were demonstrated in normal subjects.¹ Sir Thomas Lewis showed in 1927² that intracutaneous morphine elicited a triple response similar to that induced by histamine. Histamine release by opium alkaloids has been demonstrated in isolated cat skin and muscle preparations.³ Elevated plasma levels of histamine have been measured in intact dogs following the administration of morphine and pethidine.⁴ A significant decrease in the lung capacity of intact dogs has been observed following the administration of morphine and pethidine—an effect most likely to be due to bronchoconstriction.⁵ The mechanism of opiate-induced bronchoconstriction may include central vagal stimulation, histamine release leading to enhanced bronchomotor tone and pulmonary vascular congestion, and histamine-induced reflex enhancement of vagal tone.⁵

In view of this evidence and the availability of alternative sedatives, we feel that the use of opium alkaloids in asthma is unjustified and should be avoided.—We are, etc.,

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Treatment of Typhoid

SIR,—We read with interest the article on chloramphenicol combined with ampicillin in the treatment of typhoid by Professor F. De Ritis and others (7 October, p. 17). We conducted a similar trial in Madras.¹ The patients were studied in three treatment groups: group 1 was given chloramphenicol alone (30 mg/kg/day); group 2 ampicillin alone (125 mg/kg/day); and group 3 a combination of chloramphenicol (20 mg/kg/day) and ampicillin (80 mg/kg/day). The mean duration of pyrexia after starting the treatment in the three groups was 5.6, 4.8, and 5.4 days respectively. Though the difference between the treatment groups was not significant the average dose of chloramphenicol and ampicillin was smaller in group 3. If the patients had been given full doses of chloramphenicol and ampicillin, as in the study of Professor De Ritis and his colleagues, the pyrexial period might have been shortened significantly. Furthermore, the need for steroid supplementation to control toxæmia after antibacterial treatment only for the first 72 hours was less in those on combined therapy than in those on chloramphenicol alone or ampicillin alone. One patient in each of the first two groups relapsed and none in the third group.

We also studied the use of furazolidone in enteric fever in a similar way.² Patients in group 2 were given chloramphenicol (43.5 mg/kg/day); those in group 2 were given furazolidone alone (17 mg/kg/day); and those in group 3 chloramphenicol (39 mg/kg/day) and furazolidone (12.5 mg/kg/day).

day). The mean duration of pyrexia after starting treatment was 4.6, 5.9, and 3.5 days respectively, the difference being statistically significant in favour of the combined therapy. No patients in group 3 relapsed, but one did so in each of the other groups.

Combined therapy seems therefore to be superior to single drug therapy. The possible advantage of a reduced dosage of the individual drugs in the combination, especially of chloramphenicol, is also to be considered. With an increasing number of reports of resistance of *Salmonella typhi* to chloramphenicol it will probably be wiser to start patients, at least those who are very ill, on all three drugs, as it is done in some other infections. When economy is also a consideration chloramphenicol and furazolidone, being cheaper, can be given in preference to the combination containing ampicillin.—We are, etc.,

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Constraints on Consultants

SIR,—I disagree with the first sentence of your leading article (3 March, p. 501), in which you say that the consultant alone has the right to decide on the line of treatment for his patients.

In my opinion the patient has the right to accept or reject a particular line of treatment even when it has been explained to and understood by him. If he is not capable of accepting or rejecting treatment by virtue of his understanding or disposition such decision should be made by his next of kin. This is the procedure adopted in surgical and in medical wards but does not dispose entirely of the ethical and legal hazards.

