SIR,—I should like to comment on the statement made in the leading article on tetracyclines (28 November, p. 509). "Because of serious effects on tooth development, tetracyclines are absolutely contraindicated for children aged under eight and for pregnant or lactating women."

Reference 9 attributes this to A. Manten, in *Side Effects of Drugs*, edited by L. Meyler and A. Herxheimer, Vol. 6, p.283. Unless I am mistaken this would appear to be a misquotation, as I am unable to locate any reference to work by Manten in the section relating to the effect of tetracyclines on teeth and bone. I do note a comment that "at any time between the 4th month of gestation and the 7th or 8th year of life . . . discoloration of teeth" may be caused. Also on page 286, the rather mildly worded advice appears that "Tetracyclines should preferably not be given to children younger than 8 years. . . ."

This is very different from your leader writer's comment that they are "absolutely contraindicated", and I should appreciate clarification as to how these two diverging statements can be reconciled.—I am, etc.,

JOHN MOODIE,
Medical Director,
Bristol Laboratories Ltd.
Slough, Bucks.

Hyperpyrexia after Anaesthesia

SIR,—The letter from Dr. G. M. Hall (5 December, p. 622) raises the following points concerning hyperpyrexia and malignant hyperpyrexia. Hyperpyrexia has no agreed definition. Some suggest a temperature of 105° F. or 106° F. (40·6° C. or 41·1° C.) while others also specify the site where it should be taken. Malignant hyperpyrexia has not been defined either in terms of duration or height of fever, or clinical features. There is a tendency to use the phrase in connexion with fatal hyperpyrexia associated with anaesthesia, but similar clinical states (including rigors or muscle rigidity) arise in other situations. Hyperpyrexia is like hypertension in that it has many causes and will, if persistent, become clinically malignant. Like a raised blood pressure it may represent a physiological response to an abnormal environment or activity, or to a disease state. It is not a disease in itself, as "true malignant hyperpyrexia" might imply. If by the latter phrase is meant the commonest clinical variety of hyperpyrexia occurring in patients under anaesthesia, who develop muscle rigidity and who often die despite prompt treatment, why not call it "true *anaesthetic* malignant hyperpyrexia"? The phrase is otherwise misleading and is not a usefully descriptive name for the syndrome.

There is evidence of an upper limit to physiological fever, set between 105 and 106° F. If pyrexia exceeds this, it represents a pathological response and might imply failure of heat homoeostatic mechanisms. A useful definition of potentially malignant hyperpyrexia might be a temperature of 106° F. (41·1° C.) (rectal), persisting despite cooling treatment for two hours. This definition should exclude entities such as malarial rigors, and it emphasizes the failure of heat loss mechanisms. High fever may complicate hypovolaemic shock as a result of heat retention, caused by peripheral vasoconstriction impairing heat loss. Hypovolaemia of more gradual onset may be difficult to detect, especially in younger patients who compensate for longer periods by increased vasoconstriction. This explains the higher incidence of malignant hyperpyrexia in the young. Pulse arterial and central venous pressures may show noticeable changes only after decompensation has occurred. Early detection is by differential temperature monitoring, and treatment is by transfusion and induction of peripheral vasodilatation with chlorpromazine.[1,2]

While emphasis has been given to the muscle abnormalities in true anaesthetic-induced malignant hyperpyrexia, less has been given to the resistance to cooling which is a feature of most types of persistent hyperpyrexia. If the body can cope with the metabolic storms of squash games, marathon running in the sun at high altitude, or continuous heavy labour in hot humid South African mines, why should it be unable to cope with widespread muscle fasciculation under anaesthesia? Heat homoeostatic mechanisms are impaired under anaesthesia and may be as important a factor as intense muscle activity in causing the resistance to cooling therapy. In view of the high mortality it is not surprising that the literature is reticent regarding treatment. What does seem surprising is the frequent failure to mention the use of chlorpromazine in severe cases. It is stated to be of value in high fever and heat hyperpyrexia in current American and English texts, and it has been used to induce hypothermia. It would seem to be logical to use it in resistant cases, particularly where peripheral vasoconstriction is present.—I am, etc.,

J. C. ROBERTSON.

Good Hope General Hospital,
Sutton Coldfield,
Warwicks.

