units were isolated; this is of doubtful importance and laboratory contamination could not be excluded. The same phial was sterile on subsequent reculturing. No other important growth was obtained and clinical evidence of infection was absent.

This detailed study of a small number of patients has further failed to find any evidence that the practice of reusing plastic insulin syringes is associated with significant microbial contamination.

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- 1 Allwood MC. Re-use of plastic insulin syringes. *Lancet* 1983;i:712-3.
- 2 Collins BJ, Richardson SG, Spence BK, et al. Safety of reusing disposable plastic insulin syringes. *Lancet* 1983;i:559-61.

Dihydrocodeine in renal failure

SIR,—I read with interest the paper by Dr J N Barnes and others (9 March, p 740), who point out the possible hazards of adopting a normal dosage regimen for dihydrocodeine in patients with renal failure. (Previous work has shown such patients to be sensitive to normal doses of morphine.) The conclusions they draw—that distribution and elimination characteristics of dihydrocodeine are altered in severe renal failure—are probably true but they cannot be totally substantiated from their data.

Each subject and patient in the study was given a fixed dose (60 mg) of dihydrocodeine without adjustment for body weight. If the mean weight of the normal subjects was greater than that of the renal patients the latter group would show a lower mean volume of distribution for the drug and higher plasma drug concentrations. Total body clearance of drug, being partly dependent on distribution volume, would correspondingly be less in a lighter group of patients. Alteration in plasma protein binding of highly bound drugs in renal failure may account in part for differences in distribution and elimination. Opiates bind to several plasma proteins, including albumin; a decrease in protein binding is expected to lead to a reduction in total (bound and unbound) drug in the plasma—a result not observed in the study. Finally, any potential drug-drug interactions within the study groups which could have influenced plasma drug values were not mentioned by the authors. Drugs commonly administered to renal patients (3 blockers, cimetidine) may adversely affect hepatic blood flow or inhibit metabolism of drugs (such as opiates) with high intrinsic clearances.

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- 1 Olsen GD, Bennett WM, Porter CA. Morphine and phenytoin binding to plasma proteins in renal and hepatic failure. *Clin Pharmacol Ther* 1975;17: 677-84.

*.*Dr Barnes replies below.—ED, BMJ.

SIR,—Mr Brown has raised some important points. We elected to give a fixed 60 mg dose of dihydrocodeine and to weight match our two groups. The mean (SEM) weight of our normal subjects was 65.6 (2.7) kg and that of the renal patients 62.3 (3.1) kg. We think it unlikely that the inevitable small difference in weight between the two groups explains

the differences in pharmacokinetics of dihydrocodeine observed. The comment about the possible effect of alteration in plasma protein binding in renal failure concurs with the similar point raised in our discussion.

We agree that drug-drug interactions could have influenced plasma drug values, and subjects were excluded from study if they were taking drugs likely to have such an effect. Six of our patients were taking aluminium hydroxide and this was discontinued 48 hours before the study. All the patients were taking ferrous sulphate, which was also discontinued 48 hours before study. We think it unlikely that these drugs would have had a continuing effect on the pharmacokinetics of the dihydrocodeine.

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Management of acute gastroenteritis in children

SIR,—Conventional management of acute gastroenteritis entails a period of rehydration with clear oral fluids followed by gradual reintroduction of milk. Dr Khin-Maung-U and others (23 February, p 587) have shown the beneficial effect of continued breast feeding in Burmese children, but in our experience in London few children admitted with acute gastroenteritis are breast fed. We were concerned about the extra time spent in hospital as a result of gradual regrading with increasing strength milk and we have conducted a study comparing this conventional regimen with reintroduction of full strength milk 24 hours after admission.

One hundred and eighty one children with mild gastroenteritis were admitted to our study. After a thorough clinical assessment oral glucose electrolyte solution (Dextrolyte, Cow and Gate) was given for 24 hours followed by random allocation to either a regimen consisting of quarter, half, and full strength milk, increasing at 24 hour intervals (slow regrading), or a regimen in which full strength milk was reintroduced immediately (fast regrading). Clinical assessment, including body weight and stool and vomiting frequency, was made every 24 hours, and stools were examined for pathogenic organisms. Children were discharged home when parents and the clinician in charge were satisfied with the child's clinical condition.

