fatality rate) and the mortality rate per number of individual electrical treatments given (treatment-fatality rate).

Using a questionnaire, Barker⁵ and Baker⁶ investigated retrospectively nine deaths which had occurred over a two-year period in 55 hospitals as a result of E.C.T. These deaths were distributed over more than a quarter of a million treatments. Amongst the conclusions from this study (which must be one of the largest in existence) was that the E.C.T. mortality rate was extremely low—one death per 28,000 treatments, which is equivalent to a treatment-fatality rate of 0.003%. This might imply that the mortality rates from E.C.T. and that arising from tranlycypromine are of approximately the same order (0.003% as opposed to 0.001%), whereas it is of course impossible to compare the incidence of death resulting from tranlycypromine against a mortality which is expressed according to the number of E.C.T. treatments which have been administered.

Also it would seem inappropriate to compare the fatality rate resulting from a monoamine oxidase inhibitor taken several times a day, alone or in combination with other powerful psychotropic drugs, over a period of several months or years, with that resulting from E.C.T., which may also be given alone or in conjunction with drugs (usually 2 or 3 times a week for much shorter periods). Too many variables are introduced. For instance, among many other considerations the age of the patient may be much more important in relation to the E.C.T. fatality rate than to the incidence of death associated with tranlycypromine.

Far more information about this subject is required before any lasting conclusions may be drawn. The position of the elusive decimal point is, however, of considerable importance.—I am, etc.,

Shelton Hospital,
Shrewsbury.

J. C. BARKER.

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Attempted Suicide with Cheese

SIR,—Many reports have appeared lately dealing with possible side-effects of "par-nate" (tranlycypromine).

So far, however, I have not heard of a similar case to that of a depressed young woman recently admitted to this hospital. Prior to admission she was having tranlycypromine, and had been naturally warned about the risks of cheese concurrently with that drug. Unfortunately she suffered an acute deterioration of her illness and attempted suicide by swallowing some tablets of tranlycypromine. A few days after her admission she confessed to the staff that she had not only taken the tablets but also a "chunk of cheese." Nothing happened to her.—I am, etc.,

Stone House Hospital,
Dartford, Kent.

J. ASENSIO.

Ampicillin in Typhoid Fever

SIR,—Your leading article on ampicillin (18 January, p. 132) states that since the discovery of ampicillin (alpha-amino benzyl penicillin, "penbritin") in 1961¹ no full-scale results of clinical trials of ampicillin in typhoid fever have been reported. I would like to draw attention to a controlled trial of ampicillin treatment in typhoid fever carried out at the Mulago Hospital, Kampala, the results of which I presented at the Third International Chemotherapy Conference held in Stuttgart, West Germany, in July 1963² and which will be published in the proceedings of that meeting. The trial was controlled in that patients were allocated to treatment with ampicillin or chloramphenicol on a random basis. The criterion for the final diagnosis and inclusion in this trial was a positive blood culture of *Salmonella typhi*. Fifty patients were studied, 25 in each group. Both drugs were given orally. Ampicillin was given in the dose of 2.25 g. per day, and chloramphenicol 3.0 g. per day, till the pyrexia subsided. Thereafter ampicillin dosage was reduced to 1.5 g. per day, and chloramphenicol to 2.0 g. per day, and this was continued for one week. Children under 10 years of age were given half the adult dose. The series consisted of 36 males and 14 females. The age range was from 8 to 50 years.

In the patients treated with ampicillin the duration of illness before the start of the treatment had great effect on the response to the drug; the early cases responded much better than the late cases. On the other hand the response to chloramphenicol was uniformly good, regardless of the duration of illness before treatment. In nine patients who were ill for less than seven days before the start of the treatment the response to ampicillin therapy was good, and the average duration of fever was five days. This was noted in all patients irrespective of the severity of the illness. In 16 patients who were ill for more than seven days the response to ampicillin therapy was slow, and the average duration of fever after the start of treatment was nine days. The average duration of fever after the start of chloramphenicol was 5.5 days, regardless of the severity or duration of the illness.

In the ampicillin-treated group nine patients responded satisfactorily; the response was slow in 13 patients and poor in three. These three all did well on chloramphenicol. Blood culture of one of these patients showed *S. typhi* resistant to ampicillin and sensitive to chloramphenicol. One patient had a relapse and responded well to another course of ampicillin. One patient died of intestinal haemorrhage. In the chloramphenicol-treated group, the response to therapy was considered good in 21 cases, slow in three, and poor in one. The blood culture of the patient who showed the poor response grew *S. typhi* organisms which were found to be resistant to chloramphenicol and sensitive to ampicillin; he subsequently did well on ampicillin.³ Two patients relapsed, but responded well to second courses of chloramphenicol. Two patients had intestinal haemorrhage, and this was fatal in one. One other patient died of intestinal perforation. Four further cases of typhoid fever were treated with the bigger dose (4.0 g. per day) of ampicillin. No improvement in the response was noted.

