

Autism, a variant of kernicterus?

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Stereotyped motor mannerisms in children with autism may reflect impairment of the basal ganglia [1-3]. Damage of the basal ganglia, associated with jaundice in the newborn period, leads to kernicterus, a severe affliction of motor development [4]. Hemolytic disease of the newborn, caused by maternal antibodies that cross the placenta, is the best known cause of kernicterus [5]. However, development of RhoGAM to prevent maternal antibody formation to Rh-factor has not eradicated the problem [6]. Hansen (2000) pointed to an increase in kernicterus since 1994, which he even referred to as a new "epidemic" [7, p1156].

Jaundice caused by elevated bilirubin levels is common in newborns. Why damage occurs in some but not all infants remains an important question [8]. Zimmerman and Yannet (1933) summarized a large number of case reports and concluded that injury by anoxia or sepsis often precedes bilirubin staining of subcortical nuclei, and stated, "This differs in no way from the well known fact that any intravital dye will localize in zones of injury and will leave unstained tissues which are not damaged," [9, p757].

The blood-brain barrier normally prevents bilirubin from getting into the brain anywhere, but if breached, according to Levine et al. (1982), "Other toxic substances may also enter the brain, but they could go unnoticed if they are colorless." [10, p258]. Thus substances other than bilirubin should be looked for that could result in kernicterus-like injury of subcortical nuclei.

Kernicterus has been reported in infants with very low levels of bilirubin [11], and kernicterus was found in newborn infants following treatment with sulfisoxazole antibiotic, and with synthetic vitamin K [12-14]. Factors that might trigger breakdown of the blood-brain barrier should be looked for as the real cause of kernicterus.

The basal ganglia are among a rank order of subcortical structures that comprise the most metabolically active sites in the brain [15, 16]. Factors that disrupt aerobic metabolism during development also impair these centers of high metabolic rate [17, 18]. The same subcortical nuclei were also damaged in experiments with monkeys on asphyxia at birth, in the first of which Ranck and Windle (1959) noted, "The human neuropathologic entity most closely resembling the effects of asphyxia neonatorum in the monkey is kernicterus" [19, p153].

Lucey et al. (1964) injected monkeys with bilirubin "every 6 hours from 1 to 3 hours after birth for as long as 4 days" [20, p43], and neither kernicterus nor any neurological signs were seen. Monkeys subjected to asphyxia before being made hyperbilirubinemic, developed severe neurological deficits and were found to have kernicterus. Lou et al. (1977, 1979) also demonstrated entry of Evans blue dye into the brains of fetal sheep, but only after breakdown of the blood-brain barrier by asphyxia [21, 22].

Evidence of anoxic birth in children who later develop autism is abundant [23-44]. Could the repetitive and stereotyped mannerisms observed in children with autism represent a variant form of kernicterus? The role of perinatal compromise, with consequent anoxia, plus exposure to toxic substances in the neonatal period, merits serious attention as predisposing factors for development of autism.

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