this technique is therefore cholesterol → 22-hydroxycholesterol → 20,22-dihydroxycholesterol → pregnenolone.

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**Cholesterol Transformation to Biliary Acids in vivo in the Rat**

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The cholesterol transformation into biliary acids is one of the major processes of cholesterol disappearance in an organism. Its chemical pathways have recently been extensively studied (Mosbach, 1977). As cholesterol 7α-hydroxylase is the rate-limiting...

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enzyme of biliary acid synthesis (Shefer et al., 1970), in many studies an attempt has been made to define more clearly the factors which modulate its activity (for example, see Mosbach, 1972; Mitropoulos et al., 1972, 1973; Boyd et al., 1973; Shefer et al., 1973; Danielson, 1972, 1973; Danielson & Johansson, 1974; Takeuchi et al., 1974; Gielen et al., 1969, 1975; Mayer & Voges, 1972). From this physiological point of view the question arises as to the characteristics in vivo of the process considered. To approach this problem with precision, the definition of a dynamic system must be recalled and subsequently the cholesterol dynamic system must be described. (a) The simplest dynamic system is an open unregulated compartment with one inflow (order) and one outflow. Its dynamics are governed by a determinative process characterized by a parameter. Thus the outflow depends on the state of the system. The system is defined by two equations: a balance (or state) equation and a structure equation. (b) The cholesterol system is described as a mammillary system of which the central compartment is the plasma (Chevallier, 1977). It is assumed that the cholesterol in the plasma is a homogeneous compartment. When the system is in a steady state, there are three main net outflows from plasma to the liver, the digestive tract and the glands. The cholesterol of each of these organs constitutes a compartment. Its determinative process results in an outflow of biliary acids, or of cholesterol in the faeces, or else of sterols in the urine. In the liver it is finally assumed that the non-esterified cholesterol is the precursor of biliary acids and it constitutes a homogeneous compartment.

As the flows of cholesterol in rats in various dynamic equilibria are known (under 60 or more different experimental conditions) (Chevallier, 1977), it can be deduced firstly that the transformation of cholesterol into biliary acids is an unregulated process (‘regulation’ is used with its original physiological meaning, that is, to maintain constant a variable). Secondly, it can be shown that the three main outflows are governed by determinative processes of the same nature. The parameter of each of them is a function of the flow of synthesized cholesterol in the plasma. Hence the plasma cholesterol system is not linear (Chevallier, 1977; Chevallier et al., 1976). Moreover, the transfers of the plasma lipoproteins into the organs corresponds very probably to the determinative processes of plasma cholesterol system. These transfers are simultaneously orders for the organs. The liver, for instance, transforms automatically the net flow of cholesterol which enters into it. In other words, physiologically the process governing the net transfer of cholesterol from the plasma to the liver is the limiting step of the cholesterol transformation into biliary acids.

The cholesterol system has also been examined when it was in transitory states created by a temporary loss or gain of cholesterol. When cholesterol is eliminated in the milk of lactating females, the biliary formation is proportionally decreased. The case of a taurocholate chronic ingestion is particularly noteworthy because in such a condition, esterified cholesterol increases in the liver (Lutton et al., 1973). Where the ingestion is unique, we observed an initial increase followed by a decrease of the esterified cholesterol (Mathé & Chevallier, 1977). Considering the kinetics of these variations and those of biliary-acid production that accompany them, three arguments are supplied in favour of an initial action of exogenous taurocholate on the enzyme of cholesterol esterification or of esterified cholesterol hydrolysis. A fourth argument is based on the laws of the dynamics of esterified cholesterol in the liver (Chevallier, 1977). The decrease of biliary-acid production, which follows taurocholate ingestion, is a normal response of the system to the loss of cholesterol that constitutes its esterification.

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