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The Several Viruses of Post-transfusion Hepatitis

The introduction of routine screening of donor blood for the hepatitis B surface antigen (HB_sAg) raised hopes for the eventual control of post-transfusion hepatitis. However, though reductions in frequency of up to 75% are possible,[1] cases of post-transfusion hepatitis still occur. In some instances HB_sAg may be found in the serum even when the transfused blood had been passed as free of antigen by the most sensitive techniques currently available—passive haemagglutination[2] and radioimmunoassay.[3] In most such cases, however, tests for HB_sAg are negative, and the absence of an antibody response either to the surface or to the core antigen means that the hepatitis B virus is extremely unlikely to have been responsible.[4 5] This has highlighted the question of what the cause of the hepatitis is in these circumstances.

One obvious candidate is the hepatitis A virus; but, while the incubation period in some cases of post-transfusion hepatitis is short,[2] in many cases it has been longer than the six-week limit generally accepted[2-1] for infection with the A virus. Recently, Feinstone *et al.*[5] have examined directly the role of this virus in 22 patients with HB_sAg-negative post-transfusion hepatitis using immune electron microscopy to detect antibodies to the faecal particles currently thought to represent the A virus. They found that sera from 13 of the cases were positive for such antibodies before developing acute hepatitis and that the titre did not subsequently increase, while sera in the other nine patients were negative throughout. Furthermore, the incubation period in more than half the patients was greater than six weeks.[5] These findings, together with the known predilection of the A virus for transmission by the faecal-oral route, make it clear that it cannot be a common cause of HB_sAg-negative post-transfusion hepatitis.

Other possibilities that must be considered are the herpes viruses, which include herpes simplex, the Epstein-Barr virus, and cytomegalovirus. Herpes simplex hepatitis usually occurs in newborn or young children, and has been reviewed recently in these columns.[6] The Epstein-Barr virus may be carried in latent form in the circulating leucocytes of healthy persons, and may occasionally be transmitted by blood transfusion.[7] However, 80-90% of individuals will have acquired antibody to this virus by adulthood, and it can therefore be only a very infrequent cause of post-transfusion hepatitis. In contrast, cytomegalovirus does appear to account for a small number of cases,[7] and since only about half the general population possess antibodies seroconversion is much easier to observe than with the Epstein-Barr virus. There are, however, a number of problems. Firstly, seroconversion does not necessarily prove infection, since it is also observed in equal or greater frequency after transfusion both in patients who subsequently develop typical HB_sAg-positive hepatitis due to the B virus and in those who never contract acute hepatitis.[4 8] Secondly, it is still uncertain in the cases that show seroconversion whether the disease is transmitted de novo or reflects merely a reactivation of pre-existing infection—though the observation that the frequency of seroconversion increases with the number of units transfused and that the antibody is often of IgM class favours a primary infection.[8] Finally, the incubation period of cytomegalovirus is about 2-4 weeks, much shorter than that observed in most cases of hepatitis after transfusion. Thus the exact role of cytomegalovirus in post-transfusion hepatitis remains uncertain.[4 5 8] These considerations have led Prince *et al.* to suggest that HB_sAg-negative cases with a long incubation period may be due to another as yet unidentified hepatitis virus—so-called type C.[4]

The management of post-transfusion hepatitis, once the diagnosis has been made from other causes of postoperative jaundice such as halothane hypersensitivity, benign intrahepatic cholestasis, and mechanical obstruction of the intrahepatic biliary tree, is less of a problem. Simple supportive therapy with adequate fluid and glucose intake and standard precautions against infection are usually all that are necessary. However, a close watch should be kept for confusion and drowsiness, the warning signs of encephalopathy, which are indicative of a fulminant course with high mortality and requiring more intensive therapy. Occasionally, abnormalities of biochemical liver function may persist for some months after apparent clinical recovery. This is particularly apt to occur in patients with persistent HB_s antigenaemia, and further investigation by liver biopsy is essential to identify patients in whom progression to chronic hepatitis is occurring and who require immunosuppressive therapy.

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High Altitude Retinal Haemorrhage

Exposure to high altitudes carries a number of health hazards, the most recently described of which is retinal haemorrhage.

