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in solid myeloma tumours but also for metastatic spread of myeloma. This notion is not in conflict with recent knowledge of the heterogeneity, development, and migratory habits of B-cell subpopulations. There is no doubt about the presence of circulating tumorigenic cells in mice bearing myeloma tumours. However, the exact identity of these cells is not known. The simultaneous detection of malignant change and idiotypic structures in circulating lymphocytes is difficult. Nevertheless, lymphocytoid cells bearing some tumour-cell markers have been demonstrated. The number of lymphocytes whose Slg was altered by tumour r.n.a. is probably much greater than the number of tumorigenic cells estimated in other experiments. Although it is highly likely that Slg-id+ neoplastic stem cells circulate in human myeloma, the bulk of the Slg-id+ lymphocyte population may be partially differentiated and therefore relatively benign. In addition, many circulating tumorigenic cells could be in a non-growth phase or equivalent state, and probably very few of those which are in the cell cycle successfully initiate a focus of tumour because of immunological inhibition and/or ecotactic preference.

Definitive experiments are needed to detect and isolate myeloma CFU-c stem cells from human peripheral blood, and attempts should be made to propagate these in nude mice. Further characterisation of peripheral lymphocytes from myeloma patients must be undertaken because of their possible value in diagnosis and therapy.

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1056 babies were examined, of which 343 (32.5%) contained rotaviruses. Bacteriophages but no other virus particles (astroviruses, caliciviruses, coronaviruses, adenoviruses, small round virus particles) were detected, in contrast with our findings among older children. The number of rotavirus particles detected varied considerably: of 104 consecutive rotavirus-positive infants studied during the winter months, 41% excreted $10^7$–$10^8$ particles/g of faeces, but the stools of 20% of the infants contained more than $10^{10}$/g which is what we usually find in rotavirus-infected children with acute gastroenteritis.

Infection had a seasonal variation, reaching a peak during the winter of 1976–77 and the lowest level in summer, 1976 (fig. 1). The proportion of bottle-fed babies excreting rotaviruses during the winter months was particularly high (76% and 75% for December, 1976, and January, 1977, respectively).

Because patients were transferred from Mary 1 and Mary 3a and b wards in the south wing directly to Haydon and Mary wards in the new north wing, it was not surprising that rotavirus excretion was detected in babies in these wards immediately after they were opened and persisted throughout the study (fig. 2). After the transfer of some patients from Haydon and Mary wards to Bowes ward rotavirus was detected in babies in Bowes. Wrigley and Garland wards accepted only new patients; Garland remained apparently free from virus for a month, but rotavirus was detected within a few days of Wrigley's opening.

Rotavirus infection was significantly less frequent ($\chi^2=127; p<0.01$) among babies who were breast fed (22% positive of 751) than among bottle-fed babies (58% positive of 305). Virus particles in the stools of breast-fed babies were often clumped, which prompted us to examine a consecutive series of infants excreting rotaviruses: 19 (14%) of 135 contained clumps, and 18 of these 19 were from breast-fed babies. In 15 of the 19, the clumps were of complete "smooth" virus particles and the "rough" particles were unclumped. The reverse was true in the remaining 4 specimens. Bottle-fed babies who were rotavirus positive excreted greater amounts of virus (see table).

Analysis of feeding charts from one of the new wards (Haydon) in the north wing showed that rotavirus infection among newborn babies was mild or more often symptomless. Only 15 of 189 (8%) babies in this ward who excreted rotavirus passed frequent loose or offensive stools or vomited and there was no obvious correlation between the amount of virus excreted and the presence of gastrointestinal symptoms. Such symptoms were noted in 5 (2%) of the 254 rotavirus-negative children in the ward.

In Haydon ward rotavirus infection among newborn babies was mild or more often symptomless. Only 15 of 189 (8%) babies in this ward who excreted rotavirus passed frequent loose or offensive stools or vomited and there was no obvious correlation between the amount of virus excreted and the presence of gastrointestinal symptoms. Such symptoms were noted in 5 (2%) of the 254 rotavirus-negative children in the ward.

**Discussion**

In other reports of rotavirus infection,8–10 the proportion of newborns with diarrhoea was variable, but usually greater than in our series. However, the significance of this is difficult to assess since newborn babies, although apparently in good health, pass a variable and often frequent number of stools of varying consistency. The assessment of reports of "diarrhoea", "loose stools" or "frequent stools" is thus difficult particularly if, as in our study, assessment is made retrospectively by examining feeding-charts or case-notes. Although we may have underestimated the frequency of diarrhoeal episodes, it is certain that no infant was sufficiently ill to require treatment.

