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ABSTRACTS

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Special Sessions

NEUROLOGY

Effect of Xylocaine on infant rat brain mitochondria. Arnold L. Smith. *Children's Hosp. Med. Ctr., Boston, Mass.* (Intr. by David H. Smith).

Local anesthetics are widely used in obstetric practice to facilitate painless delivery. Their usage has been associated with neonatal respiratory depression and, in the case of fetal injection, with neonatal seizures. Because of these observations the effect of Xylocaine on infant rat brain mitochondrial enzymes was investigated.

The neurochemical development of 5- to 10-day-old infant rats approximates that of the human newborn. Xylocaine was administered intraperitoneally to infant rats at this age in doses calculated to produce blood levels comparable to those in human newborns with toxic signs and symptoms. Two hours after injection there was a 65% decrease in brain D(−)-beta-hydroxybutyrate dehydrogenase (HBDH) activity and a 40% decrease in succinic dehydrogenase (SDH) activity. Brain cytochrome oxidase (CyO) activity was not significantly decreased. Temporal examination of these enzymes after injection suggested that HBDH was the first enzyme inhibited. These observations are in contrast to the lack of inhibition of liver HBDH, SDH, and CyO. The inhibition of oxidative enzymes in infant rat brain mitochondria persists up to 5 hours after injection. This enzyme inhibition is also demonstrable in measurements of respiration of intact brain mitochondria. Oxygen consumption of normal infant rat brain mitochondria is best supported by D(−)-beta-hydroxybutyrate (BOH), but succinate was also effective. BOH dependent respiration of infant rat brain mitochondria was inhibited by Xylocain in vivo and in vitro. The data suggest that further studies of Xylocaine usage and effects in the perinatal period are indicated.

Multiple sulfatase deficiencies, the enzymatic basis of a new disorder. Jerome V. Murphy, Marcia Williams, and Hugo W. Moser (Intr. by R. Michaels). *The Mass. General Hosp., Boston, Mass.*

Since 1961 seven patients have been reported with both generalized neuronal storage and metachromatic degeneration of white matter. These patients have the onset of their degenerative disorder during their second year of life with loss of motor skills. Deafness and seizures ensue. Associated findings include icthyosis, minor skeletal anomalies, and hepatosplenomegaly. Alder-Reilly bodies are seen in the white blood cells and the urine contains excessive amounts of cerebroside sulfate and glycosaminoglycans.

Frozen post mortem tissues from two unrelated patients with this disorder were available for enzymatic studies. Aryl sulfatases A and C were absent in all tissues studied. Aryl sulfatase B was deficient in liver, but relatively absent in brain and kidney. Steroid, cholesterol and estrone sulfatase activities were absent in liver. Mixing experiments failed to reveal a factor inhibiting these sulfatases. Enzymatic study of parental white blood cells failed to identify the carrier state. Several accumulated substrates could be specifically associated with an enzymatic deficiency.

Explanations for the absence of these lysosomal and microsomal enzymes are theoretical, but other disorders of multiple enzyme deficiencies have been reported.

Brain glucose metabolism in undernourished rats. H. Peter Chase, Vijay Kumar, Denis O. Rodgerson, and Geoffrey P. Cheung. *Univ. of Colo. Med. Ctr., Denver, Colo.*

Glucose is the primary substrate used by the infant brain either as a source of energy or for lipid and amino acid synthesis. The in vivo conversion of glucose U-^{14}C, 2.5 μCi/60 g of body weight injected intraperitoneally, to lipids and amino acids was measured in the brains and livers of poorly nourished and control infant rat pups at ages 6, 10, 17, and 24 days, and in adult animals fed a control or 8% protein diet for 3 months. Brain lipid formation was decreased 50 to 75% from ages 6 to 17 days, and brain amino acid formation was reduced 60% in 10-day-old rat pups. Reduced in vivo hepatic conversion of glucose U-^{14}C to lipids and amino acids was found only at ages 6 and 10 days. In vitro production of $^{14}CO_2$ from glucose U-^{14}C incubated with brain slices was not altered in 10- or 20-day-old malnourished animals (1.58 ± .26 *vs.* 1.14 ± .07). Brain ATP, phosphocreatine, and glycogen levels were not reduced at either age 10 or 20 days. Mitochondrial glutamate dehydrogenase activity catalyzes the formation of amino acids from α ketoglutarate in Krebs cycle, and was reduced 21 to 30% in the brains of malnourished animals, and 49 to 81% in the livers. Supernatant NADP-isocitric dehydrogenase activity, believed to produce TPNH for lipid synthesis, was not reduced in the brains, but was reduced in the livers of malnourished infant rats. Pyruvate kinase, one of the rate limiting enzymes of glycolysis, showed reduced activity in liver and muscle of malnourished animals, but not in brain.