contain two amphetamine tablets (10 mg.) and two Parlate (tranylcypromine) tablets (10 mg.).

Her temperature continued to rise to 109.4° F. (43° C.). She was treated by immersion in ice water and the infusion of intravenous salicylate. Therapy was instituted in order to correct the marked dehydration, acidosis, hyperkalaemia, and subsequent hypotension that she suffered. Her blood-pressure remained unobtainable in large doses of metaraminol, but did respond to L-norepinephrine. After about 20 hours of therapy the patient began to support her own blood-pressure, carry on normal respiration, and respond feebly to simple commands. During the second day in the hospital she rallied dramatically and by its end was recognizing and conversing with relatives. Once her sensorium was clear, the patient related a detailed story of her ingestion of amphetamines and tranylcypromine. She had apparently been using amphetamines intermittently for both diet and mood-elevating effects. A few days before she became ill she started to ingest 10 mg. tranylcypromine tablets once or twice a day. She had taken one amphetamine and one tranylcypromine tablet just before going on duty the night that she took ill. This was the first time that both drugs had been taken together. The patient had obtained the drugs as samples in the hospital clinics.

The patient recovered completely. Her mental status during convalescence was normal and she gave us no reason to doubt her story.

At the time of her admission extensive blood, urine, spinal-fluid, and stool cultures were negative. A lumbar puncture had been normal. A variety of drugs were looked for, including salicylates. None were found. Unfortunately no assay for amphetamine or tranylcypromine was done.

I believe that this case represents an example of near-fatal hyperpyrexia caused by the ingestion of therapeutic amounts of tranylcypromine and amphetamine. In the full appraisal of the clinical usefulness of antidepressant agents, such cases must be given proper consideration.—I am, etc.,

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EDMUND LEWIS.

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Oral Contraceptives and Liver Injury

SIR,—In your leading article (29 May, p. 1391) you refer to the enormous numbers of women who are now taking oral contraceptives, and, of course, very many of these women are taking them without medical indications. Those of us who are concerned about the possible long-term effects of this wholesale use of hormones will not be very greatly reassured by your article. It may be true that liver damage is the least of the risks (I think there are more important possibilities), or it may be that there is no danger at all, but surely the evidence is insufficient to warrant the conclusions you draw.

The investigations reported by Dr. G. I. M. Swyer and Dr. V. Little (29 May, p. 1412) are extremely valuable, but we cannot say the risk is negligible merely because twelve women have taken these pills for a few years without demonstrable liver damage. Would it not have been as logical to have argued, say ten years ago, that because twelve men had smoked heavily for three to six years and none had developed cancer, there was there-

fore no harm in smoking? Such a conclusion would plainly have been dangerously incorrect, but it would have had this in common with the other conclusion: it would have been in accordance with what people wanted to hear and to believe.—I am, etc.,

Banbury, Oxon.

J. M. GATE.

Action of Bismuth Aluminate

SIR,—The paper by Dr. S. G. Flavell, Matts and his colleagues (20 March, p. 753) demonstrates statistically significant clinical results in favour of bismuth aluminate. Although the exact mode of action of this new bismuth compound is not understood, the authors' hypothesis suggesting that the good therapeutic results may be due to a coating effect providing a local antipepsin action at the site of the ulcer is an interesting possibility.

Bismuth aluminate has been used in this department in following up our studies on the effect of aspirin on gastric secretion.¹ Our initial objective was to determine whether bismuth aluminate would provide protection against gastric mucosal damage caused by the administration of aspirin. Our results in this respect were negative, but some of our experimental findings may have a bearing on the hypothesis put forward by Matts and his colleagues.

In one series of our cat experiments the animals were given either bismuth aluminate or aspirin, or a combination of the two drugs, prior to histamine infusion and tests for gastric function. The experimental technique was basically the same as that reported in our paper on histamine secretory tests in cats.² The bismuth aluminate or aspirin was suspended in about 50 ml. of water and injected into the stomach. After 1½ hours the stomach was opened and all residue of the drug was removed.

