dialysis¹ is most likely to be due to the high dialysis clearance of unmetabolised drug. This also explains why the peak plasma level of cyclophosphamide is within the range previously reported in patients with normal renal function.³

The action of cyclophosphamide depends on biotransformation in the liver⁴ to aldophosphamide⁵ and other active metabolites with alkylating activity. For a given dose, in a patient with chronic renal failure we would predict much higher plasma availability of both cyclophosphamide and active metabolites on days when the patient was not on dialysis. These observations have particular relevance to the renal transplant patient being given cyclophosphamide as immunosuppression.

M R BENDING
R E FINCH

Department of Medicine,
Department of Therapeutics,
Westminster Hospital,
London SW1

¹ Milstead, R A V, and Jarman, M, *British Medical Journal*, 1978, **1**, 820.

² Bagley, C M, Bostick, F W, DeVita, V T Jun, *Cancer Research*, 1973, **33**, 226.

³ Jarman, M, et al, *Clinical Chimica Acta*, 1975, **58**, 61.

⁴ Brock, N, and Hohorst, H J, *Arzneimittel-Forschung*, 1963, **13**, 1021.

⁵ Hill, D L, Laster, W R Jun, Stuck, R F, *Cancer Research*, 1972, **32**, 658.

Staphylococcus aureus in raw human milk for neonates

SIR,—Dr A Lucas and others (25 March, p 781) understandably take us to task on the subject of acceptable limits for *Staphylococcus aureus* in raw human milk.

We should like first to point out that, unfortunately, an error appeared in our paper (18 February, p 393). Under the heading "Raw milk" on p 395 we give three main criteria for the acceptance of human milk to be fed raw. The second of these appears as: "It should not contain more than 10×10^5 colony-forming units of *Staphylococcus aureus*/l." The figure of 10×10^5 is repeated twice more in the same paragraph. In all three cases it should be 10^5 colony-forming units/l (that is, 10^2 /ml). After experience with more sensitive methods, we eventually chose to use a screening test employing a standard loop (0.01 ml of milk), with the result that 10^5 colony-forming units/l is the lower limit of sensitivity of our method.

It is not easy to obtain human milk that does not contain small numbers of *Staphylococcus aureus*. The organism is hardly likely to be derived from the alimentary tract since it is not a common intestinal pathogen, and its presence therefore would not indicate the likelihood of faecal contamination, which is the case with the enterobacteria. In addition, there are good reasons for thinking that all human milk possesses antistaphylococcal properties.¹ The protective effect of human milk against *Staphylococcus aureus* may extend throughout the gut of breast milk fed infants, since in a study of the faecal flora of seven-day old full-term breast fed infants *Staphylococcus aureus* was much less frequent as a significant component of the faecal flora than in an equivalent group of formula-fed infants (5% as against 34%).² It is well known that a high proportion of newborn infants rapidly become nasal carriers of *Staphylococcus aureus*³ and small numbers of these organisms must

normally pass into the intestinal tract. These factors convince us that the feeding of carefully selected raw milk containing at most only small numbers of this organism is unlikely to present a hazard to the infant's health. We would agree, however, that further investigative work is necessary to clarify the situation more fully.

Our reasons for using raw milk are partly nutritional and partly immunological. Pasteurisation, it is true, preserves part of the antimicrobial components of milk, but these are more fully retained when untreated breast milk is deep frozen.⁴ It is difficult to reconcile the misgiving of Lucas *et al* that immunological properties retained by raw milk may on the one hand be deleterious and yet be beneficial if the milk is pasteurised. It is also difficult to be sure of what "foreign (? undesirable) cellular components" (apart from a strictly defined number of bacteria) are present in deep-frozen raw milk that are not found in pasteurised milk.

We feel that, until proved otherwise, careful collection methods and bacteriological surveillance such as those we advocate should be rigorously applied by anyone thinking of establishing a milk bank. Reliance on pasteurisation itself to render the milk safe may not be adequate if bacteriological screening is postponed until after the procedure. Unless one can be reassured by prior screening that the count of *Staphylococcus aureus* in the milk is low prior to pasteurising, enterotoxin production may constitute a cause of unexpected gastrointestinal problems such as those we are all trying to avoid.

