

Hypoxic brain damage in fetus and newborn. Morphological characters. Pathogenesis. Prevention.

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In the newborn, cerebral lesions of hypoxic-ischemic type present essentially under two aspects: Necrosis of white matter or leukomalacia and neuronal necrosis. In their pure form these two types of cerebral injury differ not only in their morphological characters but also in many other aspects.

I - LEUKOMALACIAS usually occur in infants born prematurely who develop, after birth, repeated apneas, episodes of hypotension associated or not with respiratory distress. In more mature infants, leukomalacias are found in I.U.G.R. and hypoglycemia and meningo-encephalitis.

In the acute phase the lesion presents in the form of coagulation necrosis and, at this stage, the axons are already damaged; later follow microglial, astrocytic and macrophagic reaction (2). The lesions are located in the deep periventricular white matter corresponding to the border zones between ventriculofugal and ventriculopetal arterial systems (8), in non-myelinated regions which have a high water content and are very fragile. With intensive neonatal care, mortality and morbidity rates have considerably decreased over the past 15 years. In Port-Royal Unit in Paris the mortality rate has fallen from 30% to 15% in spite of the increasing number of low-birth-weight infants. Meanwhile, infants who die have survived longer than years ago = about 10% survived more than 10 days (1957-1967), 15% (1967-1974) and 25% (1975-1980). Concomitantly the frequency of leukomalacia in premature infants has increased: 20% of autopsies in the first period, 22% in the second and 34% in the third.

The clinical picture is non-specific in the acute period. CT-Scan and ultrasonography are unhelpful. The presumptive diagnosis is based on the poor development of the child and the non-maturation of cerebral electrical activity. The course is rapidly fatal if leukomalacia is associated with massive intraventricular hemorrhage or with meningo-encephalitis. If the child survives or if leukomalacia occurs in the isolated form, the lesions progress either to sclerosis of the centrum semi ovale with dilatation of the ventricles, or to multicystic leukoencephalomalacia (7). Clinically, the outcome will be some form of spastic cerebral palsy, varying from monoplegia to quadriplegia. In this later stage, CT-Scan and U.S. provide a mean of evaluating the extent of the anatomical lesions (5).

With the general availability of intensive neonatal care the pure forms of spastic monoplegia and diplegia have certainly become less common. But prolonged survival of very sick babies leads, too often, to severe brain damage. In our autopsy material sclerosis of the C.S.O. and multicystic encephalopathy related to the overall

incidence of leukomalacia, increased from 2.2% (1956-1966) to 7.2% (1967-1973) and to 14.4% lately (1974-1979). Prevention consists in preventing prematurity and rapidly correcting states of hypoxia, hypotension and acidosis.

One particular form of leukomalacia, well known to pathologists, supervenes ante-natally and is now being diagnosed at birth, by CT-Scan. The pathogenesis is obscure.

II - NEURONAL NECROSIS is observed primarily in infants born at term following a normal pregnancy but after difficult labour delivery (6). The morphological characters of the cellular lesions are the same as in the adult but images of karyorrhexis are frequent in the subiculum, the gray matter of the pons and the internal granular layer of the cerebellar lamellae. Cortical necrosis may be laminar or patchy, often accentuated in the depth of the sulci. The basal ganglia and the entire brain stem including the inferior colliculi are also very vulnerable. Cerebral oedema is nearly always associated with severe necrosis.

The arterial network of adult type, the advanced maturation of cells and their neuropile, the onset of activity of oxydative enzymes (3) explain, in part, the vulnerability of neurones in the fullterm infant.

From the first day of life the clinical picture is typical: The child is in coma or in status epilepticus (clinically manifest and/or revealed by E.E.G.). CT-Scan and U.S. may show oedema with collapse of ventricles and sulci. The course is usually fatal within a few days due to superimposed cardiac failure or respiratory problems. In case of survival the neurological sequelae are generally very severe: Choreoathetosis, quadriplegia, brain atrophy and mental retardation.

The incidence of these accidents has diminished remarkably in the course of the last 15 years i.e. = 1.6 per 1000 fullterm deliveries in 1962 to 0.7 in 1980 in two maternities Hospital in Paris (1). But the number of sequelae is, to some extent, determined by the individual policy of each intensive care unit. Prevention is essentially a matter of obstetrics. In conclusion, over the past 15 years, there has been a changing panorama of hypoxic-ischemic brain damage in neonates, both in terms of morphological criteria and in relative frequency. Neuronal necrosis in fullterm is tending to disappear, while, in premature infants, maintained on mechanical ventilation for a long period of time, the occurrence of severe brain destruction is apparently increasing (4).

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