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.

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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.

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* * * 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.

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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'