There were no manifestations of hypersensitivity reactions noted during the administration of ampicillin. This is at variance with the experience of W. P. U. Kennedy and his colleagues,⁴ who encountered a high incidence of hypersensitivity reactions to ampicillin.—I am, etc.,

KANTI M. PATEL.

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Medical School,
Mulago Hospital,
Kampala, Uganda.

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Trial of Oxethazaine

SIR,—The findings of Dr. G. V. Balmforth and his colleagues (8 February, p. 355) do not surprise me, for I have had some experience of the mixture of the local anaesthetic oxethazaine in a gel of aluminium and magnesium hydroxide ("mucaine"). They found that the local anaesthetic added no benefit to the plain gel in patients with a duodenal ulcer. On the other hand they also showed that the local anaesthetic mixture was no worse.

In a double-blind trial I found that mucaine was significantly superior to the same gel without the local anaesthetic in cases of heartburn of pregnancy. Since that trial ended I have used this mixture in over 50 similar cases and rarely found it not to satisfy my patient. I have also found mucaine to be useful as a symptomatic treatment of heartburn due to other causes, usually hiatus hernia, though the number of such cases in my practice is not sufficiently great to prove anything statistically. Patients with a duodenal ulcer do not often get a reflux oesophagitis and rarely complain of heartburn, so I would not expect a local anaesthetic to add any benefit to the plain gel in these cases.

The enthusiastic response new drugs sometimes evoke should not cause us to condemn them if they fail to come up to every expectation. Safe symptomatic remedies have a place in the therapeutic armamentarium of all physicians.—I am, etc.,

London W.12.

STUART J. CARNE.

Fluoridation Falsified

SIR,—I am now told by Mr. W. Stewart Ross (21 March, p. 766) "that 1½ g. of sodium fluoride would have to be ingested in water containing 1 part per million sodium fluoride" for toxicity, and that this volume of fluid cannot be drunk. The second part of this is true; the first I believe to be untrue. I cannot concede his "elementary point" until he explains why he chose two and a half bathfuls of water, rather than (say) two, as the minimum daily amount that will provide a toxic amount of fluoride. Will he please give the evidence for this figure? His 1½ g. of NaF is about 700 mg. of F; the B.D.A. states that 20 mg. of F causes chronic poisoning, and this is contained in 20 l. (about 35

pints or one-fourteenth of a bathful) of water at 1 p.p.m. F.

It is certainly remarkable and not irrelevant that he chose as the minimum chronic dose that could produce toxicity the amount chosen by the Ministry as the acute toxic dose. My doubts about his dosages are strengthened by the elementary error in the words he has italicized, since 1 p.p.m. of *sodium fluoride* is about the same as 0.45 p.p.m. F, less than half the amount proposed to be added to public water supplies.

Dr. D. J. Galagan, a proponent of fluoridation, found in Arizona that concentrations in the water supply above 0.8 p.p.m. F resulted in objectionable dental fluorosis.¹ He attributed this to the increased water consumed in the hot atmosphere. I have stayed in Arizona and believe this interpretation is correct. But the inhabitants do not drink 2½ bathfuls daily. So how does Mr. Ross explain this toxic result of the ingestion of water containing not more than 1 p.p.m. F? The occurrence of serious chronic poisoning in persons using rather greater concentrations (e.g., about 1 to 2 p.p.m. in Qatar,² and 6 p.p.m. in Aden³) has also been attributed mainly to increased consumption of water, perhaps combined with malnutrition. In this country a stoker or professional dancer may allegedly drink 30 pints (17 l.) of water daily (17 mg. of F at 1 p.p.m. F). So I propose that Mr. Ross and I do a controlled experiment as he suggests: I will ingest 35 pints (20 l.) of water daily for six months while he ingests the same amount of water containing 2.2 p.p.m. NaF (1 p.p.m. F), and to check that neither of us inadvertently cheats (e.g., by the addition of chalk) a neutral observer should measure daily the volume of urine and its content of creatinine and fluoride. Will he agree to this simple and realistic test of the chronic toxicity?

I note with surprise that Dr. Dalzell-Ward thinks "it would be difficult for an individual to consume three times the daily optimum dose of fluoride. . . ." For an adult there is no optimum dose, since it is generally agreed that after adolescence water at 1 p.p.m. F does not benefit the teeth. There are certainly persons in this country who ingest more than three times the average amount of water. He cannot explain away his erroneous statement about safety by saying it was framed in terms of sociology. He made to a scientific meeting and published in a scientific journal the statement that "the safety margin exceeds that offered by any other prophylactic procedure." He agrees that the addition of thiamine to white flour is analogous (I could have chosen other prophylactic measures). He tells us that the "optimum daily dose" [for an adult man about 1.4 mg. from water at 1 p.p.m. F] is rather less than one-thirtieth the amount that causes chronic poisoning [apparently, therefore, about 40 mg. F, which is double the figure given by the B.D.A. but only an eighteenth that of Mr. Ross]. Since the average prophylactic amount of thiamine for an adult is at least a thousandth of the amount that could produce toxicity, by what criterion does the safety margin of fluoridation exceed that of the addition of thiamine to white flour? Will he either substantiate or withdraw his statement?