It is not known why rotavirus infection is mild or symptomless in the newborn human. It is often severe in newborn calves and piglets, particularly if they are colostrum-deprived,11 and unlike humans, these animals do

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**TABLE 1**

| Approx. no. virus particles/g | Breast fed | Bottle fed |
|-----------------------------|------------|------------|
| $10^7$                      | 15         | 5          |
| $10^8$                      | 11         | 12         |
| $10^9$                      | 12         | 12         |
| $10^{10}$                   | 4          | 12         |
| $10^{11}$                   | 2          | 19         |
| **Total**                   | 44         | 60         |

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**Fig. 1**—Monthly percentage of neonates excreting rotavirus, May, 1976–May, 1977.

**Fig. 2**—Occurrence and spread of rotaviruses in newborn nurseries. ---rotavirus detected, --rotavirus not detected. Figures in parentheses show frequency of positive rotavirus findings.

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11. Colostrum-deprived calves are those born to mothers that have been deprived of colostrum, a thick, yellowish fluid that is produced by the mammary glands of cows shortly after giving birth. It is a rich source of antibodies and other substances that provide neonates with passive immunity against infectious diseases. Colostromal deprivation in newborn calves can lead to severe and sometimes fatal infections.
not acquire antibodies transplacentally. Rotavirus antibodies present in the sera of almost all human adults may protect the newborn after transfusional transmission. Although it may appear surprising that serum antibodies rather than secretory antibody protects against infection localised in the small intestine, vaccine-induced circulating antibodies protect the gut against cholera and the respiratory tract against influenza. However, although newborn infants are protected from disease, they are not protected from infection: 33% in our study of excreted virus, occasionally in very large amounts. Symptomless infection with excretion of large quantities of virus also occurs with cytomegalovirus and hepatitis-B virus. Holmes has suggested that the intestinal brush-border enzyme, lactase, acts as the host-cell receptor for rotavirus. In-vitro trypsin treatment enhances the in-vitro infectivity of porcine and bovine rotaviruses. However, there is no evidence that human neonates are deficient in these enzymes.

It is possible that the rotavirus strains circulating in our nurseries were avirulent. Pig rotaviruses may vary in virulence. However, the demonstrations of mild or symptomless infection in newborn infants but frank diarrhoea in older children in the U.K., Australia, and India do not support this hypothesis. Furthermore, in our hospital there is concurrent rotavirus infection among symptomless newborn infants and among older children with gastroenteritis in the ward only one floor above the newborn nurseries. Breast-fed babies excreted rotavirus significantly less frequently and, when infected, generally shed less virus than bottle-fed babies. Breast-fed babies may be protected by maternal secretory antibodies in colostrum and breast milk during the newborn period, or by non-specific antiviral factors distinct from antibody or interferon in breast milk.

In a rural Bangladesh environment heavily contaminated with rotavirus transmissions to hospital with rotavirus-induced diarrheal disease is rare before the age of 6 months. How rotaviruses induce diarrhoea in humans is not clearly understood but the newborn’s gastrointestinal tract may have physiological characteristics not found in older children which allow symptomless infection. Discovery of the mechanism by which young infants are protected might provide an alternative to vaccination.

Although it is uncertain how infection was introduced into the newborn nurseries, transmission of infection by medical or nursing staff from infected older children in the general wards seems likely. Studies in Toronto have shown that rotavirus infection, a common cause of hospital-acquired gastroenteritis among older children, was probably transmitted by medical staff. We found infection occasionally in infants in the newborn special-care nursery. Premature babies also had symptomless infections but in this unit many are in incubators and active measures are taken to prevent cross-infection, so rotavirus spread is likely to be rare.

We are now investigating whether our newborn rotavirus-infected infants are “immunised” as a result of infection. Follow-up studies on 20 babies who excreted rotavirus neonatally have shown that I had rotavirus-induced diarrhoea when aged 14 months, and we are attempting to determine whether the two virus strains are antigenically related. Serotyping by ELISA of groups of 3 rotavirus-positive stool samples from the 1975 and 1976–77 surveys of neonatal nurseries and from current episodes of diarrhoea among older children has been carried out by Dr R. H. Yolken, N.I.H., Bethesda, U.S.A., and has shown that all viruses are type 2. This type appears to be the predominant serotype associated with symptomatic disease in most parts of the world.

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PREVENTION OF IRON LOADING IN TRANSFUSION-DEPENDENT THALASSÆMIA

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Summary Urinary iron excretion after single intramuscular (i.m.) bolus injections or 12 h subcutaneous (s.c.) infusions of desferrioxamine (D.F.) was determined in sixteen homozygous \( \beta \)-thalassaemia patients whose ages ranged from 10 months to 23 years. At all ages the s.c. infusions resulted in greater iron loss than identical i.m. doses. With doses of 0.5–1 g of D.F. as s.c. infusions eight out of nine children aged less than 6 years with a total transfusion iron load of less than 10 g excreted sufficient iron to achieve iron balance. These results suggest that iron loading in transfusion-