## **Development of the Human Intrahepatic Biliary System**

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## **Abstract**

In the development of the human biliary system, the extrahepatic bile ducts (EHBD) develop from the embryonic hepatic diverticulum, while the intrahepatic bile ducts (IHBD) originate within the liver from the ductal plate. The ductal plate is a flat muralium of primitive biliary epithelium that develops in the mesenchyme along the branches of the portal vein, by a process which requires a delicate balance between cell proliferation and death. The ductal plate is thus remodelled into the adult system of tubular anastomosing bile ducts and this process is called ductal plate remodelling.

Computerised three-dimensional reconstruction of the developing ductal plate has shown that the ductal plate remodelling process starts at the porta hepatis around 11 weeks of gestation and progresses towards the periphery of the liver. The extrahepatic biliary system is in direct luminal continuity with the developing intrahepatic biliary system throughout gestation and does not have a "solid stage" as suggested previously.

The ductal plate remodelling is controlled by many biochemical and molecular factors, some of which have been identified and studied. It has been suggested that abnormalities in the development of the IHBD could lead to a spectrum of diseases called ductal plate malformation. Biliary atresia is one of the conditions in this spectrum. Currently, we are studying the IHBD in biliary atresia in comparison to the normal developing IHBD, the results of which are presented in this review. Both morphologically and biochemically the IHBD in biliary atresia resembles the primitive foetal ductal plate suggesting a disruption in ductal plate remodelling.

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