new (*sic*) drug the doctor can not only ease the burden of the chronic bronchitic, but postpone or prevent his eventual hospitalization."

So far as I know, there is no evidence that amiphenazole is of the slightest value in the management of the ambulant chronic bronchitic.—I am, etc.,

J. G. SCADDING.

Institute of Diseases of the Chest,
London S.W.3.

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- Simpson, T., and Hawkins, W., *Brit. med. J.*, 1959, 1, 508.
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Cyclophosphamide

SIR,—Your special correspondent reporting on the symposium on cyclophosphamide held at the Royal College of Surgeons on October 4, 1963 (November 9, p. 1189), quotes me as follows:

"Dr. G. H. Fairley (St. Bartholomew's Hospital) felt it was too early to draw any conclusions on 62 cases of Hodgkin's disease that had been treated with cyclophosphamide over the past three years because in only eight of these had it been the first form of treatment."

This is incorrect and misleading. Since early cases of Hodgkin's disease are usually treated with radiotherapy it is

not surprising that cyclophosphamide was the first form of treatment in only eight of our 62 cases. What I in fact presented was an analysis of the results of treatment when cyclophosphamide was used for the first time regardless of previous radiotherapy or chemotherapy; in most cases cyclophosphamide was the first form of chemotherapy used. To say that I felt it was too early to draw any conclusions is quite untrue, as the results showed that cyclophosphamide, like other nitrogen mustards, is a most valuable drug in the treatment of patients with Hodgkin's disease and is likely to prove effective the first time it is used.—I am, etc.,

G. HAMILTON FAIRLEY.

St. Bartholomew's Hospital,
London E.C.1.

Apparatus for Oxygen Administration

SIR,—As Drs. D. C. Flenley, D. C. S. Hutchison, and Professor K. W. Donald (November 2, p. 1081) have clearly shown, the performance of the current production version of the Venturi mask is not satisfactory. We too have noticed this and I would like to amplify their observations.

The current mask differs from the prototype in having a shorter barrel and a narrower (and therefore higher velocity) additional oxygen nozzle. On returning to the dimensions of the prototype we have, however, found that the performance, although better, is still unsatisfactory. It seems that the measurements I reported in 1960¹ were misleading because, not having a rapid oxygen analyser, I used a technique of multiple sampling which gave only an average concentration in the mask. We are now able to explore the whole air-stream using a mass spectrometer which gives a virtually instantaneous measurement of oxygen concentration. This instrument has shown us that it is difficult to eliminate regional variations due to inadequate mixing in a mask with two oxygen sources. In view of the other disadvantages of this mask, such as the need for a double regulator, its lack of robustness, and its cost, we have suggested to the makers that it be replaced.

We are developing other approaches to the problem. The first to reach production is a single-concentration single-nozzle Venturi mask ("ventimask," Oxygenaire), which can be used with any regulator and is sufficiently inexpensive (7s. 6d) to be regarded as disposable. The concentration delivered by this mask is intended to be 27% at an oxygen flow of 4 l./min. We have analysed the concentration in six masks taken at random from stock. At an oxygen flow of 4 l./min. the observed concentration was 26.6% (S.D. 0.51); on reducing the oxygen flow to 2 l./min. the concentration fell by 0.15% (S.D. 0.27), and on increasing the flow to 8 l./min. the concentration rose by 0.45% (S.D. 0.26). There was little variation in composition