CONGENITAL CHICKENPOX

By I. M. LIBRACH, M.B., B.Ch., D.P.H., D.C.H.

Medical Officer in Charge, Ilford Isolation Hospital

Transplacental immunity has been considered sufficient to protect the newborn infant at birth and for some considerable time afterwards. Shuman (1939) thought that active immunity of the foetus *in utero* can occur even in late pregnancy. If, however, a mother develops an infectious disease just before her child is due to be born, then such maternal antibody as is formed may be insufficient to protect her infant *in utero*. In rare cases, the mother may be suffering from a/or hypogammaglobulinaemia and this may mean inability to form antibody at all or only in insufficient amount. From the point of view of the infecting organism two other factors must be reckoned with: (1) its ability to become blood borne, and (2) its ability to penetrate the placental barrier. The size of the organism would at first sight seem to determine the latter process, but if we take the size of a staphylococcus, $1,000\mu$ as a standard, then parasites as large as *P. malariae* or as small as polio virus 30μ are known to be capable of placental penetration. Is the process purely mechanical? This is easily understandable in relation to a small virus, but much less so when it comes to a large bacillus or protozoon. The foetal and maternal blood currents do not intermingle, being separated by the delicate walls of the foetal placental villi, which project into the intervillous space or marginal sinus, containing maternal blood from the uterine vessels. These vessels of the villi are surrounded by a layer of mesoderm covered with the two strata of the trophoblast. This is replaced after the fifth month by a single layer of flattened cells. It is easy to see how an organism can reach the intervillous space via the uterine arteries as a result of maternal bacteraemia or viraemia; it is more difficult to understand how it can penetrate the single layer of flattened cells in a foetal villus and so gain access to the foetal circulation. The same speculation might apply to maternal antibody whether from an organism or a blood factor such as Rh. Theoretically, it would seem that they must go in one of two ways: (1) between the cells of the villus, or (2) through them. All membranes have lipid characteristics allowing

passive diffusion of lipid soluble substances. Insoluble substances permeate with difficulty unless facilitated by some transport mechanism such as an enzyme, e.g. cholera R.D.E. (receptor-destroying enzyme—Burnet, 1953). This concept makes the transcellular theory more feasible. In any event, the placenta itself must be infected at some stage in the transfer. Schaeffer *et al.* (1954) demonstrated Type 1 polio virus in the placenta and aborted foetus of a mother with poliomyelitis. Once through the villus it is in the foetal circulation and its further progress is again easy to understand if it is capable of blood-borne carriage.

Chickenpox is very common. The virus is very small, 230μ . It seems surprising that few congenital infections have been reported—something of the order of a dozen or so instances up to 1958. This may be because most mothers must have had the disease in their infancy. Statistics are hard to come by. From 1935 to 1938 2,200 cases of chickenpox were admitted to the Willard Parker Hospital, New York, but only one was aged two days. Even in the second week of life the disease is rare. Hubbard reported a case—said to be the first—in a one-day-old infant in 1878, and in 1913 Pridham reported another in an infant four hours old, but the mother did not have chickenpox at the time of delivery, although a 14-year-old boy in the same house had the disease. Most other authorities describe cases in infants 8-14 days old. In each case the disease was present in the mother eight days before to one day after birth. A further possible example is reported.

Case Record

S. D., aged 26 years, was admitted in labour on August 31, 1958, having had a vesicular rash for 10 days. Two other children, aged 2 and 5 years, also had the disease at home. On examination (T. 97, P. 80, R. 20), a pleomorphic rash, maximal on the trunk and scanty on the limbs, was present—macules, papules, pustules, many scabbed. B.P. was 106/80. Abdomen, full-term pregnancy. She was delivered at 9.35 p.m. on the same day of a normal healthy male child

weighing 7 lb. 1½ oz. showing no lesions of any kind. The placenta and membranes were macroscopically normal. The former were not saved. Four days later (September 3, 1958) a few papules were noted on the legs and trunk of the infant. None further occurred. The progress of both mother and child was uneventful, both being discharged well on September 9, 1958, i.e. 10 days after admission.

Discussion

In the newborn, several features may lengthen the incubation period due to the fact that exposure may occur at one of three periods: (1) At the time of the original *exposure* of the mother to the disease; (2) at the time of the *onset* of the disease in the mother; and (3) from *contact* with the mother or perhaps another case at the time of delivery or soon after. Endometrial varicella has never been reported, but if present it means that transplacental infection need not occur.

Waddington (1956) describes twins who showed no evidence of the disease at birth, but the second developed it two days later and the first eight days later! Both had been given 0.42 ml. and 0.32 ml. of gamma globulin respectively.

Baron (1935) concluded that if a woman contracts chickenpox in late pregnancy or during labour she is not able to transmit immune bodies, the infant is therefore susceptible and should be isolated. Ivenskaya (1920) thought that premature and ill infants are less likely to develop chickenpox than normal infants, but gave no sound reasons for this strange paradox (see Oppenheimer's case below). Most authors seem to agree that pustulation in babies does not occur. This was the case in the present instance. Differential diagnosis from papular urticaria is an obvious difficulty, which can only be resolved satisfactorily if easy methods of isolation and cultivation of the virus are discovered. Visceral lesions, however, may appear before the cutaneous ones. The rash in infants is similar to that found in children and adults, first appearing on the torso and then spreading centrifugally. The vesicles are said to be less tense and less resistant to rupture, possibly because of the delicate nature of the neonatal skin. Chickenpox mainly affects epithelial structures causing intranuclear inclusions and necrosis. The first histological description was that of a skin lesion by P. G. Unna in 1894. Intranuclear inclusions were first described 12 years later (1906) by Tuzzer. Although Schleussy (1927) and Johnson (1940) described the post-mortem appearances in the infant, the fullest account is probably that of Oppenheimer in 1944. She reported the case of a premature infant of 4 lb. who died in 11 days after contracting the disease from the

mother. At autopsy characteristic necrosis and intranuclear inclusion bodies were seen in the skin, oesophagus, stomach and intestines, liver, pancreas, spleen, thymus, adrenals, kidneys (renal tubules), lungs (bronchioles, pulmonary alveoli), rib and vertebral marrow. No C.N.S. involvement was present. She concluded that dissemination was probably due to a blood-borne virus. Johnson's case showed similar lesions in skin, oesophagus, pancreas, but also the bladder, ureters, renal pelves, vascular and lymphatic endothelium. He thought that the earliest lesion in chickenpox is not associated with cellular infiltration and that this occurs after vascular infarction and necrosis. He agreed that the virus propagates by the blood stream, localizes in tissues, predominantly epithelial in nature, multiplies at their expense and has a special affinity for the nuclear substance of the epithelial cells of the skin. Recently widespread and fatal disseminated chickenpox has been reported in patients being treated with cortisone for some unrelated condition. Whether cortisone inhibits antibody formation or facilitates intracellular viral multiplication can only be surmised. The problem is not made any easier by the descriptions of adrenal involvement in this disease.

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ADDENDUM

Since this paper was written, Steen and Pedersen