Discussion

It is clear from these cases that hepatitis B virus infection can occur with devastating consequences, even when the perceived risk of perinatal transmission of hepatitis B is low. The baby of an HBeAg positive mother has a 70% chance of becoming a chronic hepatitis B virus carrier,³ while neonates of anti-HBe positive mothers are at risk of developing acute hepatitis.² The incidence of adverse outcome in anti-HBe positive pregnancies is difficult to predict and quantify. The variable outcome cannot be accounted for by genetically determined host response alone since 97% of these babies respond well to inactivated hepatitis B surface antigen (HBsAg) vaccines⁶ and immunity to hepatitis B virus has been achieved in all ethnic groups.³ In cases 1 and 2 the mothers were known hepatitis B virus carriers who had been negative for anti-HBe in previous pregnancies. In the most recent pregnancy both mothers had seroconverted to anti-HBe, and this recently formed antibody may have been less protective to their infants. Differences in the affinity of antibody to hepatitis B core antigen (anti-HBc) have recently been observed in hepatitis B virus carriers with and without evidence of liver disease.⁷ An association of adverse outcome with recent seroconversion to anti-HBe has not previously been reported as maternal serology in previous, similar cases⁵ has usually been unknown (as in case 3).

Prevention of perinatal hepatitis B virus transmission has tended to concentrate on high risk groups,² and even the recent and more comprehensive Department of Health recommendations fail to emphasise the risk to the neonate of any hepatitis B virus carrier mother whatever her marker status and ethnic origin.⁸ Thus it should be noted that the current Department of Health guidelines recommend vaccination of the infant of a carrier mother within 12 hours of birth and at 1 and 6 months.⁸ Hepatitis B immunoglobulin (200 IU) should be given at the time of the first vaccination. Infants of mothers who have cleared the e antigen and become anti-HBe positive are included in the group of neonates

requiring post-exposure vaccination. This new and important addition to the recommendations should be highlighted for those who might not appreciate the change in policy.

A single dose of hepatitis B virus vaccine can now be produced for less than £1.¹ It is plainly cost effective to vaccinate all infants who have been exposed to hepatitis B virus, especially in the context of the costs of intensive medical support and potential cost of litigation when parents learn of the existence of an effective vaccine.⁹

In summary, these three babies developed fulminant hepatitis B from carrier mothers with anti-HBe. One baby died, another developed subacute hepatic necrosis, and the last survived after liver transplantation. We doubt if low infectivity can safely be assumed for any hepatitis B virus carrier mother, and we strongly support the vaccination of all infants of mothers carrying HBsAg.

We thank Mr J C Buckels, Dr Cowen, and Dr Kennedy for allowing us to study their patients.

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Letter from Brasília

Cholera

P D Marsden

"Of all pestilences cholera is perhaps the most awe inspiring: it may run so rapid a course that a man in good health at day break may be dead and buried ere nightfall."

With these sobering words Harold Scott opens the chapter on cholera in his book on the history of tropical medicine.¹ Today we know that for each index case of such severity there are many patients with mild or asymptomatic infections. One authority puts it at a ratio of 1:6 for the classic *Vibrio cholerae* biotype while it may be as high as 1:50 for the El Tor biotype. Man is the only known reservoir of *V cholerae*.

Cholera is known to have been endemic for two centuries in the Ganges delta of West Bengal and Bangladesh. Apart from numerous epidemics in the Indian subcontinent there have been seven pandemics in the past 160 years. The seventh began in Indonesia in 1961. It extended northward to Korea (1963) and westward through Asia to include the whole of Africa, parts of mediterranean Europe, and the gulf coast of the United States in the 1970s. The El Tor biotype of

the cholera vibrio is responsible for the current pandemic. It is hardier and more viable in water than the classic biotype.

As readers of the journal will know, El Tor has now invaded the Pacific coast of Peru and is spreading inland. In Brasília doctors are apprehensive about its possible arrival. Raw seafood is no longer popular in Japanese restaurants. Our hospital director has stock-piled electrolytes for treatment and the director of my own unit has organised a course of evening lectures on cholera. A colleague responsible for the control programme in Peru has recently visited us, and the Brazilian Ministry of Health is collaborating with Peru.

Although details are still not completely clear, it seems that in January 1990 a grain boat from the East that had unloaded at a coastal Peru port was forced to return to port by an outbreak of cholera. The captain inquired whether cholera vaccine was available (it wasn't and is of limited value) and after staying a few days to allow the crew to recuperate the ship resailed. No crew member died, but subsequent serological

REASSELECT

Cholera in Brazil may soon reach the epidemic proportions already stretching resources in Peru

testing showed high cholera antibody titres in some crew members.