REFERENCES

1 Brock, Lord, *Transactions of the Medical Society of London*, 1968, **85**, 1.
2 Ross, B. A., Brock, Lord, and Aynesley-Green, A., *British Journal of Surgery*, 1969, **56**, 877.

Calcium Metabolism in Patients with Epilepsy

SIR,—There are several possible reasons why Dr. J. C. Bowe (28 November, p. 559) was unable to demonstrate low serum calcium levels in his epileptic children at Lingfield.

The duration of anticonvulsant therapy was 1-11 years; most of the patients studied by Kruse[1] had been receiving treatment for at least 4-5 years, so a number of the Lingfield children may not have reached the stage where biochemical abnormalities are demonstrable. None of the children was receiving the drug (primidone) which was most commonly associated with osteomalacia in the studies of Kruse[1] and ourselves (10 October, p. 73).

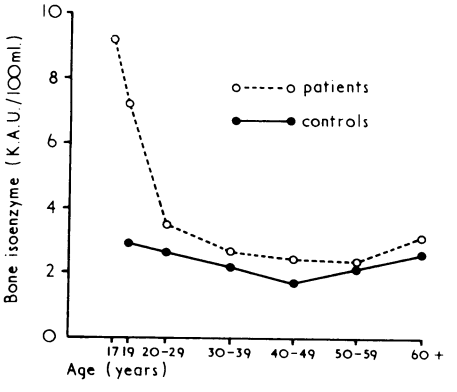
As no information is given on drug dosage, it is possible that many were receiving smaller doses than the severe epileptics studied by Kruse.[1] The normal range for serum calcium is not given nor is it stated whether corrections were made for serum albumen or specific gravity.

Despite these criticisms the results of this survey are of interest, for there are now three studies of calcium metabolism in epileptic children, one from Germany[1] showing a 15% incidence of hypocalcaemia and osteomalacia, a second from India[2] showing a significant hypercalcaemia when compared with normal children, and the Lingfield survey which has failed to show any abnormality. It is possible to reconcile these apparently conflicting reports by postulating that the acceleration of vitamin D metabolism by anticonvulsant drugs[3] may at first yield an excess of the biologically active derivative 25 hydroxycholecalciferol (producing hypercalcaemia) and only when the stores of vitamin D are depleted does a deficiency state ensue (producing osteomalacia). The older group of patients studied by us showed no evidence of hypercalcaemia. Obviously further work is required in this field, but we would suggest that routine serum calcium, phosphorus, and alkaline phosphatase levels should be performed in all patients on long-term anticonvulsant therapy.

Dr. Bowe found alkaline phosphatase levels of 14·8–41·2 King Armstrong units in his children. Before declaring these values abnormal, the age of the patient should be taken into account, for the level of this serum enzyme is high during the intense osteoblastic activity of bone growth, and electrophoretic separation of the isoenzymes[4] demonstrates very high proportions of bone isoenzyme during this period. Neverthless, in our experience the upper value given by Dr. Bowe is higher than is usually seen in children. We have recently performed routine alkaline phosphatase estimations on outpatients attending the epilepsy clinic at St. Bartholomew's Hospital, and a few examples of the results are given in the Table.

Age	Sex	Alkaline Phosphatase (K.A. units)
10	M	41
14	M	50
16	M	17
19	M	13
21	M	21
22	F	12

Serum calcium levels in these patients were normal. These figures confirm the impression from our recent survey that abnormally high alkaline phosphatase levels can occur in young epileptics without any abnormality of serum calcium. A persistent elevation of the bone isoenzyme is



frequently seen in patients up to the mid-twenties (Fig.), suggesting delayed bone maturation.—We are, etc.,

ALAN RICHENS.

