

Liver Physiology and Function in Newborn Infant

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COMMENTARY

The newborn liver is a proven model for the study of liver storage of copper and iron. We analyzed zinc concentration and distribution in the livers of newborns and infants using a systematic tissue-sampling technique. We studied 14 newborns of 26-41 weeks of gestation. One stillborn and three infants (52-90 days old). At autopsy, a longitudinal liver slice extending from the right to the left lobe was subdivided into 10 samples that were analyzed for zinc concentration by atomic absorption spectroscopy. The mean zinc concentration in the newborn liver was 639 micrograms/g of dry tissue (dt). A striking interindividual variability in zinc liver stores was observed; the hepatic concentration of the metal ranged from 300 to 1,400 micrograms/g dt. We found a correlation between zinc liver content and gestational age. In newborns of 27-32 WG, the hepatic zinc concentration was significantly higher than in newborns of 34-41 WG. Zinc stores decreased in the postnatal period; in the infant group, the mean liver zinc concentration was 148 micrograms/g dt.

The analysis of zinc concentration in 10 blocks from each liver revealed a regular distribution of the metal, without significant differences between liver lobes. Our data show that the newborn liver can be considered an interesting model for the study of zinc storage, which appears to correlate inversely with gestational age. From a practical point of view, the observed regular distribution of zinc implies that, at least in this model, zinc content determined in a small liver sample is representative of zinc content in the whole liver. The pattern of copper distribution in human newborn liver was investigated by histochemical methods (rhodamine, orcein and rubeanic acid) and by atomic absorption spectroscopy.

A significant correlation (p less than 0.005) was found between the degree of histochemical positivity and the copper concentration found by atomic absorption spectroscopy. In the majority of the 30 livers examined (first group), the copper concentration was much higher than that of normal adult liver, although exhibiting striking individual differences. No correlation between the copper content and sex, body weight or gestational age was found. From a second group of five livers, longitudinal tissue slices 0.5 cm thick were partitioned into regular blocks of about 0.5 gm, which were individually analyzed by atomic absorption spectroscopy. Copper appeared unevenly distributed within each liver, with marked differences even between adjacent blocks. However, a consistent

tendency of copper to accumulate in the left lobe more than in the right one was evident. Five additional blocks, one for each liver, were further partitioned into 10 small specimens of a final size (0.05 gm), comparable to that of a needle biopsy.

Even at this sampling level, consisting of tissue fragments taken from a small tissue area, the copper concentration appeared quite irregularly distributed. These findings may be considered for two different aspects:

- (a) The biological implications of the pattern of copper accumulation in different lobar and lobular liver compartments
- (b) The statistical inference, for diagnostic purposes, of the mean liver copper content from measurements of single percutaneous biopsy specimens.

The liver develops from progenitor cells into a well-differentiated organ in which bile secretion can be observed by 12 weeks' gestation. Full maturity takes up to two years after birth to be achieved, and involves the normal expression of signalling pathways such as that responsible for the JAG1 genes (aberrations occur in Alagille's syndrome), amino acid transport and insulin growth factors. At birth, hepatocytes are already specialized and have two surfaces: the sinusoidal side receives and absorbs a mixture of oxygenated blood and nutrients from the portal vein; the other surface delivers bile and other products of conjugation and metabolism (including drugs) to the canalicular network which joins up to the bile ductless. There is a rapid induction of functions such as transamination, glutamyl transferase, and synthesis of coagulation factors, bile production and transport as soon as the umbilical supply is interrupted. Anatomical specialization can be observed across the hepatic acinus which has three distinct zones.

Zone 1 borders the portal tracts (also known as periportal hepatocytes) and is noted for hepatocyte regeneration, bile duct proliferation and gluconeogenesis. A zone 3 border the central vein and is associated with detoxification (e.g. paracetamol), aerobic metabolism, glycolysis and hydrolysis and zone 2 is an area of mixed function between the two zones. Preterm infants are at special risk of hepatic decompensation because their immaturity results in a delay in achieving normal detoxifying and synthetic function. Hypoxia and sepsis are also frequent and serious causes of liver dysfunction in neonates. Stem cell research has produced many answers to the questions about liver development and

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regeneration, and genetic studies including studies of susceptibility genes may yield further insights.

The possibility that fatty liver (increasingly recognized as non-alcoholic steatohepatitis or NASH) may have roots in the neonatal period is a concept which may have important long-term implications. D-penicillamine was introduced to treat neonatal hyperbilirubinaemia in 1973 and to prevent retinopathy of prematurity in 1980. In this study we investigated the renal and liver functions of neonates treated with DPA and the in vitro

effect of the drug on superoxide anion generation and beta-glucuronidase release as well as on phagocytic and intracellular killing activation on human peripheral blood granulocytes. Our data concerning the renal and liver functions before and after 3 to 4 days DPA treatment reveal no pathological change during short-term administration in the neonatal period. Furthermore, none of the examined DPA concentrations influenced the phagocytic or killing activity of neutrophils.