S WILLIAMSON
E FINUCANE
H R GAMSU
J H HEWITT

King's College Hospital Medical
School,
London SE5

¹ Gyorgy, P, *American Journal of Clinical Nutrition*, 1971, **24**, 970.

² Hewitt, J H, and Rigby, J, unpublished observations.

³ Williams, R E O, et al, *Hospital Infection*, 2nd edn, p 54. London, Lloyd Luke, 1966.

⁴ Evans, T J, et al *Archives of Disease in Childhood*, 1978, **53**, 239.

* * * We regret that " 10×10^5 " arose through an error in proof correction.—Ed, *BMJ*.

Histocompatibility antigens and urinary tract abnormalities

SIR,—The observations of Drs R R Bailey and M R Wallace (7 January, p 48) with regard to the association of HLA-B12 and vesicoureteral reflux in patients with renal failure are very interesting and similar to our findings in children.

A total of 36 unrelated Caucasians (predominantly French Canadian)—34 girls and two boys aged 3–16 years—with a history of recurring urinary tract infections (UTI) due to *E coli* were tissue typed for 25 HLA specificities. Results were compared with 188 normal random subjects. In addition, four families with a total of 16 siblings (7 with UTI, 9 normal) were also tissue typed to study segregation of reflux with HLA haplotypes. HLA-A2 was significantly reduced in UTI patients (UTI v control: 48% v 25%, $P < 0.025$). On the other hand, specificities A10 (9% v 22%, $P < 0.04$) and Bw16 (3% v 14%, $P < 0.015$) showed significant increases in UTI patients. However, when UTI patients were divided into two groups,

one with reflux (16 patients) and the other without reflux (20 patients), no significant differences between the two groups were observed with regard to these three HLA specificities. Thus, our results suggest that HLA specificities A2, A10, and Bw16 may be associated with the susceptibility to UTI due to *E coli* independent of developmental anomalies of vesicoureteral origin. Although subjects with and without reflux showed deviations in several HLA specificities (B12, A9, and A11), only Aw32 was found to be highly significant ($P < 0.0001$) in our patient population. In addition, the patients with a history of recurrent UTI but without reflux showed a higher incidence of blood group A (65%) as compared to normal controls (45%). In three of the four families studied, a pair of HLA-identical siblings had a history of recurrent UTI and reflux. Although reflux segregated with HLA haplotype in all four families, no single HLA specificity or common HLA haplotype was found to be associated with reflux. Our studies suggest that a gene (or genes) other than those governing the HLA is responsible in the genesis of reflux. However, it seems to have a close linkage with the major histocompatibility complex and may be in linkage disequilibrium with Aw32.

Segregation of ureteropelvic junction obstruction (stenosis) with HLA haplotype was also recently observed in 12 siblings of a French Canadian family. The proband was a prospective renal allograft recipient who had apparently inherited stenosis from his father (ab) via HLA haplotype a. Within the family, four other siblings (two HLA identical with the proband) who shared haplotype a with the proband were also found to have stenosis, while seven other siblings who did not receive HLA haplotype a from their father were free of this anomaly. Although there was complete segregation of stenosis with HLA haplotype, the disease had variable expressivity.

Our data suggest that HLA typing may be used as a marker within a family for the presence of certain urinary tract anomalies such as ureteropelvic junction obstruction and childhood reflux.

D P S SENGAR
A RASHID
N M WOLFISH

Department of Medicine,
Ottawa General Hospital Department
of Paediatrics,
Children's Hospital of Eastern Ontario and
University of Ottawa,
Ottawa, Ontario,
Canada

¹ Sengar, D, et al, *XV International Congress of Pediatrics*, New Delhi, 1977.

² Sengar, D, Rashid, A, and Wolfish, N, *Annals of Royal College of Physicians and Surgeons*, 1978, **11**, 87.

³ Sengar, D P S, Rashid, A, and Wolfish, N M, *Clinical Nephrology*, in press.

Diseases of the respiratory system

SIR,—In his article on pneumonia, Dr C M Ogilvie (25 March, p 771) lists the antibiotics which may be of value in the treatment of pneumonia. He notes that acute fulminating pneumonia is usually caused by penicillin-resistant staphylococci or Gram-negative organisms and recommends treatment with flucloxacillin and an aminoglycoside with alternatives for patients allergic to penicillin.