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

DAVID ROWE.

University College Hospital, London W.C.1.

1 Kruse, R., *Monatsschrift für Kinderheilkunde*, 1968, **116**, 378.
2 Rudra, M. N., De, S., and Rudra, M. S., *New England Journal of Medicine*, 1969, **280**, 1242.
3 Dent, C. E., Richens, A., Rowe, D. J. F., and Stamp, T. C. B., *British Medical Journal*, 1970, **4**, 69.
4 Canapa-Anson, R., and Rowe, D. J. F., *Journal of Clinical Pathology*, 1970, **23**, 499.

Fibrosing Alveolitis and Renal Tubular Acidosis

SIR,—The paper by Dr. A. M. S. Mason and others (5 December, p. 596) on fibrosing alveolitis with renal tubular acidosis has prompted us to write of a case under our care at present. The seven cases of fibrosing alveolitis studied by them had a normal response to an ammonium chloride load. We have seen a renal acidification defect develop in a woman with Sjögren's syndrome, fibrosing alveolitis, and hyperglobulinaemic purpura.

The patient presented in 1954 at the age of 54 with keratoconjunctivitis sicca and xerostomia. Three years later she developed Waldenström's hyperglobulinaemic purpura and fibrosing alveolitis. In May 1969 she was able to elaborate urine of pH less than 5·3. She was admitted to Northwick Park Hospital on 11 November 1970 having recently had a sore throat which had made her reluctant to drink. On examination she was grossly dehydrated and confused. After rehydration she remained acidotic (plasma bicarbonate 15 m Eq/l.) and despite this her urine pH was never below 6·2.

Thus between May 1969 and now this patient has developed renal tubular acidosis. In sequence our patient presented with Sjögren's syndrome, hyperglobulinaemic purpura, fibrosing alveolitis, and renal tubular acidosis. We believe that this is the first occasion on which an acidification defect has been seen to appear in such a case. Full details are to be presented.[1]—We are, etc.,

A. M. ZALIN.
JOAN WEEPLE.
M. GUMPEL.

Northwick Park Hospital, Harrow, Middx.

REFERENCE
1 Gumpel, M., *Proceedings of the Royal Society of Medicine*. In press.

Ileorectal Anastomosis for Ulcerative Colitis

SIR,—In your leading article (5 December, p. 572) you appear to try to demolish Aylett's work in conservative surgery of inflammatory disease of the colon. I have attended discussions where the conservative and the radical schools have met in head on clash over a subject which should, of course, be a matter of judgement. I agree that there are cases in which panproctocolectomy is obviously indicated, but there are many cases that can be satisfactorily treated by ileorectal anastomosis.

Surgical treatment culminating in ileostomy can only be justified in severe cases, but the indication for resection with anastomosis may readily be widened, so offering the prospects of surgical relief to a larger number of patients who would otherwise be condemned to a life of incomplete medical treatment. The effects of recurrence or persistence of disease in the residual rectum appear trivial and easily controlled. Subsequent surveillance does not present a problem.

Although removal of the rectum certainly eradicates the disease, the danger of retention of the rectum appears to be exaggerated, and can be compared with the drawbacks of removing it. There is a high incidence of impotence in the male (and possibly in the female) following resection of the rectum. Perineal sinuses are common. Intestinal obstruction we all know occurs commonly after colectomy, while the ileostomy itself may suffer a number of mechanical complications. Having undertaken anastomosis, it may later be necessary after all to remove the rectum, but to do so although difficult should not tax the ingenuity of a proctologist.—I am, etc.,

T. ROWNTREE.

Southampton General Hospital, Southampton, Hants.