Intense histamine stimulation was started and the gastric juice collected for the next 3½ to 4 hours. At the conclusion of the experiment the stomach was opened and in 13 cats where bismuth aluminate had been administered alone a film of the bismuth compound was found to be clinging to the gastric mucosa even though the drug had apparently been previously removed from the stomach.

In another series of experiments gastric juice was obtained from dogs; peptic activity was measured and subsequently bismuth aluminate was added at a concentration of 0.05 g. per ml. Pepsin estimations were repeated at various pH levels and it was found that peptic activity was reduced by bismuth aluminate at all pH levels from 0.5 to 6.5. The gastric juice used in these experiments was obtained from denervated Heidenhain pouches and either because of this or because of species difference there was much less peptic activity than in man. This suggests that to demonstrate the antipeptic effect of bismuth aluminate on gastric juice from the lumen of the stomach in man a larger dose would be needed than that used by Matts and his colleagues. Nevertheless, our results provide some confirmation of the antipeptic action previously demonstrated *in vitro*.³

Thus it appears that bismuth aluminate could certainly provide a coating of the gastric mucosa, and this may exert a local antipeptic effect of a sufficient order to prevent auto-digestion at the site of the ulcer, even though it may not be detectable by biochemical analysis of a sample of gastric juice from the lumen. In this context it is of interest that surface mucus can have a pH of up to 9 or 10 while the pH of the stomach contents may be less than 5.

As Matts and his colleagues suggest, hyperacidity alone may be relatively unimportant in connexion with the origin of peptic ulceration which is almost certainly due to auto-digestion by acid-pepsin and possibly involving other gastric processes. Peptic inactivation is thus important, and if bismuth aluminate exerts a local antipeptolytic action at the site of the ulcer, following coating of the gastric mucosa, this could certainly account for the good clinical effect demonstrated in the double-blind trial.—I am, etc.,

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New South Wales, Australia.

G. W. MILTON.

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Sodium Fluoride and Cell Growth

SIR,—Professor W. D. Armstrong and his colleagues (29 May, p. 1435) have now broadened the scope of their earlier observations (20 February, p. 486) which refuted the evidence of Berry and Trillwood¹ for the inhibition of cell growth *in vitro* by small amounts of sodium fluoride incorporated in the culture medium. Dr. Berry and Mr. Trillwood (20 March, p. 793) had disputed the validity of the earlier observations of Armstrong and his colleagues on the ground that their own data were based upon cultures extending over three- to four-cell duplications, which was a better test of growth inhibition than the one-cell duplication originally examined by Armstrong and his colleagues.

The more recent observations of Armstrong and his colleagues go some way toward answering these objections, although only a small number of selected HeLa-cell clones were studied. Nevertheless, since Berry and Trillwood had maintained that their original biological observation had still not been validly refuted, it seemed important to repeat their own experiments—i.e., growth tests of HeLa cells growing as a monolayer attached to glass for at least four cell duplications during a week. I have now performed five such experiments with cells cultured for over six cell duplications during a week and I am unable to confirm their observation of a growth inhibition by sodium fluoride.

Five growth experiments have been performed in this laboratory with HeLa cells

Number of HeLa Cells ($\times 10^6$) after 1 Week's Growth With and Without Sodium Fluoride (1 p.p.m.).

Experiment Number	Control Cultures	Fluoride Cultures
1	3.77 3.75	3.87 4.02
2	4.65 4.90	4.82 4.80
3	5.02 4.17	4.22 4.12
4	4.30 4.80	4.50 4.00
5	4.90 4.60	4.50 4.30
Mean	4.486	4.315

Difference between means = 0.171 ± 0.120 (4% $\pm$ 2.8%).

cultured in Eagle's medium plus 10% pooled human serum. 1 p.p.m. sodium fluoride was incorporated in the culture medium of the fluoride bottles (the same concentration that is recommended for drinking-water). The experiments were performed over five successive weekly periods with an inoculum of 50,000 cells in each one of the pairs of bottles. The total cell numbers in the bottles were determined at the end of seven days (see Table). It will be seen that the difference between the mean cell numbers of all the control and fluoride cultures is not significant ($P=0.20$).—I am, etc.,

A. H. W. NIAS.

Christie Hospital and
Holt Radium Institute,
Manchester 20.