In acute fulminating pneumonia, particularly if it has not responded to antibiotic therapy appropriate for a less severe pneumonia, it is important to cover as wide a range of infecting organisms as possible (one must presume that tuberculosis has been excluded). Apart from *Strep pneumoniae*, the bacteria which are likely to be lethal in pneumonia are *Staph aureus*, *Klebsiella* spp, possibly haemolytic streptococci, and also the organism of legionnaires'

disease. The latter disease may be more common than what was conveniently known as Friedländer's pneumonia, due to infection with *K. edwardsii* or *K. atlantae*, and must be considered in all severe cases of pneumonia. For this reason and for the very wide antibacterial spectrum, I would advocate that gentamicin and erythromycin be regarded as the drug combination of choice in the face of fulminating pneumonia, particularly one which is not responding to treatment with a penicillin or tetracycline. The combination of gentamicin and erythromycin not only has the virtue that it will cover almost the whole range of bacterial infections, excluding tuberculosis, but also includes cover for at least some *Bacteroides* species, which, admittedly, are very rare causes of pneumonia, and will be effective against *Mycoplasma pneumoniae* infection, though this is rarely the cause of life-threatening disease.

The recently suggested alternative¹ of tetracycline and rifampicin might not have the same wide spectrum cover against Gram-negative bacteria.

R J FALLON

Department of Laboratory Medicine
Ruchill Hospital
Glasgow

¹ Meenhorst P L, et al, *Lancet*, 1978, **1**, 711.

The abuse of slides

SIR,—It would be difficult for anyone to dispute the excellent advice given by Miss Mary Evans in her paper "The abuse of slides" (8 April, p 905). It is a pity, therefore, that she does not practise what she preaches. Nelson's famous Trafalgar signal is reputed to have read "England expects that every man will do his duty." Perhaps if Miss Evans had looked up everything she quoted and then, as she advises, checked it, she would have seen that her quotation was incorrect.

F W A TURNBULL

Manchester Chest Clinic,
Manchester

Historical importance of outpatients

SIR,—Dr I S L Loudon (15 April, p 974) has referred very briefly to the benefit that accrued to clinical teaching from the establishment of outpatient departments in voluntary general hospitals.

The admission policy of most of these hospitals before the middle of the 19th century was that no patient should be admitted who was suffering from an incurable disease. Moreover, infants were admitted only infrequently, because of the difficulty of nursing and feeding them unless their mothers were admitted also. The result was that students were deprived of clinical teaching on a wide range of conditions they would encounter later in practice.

It was for this reason that an outpatient department was opened in Belfast General Hospital in 1848. Its first physician was A G Malcolm, who has recorded that he made it a rule to examine a number of patients in the presence of students and sometimes allowed them to make the first examination on their own. He found that before long senior students were able to diagnose with considerable accuracy cases of pleurisy, tuberculosis of the lungs, pneumonia, bronchitis, and diseases of the heart. It is, I believe, a backward

step that outpatient teaching has now ceased to be a part of the curriculum in some British medical schools.

H G CALWELL

Office of Archives,
Royal Victoria Hospital,
Belfast

Aminophylline in respiratory failure

SIR,—In his article on respiratory failure (8 April, p 898) Dr R A L Brewis advocates regimens of administration of intravenous aminophylline, which many would now regard as less than cautious. At various points in his article he advises (a) aminophylline 250 mg over two minutes; (b) aminophylline 500 mg over four hours; and (c) "intermittent intravenous injections of nikethamide and aminophylline . . . can be repeated up to every two hours." Serious toxic side effects (cerebral convulsions and cardiac arrhythmias) are known to accompany high plasma concentrations of the drug, and these concentrations arise following too rapid an injection and too high a maintenance dose of aminophylline. Several reports¹⁻⁵ and a review⁶ have drawn attention to these dangers. To achieve a plasma concentration of theophylline of 10 mg/l (which has been shown to be therapeutic in asthma) an intravenous loading dose of 6 mg/kg aminophylline slowly over 15-30 minutes has been recommended,¹ followed by a maintenance dose not exceeding 0.9 mg/kg/h. The patients with respiratory failure for whom Dr Brewis is advocating aminophylline are likely to be severely hypoxic and with diminished cardiac reserves, and may be especially at risk from toxic blood levels. In the presence of congestive cardiac failure the maintenance infusion rates should be reduced by one-third.¹

While it is appreciated that Dr Brewis was possibly advocating aminophylline as a respiratory stimulant as much as for its bronchodilator effect, safer alternative therapies probably exist for both these desired effects (for example, doxapram and nebulised salbutamol) as outlined in his article; but if aminophylline is used it should be given by slower infusion and in smaller dosages than he recommends.

