Bile Acids in Newborn and Adult Humans

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Using quantitative paper chromatography¹ taurocholic (TC), taurochenodeoxycholic + taurodeoxycholic (TCD+TD), glycocholic (GC), glycochenodeoxycholic (GCD) and glycodeoxycholic (GD) acids have been determined in human bile and intestinal contents. In 34 analyses of the bile acids in the duodenal contents of 21 newborn babies (1—7 days old) the total bile acid concentration expressed as free bile acids varied between 84 and 1182 mg/100 ml. Only conjugated bile acids could be found. With the method used free bile acids should have been detected when present as 2—3 % of the total amount of bile acids. The ratio of glycine conjugated acids to taurine conjugated acids (G/T) rose with age. Thus in children between one and four days old a mean value of 0.45 was found whereas the ratio 0.93 was obtained in children 5—7 days of age. No TD or GD could be found but an unidentified spot moving slightly faster than GD was in some cases observed on the paper chromatograms. There was approximately 2.5 times more cholic acid than chenodeoxycholic acid. When the children had reached an age of about eight months the bile acids were again analyzed in some subjects. The G/T ratio had risen to about 2 and deoxycholic acid could still not be found.

The proportions between the various bile acids in the duodenal contents of 19 medical students has been determined. No free bile acids could be detected. The mean G/T ratio was 3.1 and the proportions between cholic, chenodeoxycholic and deoxycholic acids were 1.2:1:0.6. When several analyses were made on the same subject at different times variations were noted in the G/T ratio as well as in the proportions between the different bile acids. Some factors influencing the G/T ratio will be discussed.

Cholic acid was by far dominating in human fistula bile. It was noteworthy that deoxycholic acid was usually absent. This resembles the bile acid composition of the newborn babies. In the normal adult, however, the relative amount of cholic acid is diminished and deoxycholic acid is now present. This suggested that deoxycholic acid is formed by

bacterial action on cholic acid during the entero-hepatic circulation. At the same time Lindstedt in his work on the turnover of cholic acid in man observed that radioactive cholic acid gave rise to a labelled dihydroxycholanic acid which was identified as deoxycholic acid².

1. Sjövall, J. *Acta Chem. Scand.* **10** (1956) 1051.
2. Lindstedt, S. *Arkiv Kemi* **11** (1957) 145.

The Influence of Whole Body X-Irradiation of the Biosynthesis of Cholesterol in Liver

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Earlier work¹ has shown disturbances in hepatic synthesis of cholesterol in rats after 2400 r whole body X-irradiation. We have preferred to study the effects of 400 r whole-body irradiation, considering that this would throw more light on the biochemical changes in "radiation sickness" and induce negligible histological changes. Three series of experiments are reported here.

In the first series we studied the *in vivo* incorporation of 2-¹⁴C acetate injected intraperitoneally, in liver cholesterol in mice, and the disturbances caused by whole body X-irradiation. We found a decrease in synthesis immediately after X-irradiation, probably a response to the X-irradiation, and a subsequent rise, probably a response to the liver cholesterol concentration.

In the next series we studied *in vitro* synthesis by incubation of rat liver slices with 2-¹⁴C acetate after whole body X-irradiation. Here we found an immediate rise in the rate of synthesis as a response to the X-irradiation. Subsequent changes in the rate of synthesis could be attributed to the effect of the liver cholesterol concentration. The changes in carbon dioxide metabolism were studied simultaneously.

The third series was carried out *in vivo* with mice. We studied the effects of synkavit (naphthohydroquinone) injected intraperitoneally alone and followed by irradiation. The amount of synkavit we used, 2 mg, gave an effect, similar to but greater than that produ-

ced by radiation alone. The combined treatment gave an immediate depression in synthesis rate though smaller than that produced by radiation or synkavit alone; this was followed by an increase above normal, which was not produced by either treatment alone.

1. *Progress in Radiobiology, Proc. of Fourth International Conference of Radiobiology, Cambridge (1955), p. 71.*

The Formation of Bile Acids from Cholesterol in the Rabbit

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Cholesterol-4-¹⁴C has been administered intravenously into rabbits with a bile fistula. More than 90 % of the activity in the bile acids was present as cholic acid, which normally constitutes only about 10 % of the total bile acids in the rabbit. The origin of deoxycholic acid — the main bile acid in intact animals — will be discussed.

Thiamine in Baker's Yeast

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During the anaerobic growth of the common industrial yeasts, thiamine added to the me-

dium is taken up by the cells and mainly esterified to cocarboxylase. During the aerobic cultivation of brewer's yeast and of *Torulopsis utilis*, however, the whole amount of thiamine lost from the medium has not been traced in the yeast cells by the thiochrome method¹.

A balance experiment on the uptake of thiamine by baker's yeast was performed on an industrial scale. The cultivation was performed in the usual way for the production of commercial baker's yeast under strongly aerobic conditions. Thiamine was added to two out of three batches. After cultivation, the thiamine content of the yeast cells was determined by the thiochrome method. Table 1 shows the result of the experiment.

The loss may depend on a transformation of thiamine into some compound which cannot be determined by the thiochrome method. It is known that as pyrophosphate ester thiamine has different functions under aerobic and under anaerobic conditions but it is assumed that it acts aerobic in some other form too. Myrbäck² suggested that thiamine or cocarboxylase may be transformed into a disulfide form.

In order to study the question baker's yeast was cultivated under aerobic conditions on a laboratory scale with the addition of ³⁵S-labelled thiamine. After the cultivation, thiamine compounds were extracted from the yeast with TCA at pH 1—2. The extract was examined by paper chromatography³. No thiamine disulfide compounds could be found in this extract. The only labelled compounds found in this extract were cocarboxylase and free thiamine.

1. Fink, H. and Just, F. *Biochem. Z.* **311** (1942) 61.
2. Myrbäck, K. and Vallin, I. *Svensk Kem. Tidskr.* **57** (1945) 72.
3. Paladini, A. C. and Leloir, L. F. *Biochem. J.* **51** (1952) 426.

Table 1. Balance experiment on the uptake of thiamine by baker's yeast during cultivation under strongly aerobic conditions.

	Thiamine in yeast, µg/g	Total amount of thiamine in yeast, g	Loss of thiamine, %
No thiamine added	2.8	23.8	
15 g thiamine added	3.5	30.3	43.3
30 g thiamine added	3.7	29.2	54.3