The condition was first studied in 1969 by Frayser *et al.*[1] Among 25 persons examined in a laboratory at 17 500 ft (5330 m) 9 developed retinal haemorrhage. Of these, 8 had no symptoms; the ninth had headache and a scotoma, with papilloedema, very tortuous retinal vessels, and a haemorrhage at the macula. Schumacher and Petajan[2] gave details of findings in 39 subjects who spent up to 24 days at or above 14 200 ft (4330 m) on Mt. McKinley. Fourteen of the party had retinal haemorrhage, the condition being commoner in those who were prone to vascular headache, who developed altitude headache, and who ascended rapidly above 14 000 ft (4200 m). Of note was the finding of retinal haemorrhages in six of nine climbers who made "quick dashes" to the summit from 10 000 ft (3000 m). Among 1925 people with acute mountain sickness Singh *et al.*[3] found engorgement of the retinal veins in 17, papilloedema in 4, and vitreous haemorrhage in 3. In 34

whose cerebral symptoms necessitated lumbar puncture the cerebrospinal fluid pressure was from 60 to 210 mm of water higher than the level after recovery. One patient, thought to have a cerebral tumour, proved on biopsy to have cerebral oedema.

A rapid increase in intracranial pressure may explain these ocular changes. Muller and Deck[4] concluded from necropsy studies that effusion of cerebrospinal fluid into the optic nerve sheath in cases of sudden intracranial hypertension results in compression of the central retinal vein and dilatation of the nerve sheath, swelling of which reduces the venous drainage of the eye by compressing the retinochoroidal anastomosis, producing retinal venous hypertension and haemorrhage. Cerebral oedema raises intracranial pressure and may be due to a number of mechanisms. Increased ventilation causes hypocarbia,[5] and this by decreasing cerebral blood flow may cause cerebral oedema. Sutton[6] found increased serum cortisol and postulated other hormone changes. Oliguria is an early symptom of mountain sickness and often a precursor of pulmonary or cerebral oedema. Both frusemide and spironolactone have been advocated as prophylactics of mountain sickness, while diuresis at altitude is a sign of likely freedom from this complaint. However it is produced, cerebral oedema can cause increased pressure in the retinal veins; the hypoxic retinal capillaries may then be unable to withstand the increased back pressure, and the typical splinter and flame shaped haemorrhages appear.

Acute mountain sickness, pulmonary oedema, cerebral oedema, and retinal haemorrhage are different facets of failure to acclimatize at high altitude. Rapid ascent over 8000 ft (2500 m) is hazardous. Travellers in mountains must guard against two temptations especially—going too high too quickly by aeroplane and car and the inclination to "press on regardless."

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Risk of Cot Deaths

The unexpected death of a child at home remains the major cause of death in children between the ages of 1 week and 2 years. Much of the recent work is recorded in the proceedings of a meeting held in Toronto in 1974[1] that was sponsored by the Canadian and British Foundations for the Study of Infant Deaths.[2]

No matter how complete the necropsy, about a quarter of cot deaths remain unexplained, though the same is true of many children of this age dying in hospital. Much of the basic work on unexpected death, such as Wealthall's study of apnoea,[3] applies at least as much to hospital as to home deaths.

The concept that the deaths are due to a cessation of respiration during a period of prolonged apnoea,[4] nasal obstruction,[5] or laryngeal spasm[6] has recently been extended by Tonkin[7] in Auckland. She has shown that some infants are vulnerable at the oropharyngeal level and that airway obstruction can occur during the muscular relaxation of R.E.M. (rapid eye movement) sleep. Meanwhile the chase after specific infections continues. Gardner and his Newcastle group[8] back the respiratory syncytial virus as chief culprit, while Nelson and colleagues[9] in Chicago prefer influenza A virus. There is no shortage of new hypotheses such as that the deaths are due to preleukaemia[10] or hypoimmunity.[11]

The supposition that all unexpected, unexplained infant deaths have a single cause is now yielding to the idea that they have a variety of causes. The examination of vitreous humour at necropsy[12–13] and the discovery that some infants presenting as cot deaths had severe hypernatraemia and uraemia[14] have concentrated awareness on the dangers of feeding babies overconcentrated milk and milk with increased salts,[15] and this has been a stimulus to encourage breast feeding.

Meanwhile, in some centres such as Philadelphia,[16] where there has been a longstanding interest in cot deaths, there is an indication that the numbers are diminishing, and though the figures are not yet published the same probably holds for at least one centre in Britain. In northern Europe the cot death rate seems to parallel the general infant mortality rate. But it is odd that a country such as Holland, which has a similar genetic, climatic, and infection background to Britain, has a cot death rate of about one-third,[17] and the same seems to be true of Sweden.[18]

The fact that at necropsy most babies found unexpectedly dead show the presence of some treatable disease[19] may indicate that the different death rates between Holland and Britain could lie in the home care services for children. Simply by improving these could we halve our total and unexpected infant death rate? The study by McWeeny and Emery[20] of the backgrounds of some cot deaths due to recognizable disease disclosed the existence of incompetence (social, parental, and medical) that was hinted at by a survey in Glasgow in 1970.[21] Meanwhile, as Brimblecombe points out,[22] it is possible to recognize families at risk of cot deaths[23] and to try to improve their home care.

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