MARTYN R PARTRIDGE

Department of Medicine,
Middlesex Hospital,
London W1

¹ Pfafsky, K M, and Ogilvie, R I, *New England Journal of Medicine*, 1975, **292**, 1218.

² Merrill, G A, *Journal of the American Medical Association*, 1943, **123**, 1115.

³ Bresnick, H, Woodward, W K, and Sageman, C B, *Journal of the American Medical Association*, 1948, **136**, 397.

⁴ Camarata, S J, et al, *Circulation*, 1971, **44**, 688.

⁵ Nicholson, D P, and Chick, T W, *American Review of Respiratory Diseases*, 1973, **108**, 241.

⁶ *Lancet*, 1973, **2**, 950.

Male altos and counter-tenors

SIR,—Mr Keith Norcross (25 March, p 779) had made comment in *Materia Non Medica* on counter-tenors and found that "occasionally all the counter-tenors we hear sound a little strained," and also that falsetto singing provides "a considerable strain." There is, perhaps, a slight confusion here when one understands the teachings of Russell Oberlin.

Few singers are true "counter-tenors," and most at this range are male altos. The difference is that male altos are singing in falsetto with a break between the falsetto and the normal singing voice, and true counter-tenors do not

have such a break and are singing in the true compass of their voices (or tessitura) as high tenors. It seems that Alfred Deller and James Bowman are singing as male altos and should not be called "counter-tenors" but "male altos."

MILO KEYNES

Oxford

Pensions and the freeze

SIR,—A year or two ago we heard—very justifiably—much of the "freeze" on incomes depriving some consultants of salary increments and immediate payment of distinction awards. These increments and awards would, however, finally be paid: they were, therefore, while unjustifiable and unfair (except to politicians), as well as a breach of contract, a temporary deprivation.

There is, to my mind, an even more serious situation in the pension arrangements, arising from this freezing of higher incomes (apart from the paltry £208 of the current financial year), which is permanent and cumulative. I refer to the pension of a consultant retiring after the last pay award by the Review Body, and would consider the position of a whole-time consultant with my length of service (including my war service) due to retire on 31 May 1978.

Had I retired on 31 May 1976 my pension would have been £4163.95 (£10,689 × 31 60/365 × 1/80). On 1 December 1976, an 8.8% increase brought about by index linking would make this £4530.38, and on 1 December 1977 a similar addition of 17.7% would result in my now having £5332.25. Had I retired on 31 May 1977 my pension would have been £4297.56 (£10,689 × 32 60/365 × 1/80), increasing by 11.4% from 1 December 1977 to £4787.48. Retiring on 31 May 1978 my pension will be £4517.40 (10,097 × 33 60/365 × 1/80). The later retirement takes place after the last pay award and before the next one, the worse off the individual becomes—and each time index linking takes place the greater the disparity: for a given percentage of £5332.25 will be greater than the effect on £4787.48, which will be greater than the increase on £4517.40. This calculation has purposely been made on basic pay and ignoring domiciliary visits and distinction awards—but addition of these only increases the disparity.

It seems to me that longer service means diminished pension in the peculiar world our Socialist masters have forced upon us, and this will be progressive and lifelong. On p 2 of the *Daily Telegraph* of 5 April 1978 it is reported that a Mr Graham Puttergill, chairman of a leading pension agency (Anthony Gills Pension Services) spoke of a government concession designed to prevent people near retirement becoming permanent victims of recent pay restraint—in 1974 the Government ruled that pensions could be based on what salaries would have been but for pay restraint. I believe that the BMA must call urgently for the Review Body to pronounce along these lines, and so rectify this calamitous and unfair situation.

MALCOLM S CAMPBELL

Kingston General Hospital,
Hull

Medicine and apartheid

SIR,—In reply to the letter "Medicine and apartheid" (4 February, p 306), signed by a group of doctors from London SE5, I would