His mention of morphine and aspirin is irrelevant; no one proposes to add them to public water supplies—or not yet: Sir Stanton Hicks,⁴ in opposing fluoridation of

public water supplies, has likened this to adding aspirin for the mass-headache.—I am, etc.,

Oxford.

HUGH SINCLAIR.

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Corticosteroid Eye-drops

SIR,—We read Mr. G. Everard Hewson's letter (5 February, p. 438), in which he mentions the instruction and information pamphlet on "pimafucort."

In fact we state in this pamphlet that "Pimafucort is indicated in the treatment of infections caused by bacteria, fungi or yeasts and of allergic affections of the eyelids and anterior segment of the eye." Nowhere in our pamphlet did we state that this pimaricin-neomycin-hydrocortisone ointment is indicated in the treatment of viral infections of the eye. Furthermore, at least in our country, it has become common knowledge that the use of corticosteroids in cases of, for example, ophthalmic herpes-simplex infections is contraindicated.

For these reasons it was at the time considered unnecessary to mention this fact in every instruction pamphlet.—I am, etc.,

Mycopharm-Delft,
Medical Information Department,
Delft, Holland.

L. VAN WIJK.

"Normal" Saline in Treatment of Dehydration

SIR,—“Normal” (0.9%) saline is neither normal nor physiological. Although it is isotonic with respect to the extracellular fluid (E.C.F.) the sodium and chloride content (154 mEq of each/litre) is in excess of that found in the latter, and should therefore be used with care in any state of dehydration other than that resulting from an obviously predominant electrolyte deficit.

In the interesting case of hyperglycaemia and coma associated with acute pancreatitis described by Dr. A. I. G. Davidson (8 February, p. 356) an osmotic (sugar) diuresis was not complicated by ketosis, but the clinical findings were complex, with hypotension, surgical shock, and little external evidence of dehydration. The biochemical findings indicated that the E.C.F. was hypertonic—for the normal electrolyte values were contained in what amounted to a solution of 10% dextrose (blood sugar 994 mg./100 ml.). The serum osmolality was not estimated at the time, but we may get a rough value for this by doubling the cation concentration per litre and adding to it the osmolar concentration of the blood sugar in excess of 100 mg./100 ml.—the result is 352 m.osmol./l. (normal values 290–300 m.osmol./l.). Cellular dehydration was almost certainly present in such a situation, and the use of normal saline other than perhaps initially, if no other means was available to raise the blood-pressure, would increase the severity of it; for being isotonic it contains no “free” water which could pass intracellularly, and also the excess

of ions requires excretion by the kidney, thus increasing any water deficit.

The use of 0.9% saline is virtually banned in this department, where the narrow margin of error in infants or children necessitates great caution in the correction of electrolyte imbalance; for the success of intravenous “normal” saline therapy depends on the recipient's renal function and his tolerance of moderate degrees of electrolyte imbalance.—I am, etc.,

Children's Department,
Farnborough Hospital,
Farnborough, Kent.

PETER ROBSON.

Genetics of Dupuytren's Contracture

SIR,—Your leading article (7 March, p. 578) is to be welcomed for drawing attention to R. S. M. Ling's valuable study of the genetic factor in Dupuytren's contracture. I must, however, correct the statement that “perhaps 1 in 20 of the population living to beyond the age of 75 develops signs of the disease.” The incidence in this country is in fact very much higher than that, and 1 in 5 would be nearer the mark. Actual figures from Edinburgh¹ and Manchester,² respectively, are 28.9% and 20.9% for men, 17.0% and 9.8% for women. In my series about 85% of cases in this age-group had both hands affected.—I am, etc.,

Cheadle, Cheshire.

P. F. EARLY.

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Peyronie's Disease

SIR,—I wonder if any of your more knowledgeable readers could tell me whether they have any record of Peyronie's disease (induration penis plastica) being familial. Last year I saw a patient aged 52 who had a six-week history of deviation of the penis with subsequent formation of a plaque. The appearances were typical of Peyronie's disease. Subsequently the patient wrote to state that his older brother (aged 56) had developed the same trouble at the age of 49, whilst his younger brother (aged 48) had developed the condition at the age of 45. It is probably quite irrelevant but worthy of mention that my patient's daughter has a proved Hashimoto's goitre. Possibly some expert could offer a clue to all this.—I am, etc.,

London W.1.

R. S. MURLEY.

Induction of Labour with Hypertonic Glucose

SIR,—Dr. Donald W. Briggs in his letter of 14 March (p. 701) drew attention to a maternal death from *Clostridium welchii* infection. In the case described either the organism was introduced at the time of abdominal puncture or was already in the genital tract and became disseminated soon after the onset of labour. As many thousands of abdominal amniotomies have been carried out both as a diagnostic and therapeutic procedure in Europe and the United States of America without maternal death from infection, one must conclude that this complication, if not