REFERENCE

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Monocytic Leukaemia and Phenylbutazone

SIR,—Cases of leukaemia occurring in patients treated with phenylbutazone have recently been reported. We record here very briefly a further case of acute monocytic leukaemia, with an accompanying family history of leukaemia.

In June 1955 a 57-year-old woman developed rheumatoid arthritis, which progressed in spite of treatment. By 1959 she was quite severely crippled and was treated with phenylbutazone in the dose of 300 mg. daily. The drug was maintained at 300 mg. daily for one year, and thereafter was continued at 200 mg. daily until September 1964. There was no doubt that the phenylbutazone enabled her to remain independent.

In September 1964 one of us (H. E. M.) noted that the patient had suddenly developed fever, pallor, and buccal ulcers; she was admitted as an emergency to the Harrogate Royal Bath Hospital. Examination showed a grossly anaemic, ill-looking woman, but the liver and spleen were not palpable and her lymph nodes were not significantly enlarged. A blood count showed Hb 45%, leucocytes 5,000/c.mm. The differential count showed: polymorphs—neutrophils 20%, eosinophils 1%, lymphocytes 77%, monocytes 2%.

The latex screen test was positive. A sternal bone-marrow aspiration was performed, which showed a hyperplastic marrow, in which 70% of the cells were large blasts, consistent with monoblasts. A month after admission to hospital leucocytes were 6,000/c.mm., but by then unclassified cells had appeared in the peripheral blood, varying between 50 and 80% of the total count.

Large doses of steroids produced some clinical improvement, but the patient died two months after admission. At necropsy the relevant findings were confined to the lungs, spleen, and bone-marrow. In the lungs there were many small areas of necrosis scattered throughout both lower lobes. Many small areas of necrosis contained clumps of bacteria. Around such areas there was an infiltrate of lymphocytes and macrophages; polymorphs were strikingly absent. The bronchi contained red cells and degenerating inflammatory cells. The sections of the spleen showed a marked reduction in the size of the follicles and many immature cells off the haemopoietic system in the pulp. Paraffin sections of a rib showed a very cellular marrow with little fat remaining; occasionally normal blasts and megakaryocytes were seen, but the majority of the cells were large and immature. The cause of death was necrotizing, bronchial pneumonia and acute monoblastic leukaemia.

One outstanding feature of interest in this case is that the patient's sister in 1961, at the age of

61, had died of a chronic myeloid leukaemia. The sister had never received phenylbutazone.

—We are, etc.,

J. R. GOLDING.

MARGARET G. HAMILTON.

H. E. MOODY.

Royal Bath Hospital,
Harrogate, Yorks.

Availability of Enteric-coated Aspirin

SIR,—We agree with the view expressed by Mr. W. J. Clancy (5 June, p. 1495) that enteric-coated aspirin tablets are preferable to ordinary tablets as they cause less gastrointestinal irritation. He is, however, misinformed about the availability to the public of enteric-coated aspirins. The contents of a tablet, and not its coating, determine whether a drug can be obtained without a prescription. Enteric-coated aspirins (325 and 650 mg.) are available to the public without medical authorization. The basic N.H.S. cost of 325-mg. tablets (Nu-seals Aspirin, Lilly) is 3s. 4d. per 100. Although this is rather more than the cost of ordinary aspirins, the price is not prohibitive.—We are, etc.,

ALAN BENNETT.

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London N.W.8.

SEYMOUR LAZARUS.