The only exceptions to such procedure are urgent necessity of saving life or mitigation of disruptive social behaviour.—I am, etc.,

HAROLD PALMER

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SIR,—If the concept that schizophrenia is caused by the family environment is indeed correct, then surely the appropriate solution should be group family therapy. It is therefore astonishing that you should be able in your criticism (3 March, p. 501) of the Napsbury experiment to state that the purpose of treatment was not even adequately explained to patients' relatives. There seems to have been a clear disparity between theory and practice.—I am, etc.,

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Graphic Records in Labour

SIR,—I welcome your publication of the Addington Labour Observation Chart and would like to present another example (see

fig.). This chart has been successfully used at Charing Cross Hospital for the past four years in Professor N. F. Morris's unit. It is part of the notes, which are in book form, and can be extended indefinitely with identical adhesive sheets (The gum is behind the right hand edge.)

LABOUR CHART

Name :

Contractions began at hours on

The main advantage is compactness, which has been achieved by including fetal heart, maternal pulse and blood pressure, and cervical dilation on the same graph. Clarity is retained by using red or black symbols and, rather surprisingly, the graphs do not often conflict. The time scale at the top is infinitely variable, permitting flexible spacing of observations, which is particularly useful during crises.

Considerations of space preclude the reproduction of the whole chart here, though I would be pleased to supply copies of this. The lower half includes space for recording the following: contractions (duration, interval, and strength); oxytocin (concentration and rate); drugs given (dosage); fluid intake (oral and intravenous); urine output (volume and abnormalities); and station of fetal head. The chart was designed to measure 8½ in x 11 in (21.6 cm x 28 cm) but, if applied to the new standard A4 paper, an extra ¾ in (1.9 cm) becomes available.

Several graphic variations have been suggested recently by other authors which give better display of cephalic descent or of the nature of contractions, and so on. Attempts to specify progress norms, "danger levels," etc., have been deliberately avoided since we felt that these might tend to be interpreted too rigidly. Such norms tend to vary and, I feel, are more appropriately recommended by other means.—I am, etc.,

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Breech Management with Fetal Blood Sampling

SIR,—At this hospital we support the concept of active intensive care for breech deliveries and have been working on similar lines to Dr. B. W. Eliot and Mr. J. G. Hill (23 December, p. 703). Recent correspondence on the subject prompts me to comment on the following points.

Fetal blood sampling of the breech as a means of monitoring fetal welfare is not novel and has been performed by many of our colleagues. The important point, however, is to realize that after 5 cm dilatation the blood sample from the breech differs from a scalp sample and this difference increases till the second stage.

Uniform compression of the scalp by the cervix against a firm skull jeopardizes the microcirculation, resulting in the caput. No comparable compression occurs in the breech, where the pelvis and the two limbs can be visualized as three cylinders inside a constricting circle. Compression of the vasculature sufficient to affect the microcirculation does not occur, so that no oedema of the gluteal area is seen. Blood from the scalp will have a lower pH than the breech samples; thus one must accept a higher pH level for distress in the breech. It is this level that we are trying to determine.

Once the body is delivered the placenta contracts, reducing blood supply to the fetus, and this is further enhanced when the splinting effect of the lower limbs is removed with their delivery, as then the cord is compressed against the cervical rim. Forceps applied to the after-coming head helps control during extraction and prevents head compression. When forceps are used there is no great benefit in excessive slow delivery of the head, as the most sudden decompression is when the blades of the forceps are removed. Understanding of the physiology with regard to breech management allows us to recommend an active technical, as well as chemical, management.—I am, etc.,

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Fluoride and Osteoporosis

SIR,—In your leading article (30 December, p. 748) you refer to the treatment of osteoporosis with fluoride, calcium, and vitamin D recommended by Jowsey *et al.*¹ We have been carrying out a double-blind clinical trial of sodium monofluorophosphate as prophylaxis against senile osteoporosis on 460 patients in a municipal home for aged

people over a period of eight months. Although the final results have not yet been completed, we should like in this preliminary report to draw attention to the high concentrations of ionized fluorides in the plasma resulting from this treatment.

