Developmental Expression Of Elements Of Hepatic Cholesterol Metabolism In The Rat

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Abstract

The expression of several key enzymes and receptors of rat hepatic cholesterol metabolism was studied during development. Among major findings were: acyl coenzyme A:cholesterol acyltransferase, the cholesteryl ester hydrolases, cholesterol-7 alpha-hydroxylase and the alpha 2-macroglobulin receptor (LRP) were very low in fetal livers, but all were induced shortly before birth, suggesting that these elements are important for extrauterine life. Although the other elements continued to increase, by day 6 of postnatal life, cholesterol-7 alpha-hydroxylase had reached undetectable levels. It reappeared by day 12 of suckling, placing it in the group of late-appearing activities necessary for the fully mature hepatic phenotype. Changes in acyl coenzyme A:cholesterol acyltransferase activity appeared due predominantly to changes in amount of active protein. The cholesteryl ester hydrolase (CEH) activities all showed different developmental patterns, suggesting that each was a unique activity. The bile salt-dependent CEH activity was much higher in the suckling period than in the adult where it was almost undetectable, suggesting that this CEH may have its major importance in the suckling period of development. Low density lipoprotein receptors exhibited a pattern very different from that of the alpha 2-macroglobulin receptors and did not show consistent correlation with any other elements. At some developmental time points, the relationships amongst the elements differed significantly from the adult pattern. These studies provide for the first time an integrated picture of developmental expression of key elements of hepatic cholesterol metabolism and set the stage for further studies on their modes of regulation.

Keywords

acyl coenzyme A:cholesterol acyltransferase; cholesteryl ester hydrolase; cholesterol-7alpha-hydroxylase; 3-hydroxy-3-methylglutaryl coenzyme A reductase; low density lipoprotein receptor; alpha2-macroglobulin receptor (LRP)