Cases began to appear in coastal Peru and the disease rapidly spread to Lima. From there infected carriers must have carried it by plane and road to most parts of Peru and to Colombia and Ecuador. The Peruvian estimate at the time of writing was 200 000 notified cases. It was thought that the Andes would provide a natural barrier, although the practice of chewing coca leaves in a lime base (common among Andean Indians) could lower stomach acidity and facilitate cholera infection with fewer organisms than is usually necessary. In addition, indigenous South Americans are invariably blood group O and cholera has a strong positive association with this group.

Anyway these speculations are academic since Peru has calculated that there are 20 000 cholera victims in the Peruvian Amazon and 12 000 in Iquitos, the capital of Amazonian Peru. Twenty patients have been confirmed in Tabatinga on the Brazilian border and there is talk of a patient in Mato Grosso. There are so many rumours in the air that by the time this letter is published the situation will have changed. Little seems to prevent the inevitable march of cholera down the Amazon basin. That mighty river carries one fifth of all the fresh water of the world. Other rivers might be inimical to cholera, such as the river Negro. Here the water is dark brown because of the amount of decomposed vegetable matter it has passed through and is acid (pH 5-6), which does not suit *V. cholerae*.

The great fear in Brasília is that cholera will get into the poorer satellite cities where even basic sanitation is often inadequate. If it does there will be no more of these letters as we will have patients under as well as on our beds. The conditions are worse still in some of the

conurbations surrounding the larger cities, where rural Brazilians continue to come in search of work. The Baixada Fluminense, a suburb a few kilometres north of Rio de Janeiro, shelters two and a half million people, most of whom have no proper sanitation.

What then can be done? Apart from stockpiling drugs public health efforts must be directed at urging people to act to make drinking water safe, if necessary by boiling. The difficulty is achieving adequate coverage and community response: Amazonian housewives are used to opening the boat window and throwing everything in the river. One possibility is that as soon as a case of cholera is notified in the community, measures to ensure pure drinking water are enforced and family members of the index patient treated with tetracycline to eliminate the transient carrier state. To date I have not been able to trace reliable references either to a new French vaccine (which the minister of health is alleged to have purchased) or to the Japanese rapid latex test of stool for cholera using a DNA probe. Already our Peruvian colleague estimates that his country has lost a billion dollars through a fall in exports, severely affected tourist trade, and the cost of admitting cholera patients to hospital (each patient costs over \$100 a day).

So it is a case of history repeating itself, although the doctors seem better prepared for this seventh pandemic. To return to Scott he doesn't give John Snow the importance he deserves in his section on cholera. Snow produced elegant epidemiological evidence that fatal cholera in Soho in the 1830s was related to water from the Broad Street pump—the contaminated water source. Some idea of the shocking sanitation in London for hundreds of years can be obtained from studying Hogarth's prints. Outside the John Snow pub in Soho there is a steel mark on the wall indicating where the pump was sited. John Snow removed the handle with dramatic results. So dramatic that the Centers for Disease Control, Atlanta, Georgia, has a John Snow Society to recognise this pioneer of epidemiology—the real epidemiology is always done by foot slogging not just by sitting in a chair speculating. I have entertained many American friends in the John Snow. Recently in London I passed by to have a drink there but saw that most of the memorabilia in the pub had disappeared. However, my alma mater the London School of Hygiene of Tropical Medicine has begun a campaign to restore the memory of John Snow in this famous London public house.

Since this letter was written cholera has steadily spread down the Amazon river to reach the mouth at Belém. Here hundreds of cases have been confirmed, and in Manaus the official total of confirmed cases is 1500. Air travel has resulted in dissemination to at least six Brazilian cities.

1 Scott HH. *A History of Tropical Medicine*. Vol 2. London: Edward Arnold, 1939.

ANY QUESTIONS

What side effects have been reliably associated with the flavour enhancer monosodium glutamate?

At one time it was believed that consumption of large amounts of monosodium glutamate in soy sauces caused the "Chinese restaurant syndrome," but experimental verification of these reactions has proved difficult and unconvincing. The large amounts of monosodium glutamate that were assumed to be responsible were much greater than those consumed when monosodium glutamate is used as a flavour enhancer in food.

Adverse effects of high concentrations in newborn animals—for example, neurological changes—are also

considered not to be relevant to the use of monosodium glutamate in food,² although as a precaution the enhancer is not permitted in foods prepared specially for infants and young children. As with many reports of adverse reactions to foods direct and unequivocal linking of responses to the food constituent is difficult. Some people claim to have severe reactions, but it is possible that rapid absorption of free amino acids may be the precipitating cause. Published reports suggest that adverse side effects are uncommon. — D A T SOUTHGATE, *head of nutrition, diet, and health department, Institute of Food Research, Norwich*

1 Reif-Lehrer L. A questionnaire study of the prevalence of Chinese restaurant syndrome. *Fed Proc* 1977;36:1617-23.

2 Ministry of Agriculture, Fisheries, and Food. Food Additives and Contaminants Committee. *Report on the review of flavour modifiers*. London: HMSO, 1978. (Food advisory committee report 28.)