The treated patients were given sodium monofluorophosphate in a dosage corresponding to 25 mg of fluoride per day, and sodium bicarbonate was given to the control patients. After five months the appearance of spontaneous bone fractures forced us to break the code, and it was observed that there were more side effects in the group that had received fluoride. The dose of fluoride was reduced to 25 mg twice weekly, and at the same time the plasma ionized fluoride concentration of 21 patients selected from the treated group was measured by the electrometric method² (see fig.). An x-ray revealed a recent fracture in the vertebral

Mean plasma ionized fluoride concentrations ($\pm$ S.E. of mean). (A) After five months' treatment with 25 mg fluoride a day. (B) One month later (during treatment with 25 mg twice a week). (C) Two months later (during treatment with 25 mg twice a week). (D) At the end of treatment. (E) One month later. (F) Two months later. (G) Untreated patients. (H) Untreated patients in an area with artificially fluoridated drinking water. (I) Untreated patients with renal disease in an area with artificially fluoridated water. (Numbers of patients in parenthesis.)

column of one of the patients in the treated group (plasma fluoride $5.0 \mu\text{mol/l}$), but no signs of increased calcium concentration or osteosclerosis. Two cases of fracture of the femoral neck were also found in this group (plasma fluoride 2.1 and $4.3 \mu\text{mol/l}$ respectively), and several joint collapses of thoracic vertebrae in another patient (plasma fluoride $4.3 \mu\text{mol/l}$). No cases of fracture were found in the control group of 25 patients.

Renal function was examined in patients with plasma ionized fluoride levels above $4.0 \mu\text{mol/l}$ during the initial period of treatment. In one patient with a creatinine clearance of 35 ml/min the fluoride value was found to be $9.0 \mu\text{mol/l}$, and in two patients with creatinine clearance of 46 ml/min the fluoride values were 5.2 and $4.0 \mu\text{mol/l}$ respectively. One patient who had an increased serum creatinine level (2.5 mg/100 ml) had, however, an unexpectedly low plasma fluoride level ($1.2 \mu\text{mol/l}$).

Very little information is available on the plasma fluoride levels in patients with osteoporosis. Armstrong³ reported a significant increase in total fluoride concentration in some patients and a mild increase in others. In an earlier study⁴ we found that the mean plasma ionized fluoride concentration of patients was $1.4 \mu\text{mol/l}$ in an area with fluoridated drinking water and $0.8 \mu\text{mol/l}$ in a non-fluoridated area. Patients with renal disease had an average level of $2.7 \mu\text{mol/l}$ in the area with fluoridated drinking water. In our present series renal insufficiency did not play any significant part despite the very high age of the patients.

Treatment with the high doses of fluoride recommended leads to significantly increased concentrations of ionized fluoride in the plasma. These concentrations decrease very slowly after the treatment is stopped (see fig.). We cannot, of course, conclude categorically that the fractures we observed were the direct result of fluoride retention. We think it wise, however, to draw attention to the high ionized fluoride level in these patients. The relation between this level and both the effects and the side effects of fluoride treatment should be more thoroughly investigated.

The preparation used by us was sodium monofluorophosphate, and no additional treatment with calcium or vitamin D was given. According to Jowsey *et al.*¹ oral phosphate supplementation will tend to increase rather than decrease bone resorption levels. The use of sodium fluoride instead of monofluorophosphate and a combination with calcium and vitamin D might be safer.—We are, etc.,

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Anthrax

SIR,—Professor A. B. Semple in his letter (3 February, p. 293) has rightly drawn attention to the closure of the Government Wool Disinfecting Station in Liverpool some two years ago. When I wrote my paper on anthrax (20 January, p. 157), I was unaware of this information.

Mr. Ian Macdonald, of British Charcoals and MacDonaldis Ltd. has referred me to a letter which appeared in *The Times* recently from Dr. E. S. Anderson and others¹ referring to the difficulty of sterilizing bone products and expressing the view that although the risk of anthrax infection from such products is probably small there is a need for some effective and economically viable method of sterilization. Since ethylene oxide gas is regarded as an efficient sporicidal agent, then the possibility of its industrial