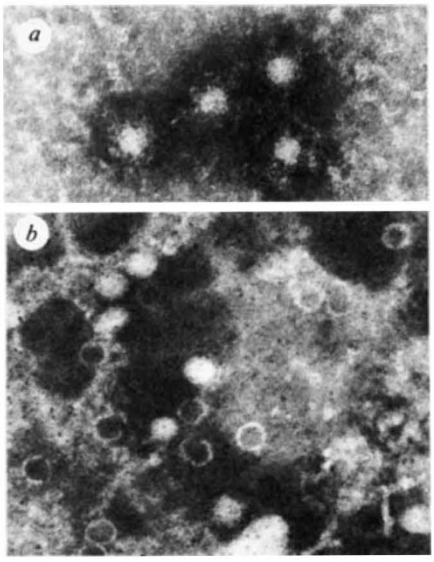

Fig. 1 *a*, 22-nm particles present in marmoset serum. These particles are apparently coated with antibody (× 168,540). *b*, 22–24 nm particles found in marmoset faeces (×168,540).

the GB agent, but antibody to these particles could not be detected in convalescent serum from the patient (GB) himself. Findings from marmoset transmission studies in this laboratory support the suggestion that the small serum particles described by Almeida may be aetiologically associated with hepatitis in marmosets.

Serum from cotton top marmosets (*S.oedipus oedipomidas*) which had been infected with the Berlin agent which is antigenically related to GB contained small aggregates of round virus-like particles approximately 22 nm in diameter (Fig. 1*a*). These particles seemed to be heavily coated with antibody. Since this serum pool is highly infectious for marmosets presumably free virus particles exist, but electron microscopy is not a sufficiently sensitive technique to be able to detect these.

Similar 22–24-nm round virus-like particles were transiently excreted in the marmoset faeces. Particles were not found in specimens collected on the seventh and twelfth day after inoculation, but a stool specimen collected from one animal on the tenth day contained both full and empty particles (Fig. 1*b*). These particles did not occur in aggregates and there did not seem to be any antibody on them. Levels of serum transaminases were first found to be significantly raised in the serum sample collected on the eleventh day.

The occurrence of 20–24-nm particles in serum of marmosets infected with both the GB and Berlin hepatitis agents, and the transient excretion of similar particles in faeces at the time when levels of serum transaminases were elevated, suggests that these small virus-like particles may have a significant role in the development of Berlin and GB hepatitis in marmosets.

Marmosets infected with the GB and Berlin agents did not develop antibody to the parvovirus-like antigen found in human sera by Cossart[3].

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1 Almeida, J. D. *et al. Nature* **261**, 608–609 (1976).
2 Dienstag, J. L., Wagner, J. A., Purcell, R. H., London, W. T. & Lorenz, D. E. *Nature* **264**, 260–261 (1976).
3 Cossart, Y. E., Field, A. M., Cant, B. & Widdows, D. *Lancet* **i**, 72–73 (1975).

DIENSTAG REPLIES,—Appleton has demonstrated 22-nm virus-like particles in serum from *S. oedipus* marmosets infected with the Berlin agent, antigenically related to the GB agent[1]. Like those in the report by Almeida *et al.*[2], the particles shown are heavily coated with antibody. Such a dense halo of antibody molecules and the large interparticle distance are characteristic of extreme antibody excess, rather than antigen excess[3]; therefore, the presence of antibody-free particles, as presumed by Appleton, is highly unlikely. Whether these antibody-coated particles have been sought in non-infectious serum (pre-inoculation, convalescent, and/or normal marmoset serum) is not detailed in Dr Appleton's communication. Even if these antibody-coated particles cannot be detected in normal marmoset serum, as Almeida *et al.*[2] reported, conclusions about the aetiologic role of these particles are unwarranted, for the same reasons we pointed out in our letter[4].

Regarding the detection of 22–24-nm particles in stool of one infected marmoset on day 10 but not day 7 or 12 after inoculation, the obvious questions are (1) whether pre-inoculation and convalescent stools were also examined, and (2) whether these particles can be aggregated by convalescent but not pre-inoculation serum from Berlin agent-infected marmosets. In our laboratory, we have detected morphologically identical 22-nm particles (Fig. 1) in normal marmoset stools, in pre-inoculation, acute illness, and convalescent stools from marmosets infected with hepatitis A virus. These ubiquitous particles bear no serological relationship to any known illness and are easily distinguished from 27-nm hepatitis A antigen particles by immune electron microscopy[5].

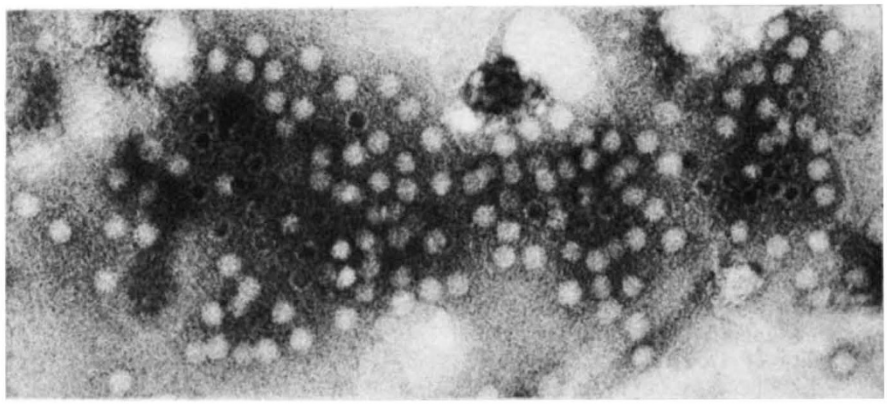

Fig. 1 Electron micrograph of 22-nm particles in the stool of a *S. mystax* marmoset. Such particles appear in normal marmoset stools as well as in stools of marmosets infected with hepatitis A virus and bear no serologic relationship to any known infection. (2% phosphotungstic acid negative stain) (×132,000).

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