Non-injury by Thermometer

SIR,—The experiences described by Dr. S. K. Dikshit (22 May, p. 1377) and Dr. A. Melinek (5 June, p. 1496) must be balanced, on behalf of this useful instrument, by the following tale.

I was called to another hospital to see a neonate, because the nurse, on removing the rectal thermometer, found the bulb to be broken. It was considered that the thermometer had broken in the rectum, as no pieces were visible on the floor or on emptying the jar-container. Furthermore, the jagged end of the instrument was so sharp that the nurse could hardly have inserted it without causing some trauma. I found no injuries of the anus and no bleeding occurred subsequently. The broken end of the thermometer I found hidden within the cotton-wool pad used in the bottom of the thermometer jar.

Perhaps this indicates how safe the procedure is in experienced hands, even with a damaged instrument.—I am, etc.,

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Guy's Hospital Medical School,
London S.E.1.

Hypsarrhythmic Children and Infantile Spasm

SIR,—Congratulations to Drs. B. D. Bower and P. M. Jeavons for drawing attention to the misuse of an electroencephalographic term, hypsarrhythmia, by its application "to a clinical entity with which it is not synonymous" (29 May, p. 1436). It is, however, unfortunate that they have spoiled the presentation of a justifiable complaint by observing that "in as many as a third of cases the E.E.G. is epileptic but not hypsarrhythmic." There is surely no such thing as an "epileptic E.E.G."—I am, etc.,

JAMES H. MARGERISON.

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

Infectious Disease

SIR,—I endorse the welcome (29 May, p. 1435) which Miss Gladys M. Sandes gave to the department for venereal and sexually transmitted diseases which was recently opened at the Middlesex Hospital. This seems a suitable time to remind the profession and its teachers that the provision for the medical care of infectious diseases in general is being neglected in a dangerous way by decreasing instruction, bed accommodation, and trained staff. At present, there is too little ambition to prevent the large amount and wide range of infections which arise in the community generally and sometimes in hospital, and to which the public press draws frequent attention. Now that the Middlesex Hospital has taken up-to-date measures to deal with one form of infection, will other leading hospitals please follow in other areas of the general field of infectious diseases?—I am, etc.,

London W.1.

J. M. ALSTON.

Test for Palatal Paresis

SIR,—May I draw attention to a simple bedside test for palatal paresis? The test consists of placing a small mirror (a vanity mirror such as is carried by the ladies in their handbags suffices well) immediately beneath the nostrils and immediately above the upper lip; it is held in the horizontal plane, the reflecting surface uppermost and with one edge applied against the skin of the face between the upper lip and the nose. The patient is instructed to repeat the word "pop" several times, two or three times per second. If the test is positive, there will appear a misting on the surface of the mirror beneath one or both nostril orifices. The validity of the manoeuvre may be checked by the examiner performing it upon himself. It is important that the patient enunciates the word "pop" as clearly and sharply as is possible, and it is preferable that the mirror be cooled before it is used.

The rationale of the test is that when positive it indicates that the soft palate is insufficiently strong to close off completely the posterior part of the nasopharynx from the posterior part of the oropharynx, primarily during the formation of the explosive consonant "p." The test is limited by the patient's ability to co-operate. False-negative results occur in the presence of marked paranasal sinusitis, nasal congestion, and in the associated presence of a facial weakness sufficient to impede the labial component of the formation of the consonant.

It is possible that this manoeuvre has been described before. Nevertheless I would still draw the attention of your readers to it, for it has a value in certain circumstances. Thus it may help to clarify the differential diagnosis between motor-neurone disease and cervical spondylosis; it may influence the classification of myopathic changes found elsewhere during the clinical examination; it may be of value in such conditions as poliomyelitis, the Lândry-Guillain-Barré-Strohl polyneuritis, and diphtheritic polyneuritis, when in the early stages it may alert the examiner to the possibility of impending bulbar involvement, and in the later stages assist in the assessment of recovery of a palatal weakness.