on the service from all parts of Britain and many countries overseas, however, it is evident that its existence is well known, at least to the great majority of consultant microbiologists in the United Kingdom.

Since Dr Foley's letter and your leading article regrettably appear to give an entirely false impression of the available facilities I should like to make it clear that the service provided at Guy's remains fully active, is publicised through the proper channels, and is freely available to all who need to use it.

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Melatonin as a marker for pineal tumours

SIR,—In our short report (29 July, p 328) my colleagues and I recorded marked elevations of circulating melatonin levels showing a diurnal variation in a patient with a proved pineal tumour. It is difficult to explain these findings in the context of current ideas outlined in Dr E Tapp's letter (26 August, p 635) but we wholeheartedly agree that "the mechanisms controlling melatonin secretion . . . are . . . incompletely understood"—and merely offer tentative explanations. As far as we could judge and as stated in the report, normal pineal tissue could not be found at necropsy and, although it is possible that some may have been inadvertently included in the tissue enzyme assays, this seems improbable. Perhaps identification of the precise origin of the circulating melatonin will have to await the development of immunofluorescent antibody techniques for melatonin in tissue slices.

It is interesting that Dr Josephine Arendt (p 635) has also found a patient with a pineal tumour and high melatonin levels, though it is disappointing that no clinical details are available. Since the initial report we have published details of an additional five patients,¹ all of whom resembled the first in having mid-day serum melatonin levels at least five times normal. As we have suggested, further study of the effects of other diseases and of radiotherapy is necessary before the full value of our observations can be determined, but at the present time we believe our results to be consistent and promising.

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¹ Barber, S G, *et al*, *Lancet*, 1978, **2**, 372.

Whooping cough

SIR,—I am grateful for Professor G T Stewart's observations (9 September, p 768) on the Keyworth whooping-cough study (19 August, p 577) and I am pleased to answer his and Professor J A Davis's points.

The population studied is remarkably isolated, geographically and socially, for a semirural area. My partners and I can recall only one case of whooping cough in the years 1974-5 and I would suggest that the 1974 cohort was not exposed to whooping cough then. The 1977 cohort, which shows the lowest attack rate, had, I believe, the lowest rate of social interaction with affected individuals. My observation of the spread of the disease in the first two months of the

Nasopharyngeal swabs

Age (years)		0-1	1	2	3	4	5	6	7	8	9	10	11	12	Adult	Total	
<i>Bordetella pertussis</i> isolated	Immunised	0	0	0	0	0	5	2	0	1	1	0	0	0	0	9	23
	Non-immunised	1	5	3	3	0	0	1	0	0	0	0	0	0	1	14	
<i>Bordetella pertussis</i> not isolated	Immunised	0	0	1	4	3	4	2	3	1	1	2	2	1	0	24	34
	Non-immunised	1	3	3	3	0	0	0	0	0	0	0	0	0	0	10	

outbreak demonstrated acquisition of the disease only from recognised cases—between siblings, neighbouring children, relatives, etc—and a closer look at the affected members of the 1977 cohort shows a consistent picture. There were 10 families in the community with a child born during 1977 in which there was also an older child who developed whooping cough. Eight of these infants developed the disease, none of whom had had any pertussis immunisation. A further case was in an only child who was in contact with a child next door with whooping cough. Two of the 10 infants exposed did not develop the disease. One had had two doses of DPT and the other was given prophylactic erythromycin (this being the only instance of antibiotic prophylaxis in the study).

The attack rate in immunised siblings under 5 was 20%, in marked contrast with the non-immunised, in whom it ranged from 50% in those born in 1973 to 88% in those born in 1976. Positive swabs were obtained more frequently from the non-immunised than from the immunised (see table above).

The group of 20 serious cases, as defined by the presence of cyanotic attacks in children under 5 years old, breaks down as follows: seven aged 1 year, eight aged 3 years, and five aged 4 years. Three lived in three-bedroomed terraced council properties and 17 in owner-occupied detached or semidetached houses.

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Arenaviruses in perspective

SIR,—Your leading article (4 March, p 529) brings the arenaviruses into perspective and at the same time raises some interesting epidemiological and diagnostic features of the disease syndrome. As you state, all these viruses cause remarkably similar symptoms. In addition to the arenaviruses and Marburg and Ebola viruses mentioned by you, haemorrhagic fever (HF) syndrome may also be due to leptospirosis, bacterial septicaemia, and viruses like yellow fever, dengue, chikungunya (mosquito-borne), Kyasanur forest disease, Omsk haemorrhagic fever, and CHF-Congo (tick-borne).¹ Because the disease is not characterised in the early phase a major problem is of differential diagnosis, particularly as the areas involved are far from free of other common pathogens.

Considering the overall epidemiological, clinical, and immunopathological features of dengue haemorrhagic fever (DHF) in South-east Asia I proposed a dual aetiology—interaction of virus and parasite infecting a human host around the same time.² It would not be too far-fetched to suggest a similar phenomenon for the serious manifestations resulting from arenaviruses and other viruses causing HF. This would explain the differences noted in clinical features—for example, gastrointestinal haemorrhages in one region, a

renal syndrome in another—as being due to the prevalence of not only a certain type of virus but also a particular type of parasite in a given region. Within a particular region the wide spectrum of clinical manifestations caused by infection with a virus may be dependent upon whether there are simultaneous infections, as also on the type and the stages of these infections.

According to this concept the ultimate outcome would be dependent on the host's immune response to such infections. For the pathogenesis two types of hypersensitive reaction are envisaged: (1) deposition of antigen-antibody complexes (both viral and parasitic) leading to complement activation and local inflammation; and (2) reagin- or IgE-mediated release of histamine from the sensitised cells leading to increased vascular permeability and vascular collapse.

Heavy parasitisation being common in the involved regions the IgE levels would be expected to be high to begin with. However, we could demonstrate significantly higher values for IgE in the sera of DHF patients from Bangkok as compared with controls.³ These were observed from the early phase of the illness, around the third day. It is suggested that an early test for IgE may help in predicting a grave prognosis among those patients who show significantly higher levels of IgE than the levels normally encountered in a particular region.

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¹ WHO Weekly Epidemiological Record, 1976, **51**, 325.

² Pavri, M, *Indian Journal of Medical Research*, 1976, **64**, 713.

³ Pavri, K M, *et al*, *Indian Journal of Medical Research*, 1977, **66**, 537.

Underdiagnosis of childhood asthma

SIR,—How often, in general practice, do we wait for our hospital colleagues to highlight a theme which is really our concern? Dr A N P Speight's revelations (29 July, p 331) about the underdiagnosis of childhood asthma have spurred us to report the current status of this condition in our own practice, which now operates a comprehensive morbidity register. We hope to publish a fuller report at a later date, but in the meanwhile your readers will be interested to know that asthma is the "market leader" in our chronic morbidity list (No 2 is hypertension). In fact 2.4% of the practice list of 7451 patients are registered as asthmatics and 36% of these asthmatics are children in the 0 to 14 age range. Moreover, random sampling suggests that 90% of these children were diagnosed as such before the age of 6 years.

Dr Speight correctly highlights some of the negative factors blocking the diagnosis. We would like to emphasise some positive factors which we believe have led us to make the diagnosis perhaps more often than other