Coagulation Failure in Pregnancy

SIR,—The significance of Dr. L. D. Courtney's experiment (31 October, p. 303) cannot be assessed without knowledge of the source of the 5 ml. of amniotic fluid, its temperature, the volume of fluid into which it was injected, and the nature of the uterine muscle preparation concerned. Fuchs and Wagner[1] found that samples of human amniotic fluid obtained at all stages of gestation had a stimulant effect on isolated myometrium from pregnant women, and concluded that the artefact of changes of ionic concentration in the bath fluid played a major role in this effect. Nearly all the literature is consistent with their finding that whole amniotic fluid has a stimulant effect on isolated uterine muscle. The exception is the work of Stamm[2 3] who observed inhibitory effects of relatively large amounts of amniotic fluid from therapeutic abortions on the isolated rodent uterus. Abrahams[4] was unable to confirm his conclusions. All authorities are agreed that any pharmacological activity found in amniotic fluid in labour is stimulant to uterine muscle.

Landesman and Wilson[5] have reviewed some of the work in the literature on pharmacologically-active polypeptides and lipid-soluble substances in amniotic fluid. More recently, Karim[6] has observed the appearance of significant amounts of prostaglandins during spontaneous labour. My own conclusion was that the amount of other ether-soluble lipid stimulants present is usually at about the threshold for activity but is markedly increased when the amniotic fluid is meconium-stained.[7]

At the present time there does not appear to be any acceptable evidence that human amniotic fluid contains a specific uterine relaxing agent of clinical significance in relation to uterine hypotonia occurring after amniotic fluid infusion.—I am, etc.,

D. F. HAWKINS.

Institute of Obstetrics and Gynaecology, London W.12.

REFERENCES
1 Fuchs, A.-R., and Wagner, G., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1963, **70**, 665.
2 Stamm, O., *Gynaecologia*, 1953, **136**, 377.
3 Stamm, O., and De Watteville, H., *Gynécologie et Obstétrique*, 1954, **53**, 171.
4 Abrahams, O. L., Ph.D.Thesis, University of London, 1966.
5 Landesman, R., and Wilson, K., *Clinical Obstetrics and Gynaecology*, 1966, **9**, 554.
6 Karim, S. M. M., and Devlin, J., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1967, **74**, 230.
7 Abrahams, O. L., and Hawkins, D. F., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1967, **74**, 235.

Alcoholism and Industrial Absenteeism

SIR,—As discussed at a recent meeting of the Royal Society of Medicine[1] and in your leading article (14 November, p. 383), in dustrial absenteeism due to sickness is causing concern in industry and commerce. You go on to point out that in addition to the cost of sickness benefit the country loses the value of the absentee's production; that some staff members have more spells of sickness absence than others, 31% having at least three spells; and "the great advantage" that would follow ". . . if those liable to [frequent] . . . short-term spells of sickness absence . . . could be identified by other factors."

Problem drinkers and early alcoholics very often have such spells of absence, quite apart from marked impairment of performance even while at work.[2] Alcoholics are found at all industrial levels, among managers as well as on the shop floor. Research and adoption of progressive policies by many American firms have shown not only the importance of alcoholism in causing great loss in industry but also that problem drinkers in industry can often be identified in relatively early phases, treated, and rehabilitated.[3] Industry in Britain remains as indifferent to the alcoholic problem today as in the past, yet the cost of alcoholism to British industry has been variously "guessed" as being between £100m. and £250m. a year.[2]

Alcoholics employed in industry stand by reason of personality and relative social stability a fair chance of marked improvement or even recovery—if recognized early and treated. Industry is in a good position by means of early diagnosis to take preventive and early therapeutic action. Much unnecessary human suffering as well at material waste can thus be avoided. There is no reason why positive action should and could not start now.—I am, etc.,

M. M. GLATT.

St. Bernard's Hospital, Southall, Middlesex.

REFERENCES
1 *Proceedings of the Royal Society of Medicine*, 1970, **63**, 1131.
2 Glatt, M. M., *The Alcoholic, and the Help He Needs*. Royston, Herts., Priory Press, 1970.
3 Christopher, D., Smithers Foundation, *Understanding Alcoholism*. New York, Scribner, 1968.