Satisfactory data were obtained in 86 children on slow regrading and 89 on fast regrading. The two treatment groups were matched for age (mean 0.9 and 1 year), sex, weight, duration of illness at home, and number of stools in the 24 hours before admission. Pathogenic organisms were identified in 56% and 42% of patients on slow and fast regrading respectively, and in more than 60% of these the organism was a rotavirus. Mean (SE) stool frequency on slow and fast regrading respectively fell from 5.6 (0.4) and 4.8 (0.3) per 24 hours before admission to 4.1 (0.4) and 3.4 (0.3) at 24 hours, 2.9 (0.3) and 3.0 (0.3) at 48 hours, 2.5 (0.4) and 2.8 (0.4) at 72 hours, and 3.2 (0.4) and 2.5 (0.4) at 96 hours. There was no significant difference in stool frequency at any time during the study.

Children on both regimens gained weight after

oral fluid repletion but this improvement was maintained consistently only in those receiving full strength milk after 24 hours. There was a significant difference in favour of fast regrading in the weight gain at 72 and 96 hours (table). The mean (SE) duration of stay in hospital was 3.6 (0.1) days on slow regrading and 2.9 (0.1) days on fast regrading and this difference was significant at the 0.1% level (Student's *t* test).

Our results agree with those reported by McDowell and Evans-Jones¹ and show that immediate reintroduction of full strength milk after 24 hours' rehydration with clear fluids is well tolerated and is associated with progressive weight gain and a shorter stay in hospital. Patients with severe gastroenteritis requiring intravenous fluid replacement were excluded from this study but they too would be expected to benefit from early feeding.² The necessity for an initial period of rehydration with clear fluids has been questioned but omission of this step was associated with a higher incidence of vomiting in the study of Rees and Brook³ and this justifies excluding milk initially.

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- 1 McDowell HP, Evans-Jones G. Is gradual reintroduction of milk feeds in gastroenteritis necessary? *Lancet* 1985;i:690.
- 2 World Health Organisation. *A manual for treatment of acute diarrhoea*. Geneva: WHO, 1980:8-12. (WHO/CDD/SER/80.2.)
- 3 Rees L, Brook GD. Gradual reintroduction of full-strength milk after acute gastroenteritis in children. *Lancet* 1979;i:770-1.

Louis Pasteur and rabies

SIR,—May I point out that the picture reproduced in the news section of 30 March (p 1009) is misleading. It shows Pasteur "preparing to vaccinate a child." In fact Pasteur never performed inoculations. He was not medically qualified and, moreover, was unable to use his arm, having been paralysed by a left sided hemiplegia in 1868.

I refer to the book *A l'Ouvre de Pasteur* written by his nephew, my father, Dr Adrien Loir. The book was published in 1934 and, I understand, was used in the making of the BBC television series *Microbes and Men*.

Professor Grancher, from l'Hôpital des Enfants Malades (Paris), was called to the laboratory by Pasteur, and it was Professeur Grancher who performed the inoculations on the first child patient (Joseph Meister) and all the subsequent ones in those early days of the treatment.

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*.*The Science Museum tells us that the picture that we published, which was sent to us, is an allegorical poster produced in 1922 and is not in the exhibition. It is made clear in the exhibition that Louis Pasteur did not give any injections.—ED, BMJ.

Percentage change in weight at given times after two treatment regimens (slow reintroduction of milk and rapid reintroduction of full strength milk) after oral rehydration. Values are means (SE)

	24 h	48 h	72 h	96 h
Slow reintroduction	+0.50 (0.24)	-0.09 (0.27)	-0.68 (0.35)	+0.14 (0.39)
Rapid reintroduction	+0.43 (0.23)	+0.42 (0.24)	+0.79 (0.35)	+1.36 (0.41)
p Value	NS	NS	<0.01	<0.05