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Composition of the Bladder Bile of Young White Mice Reared on a Diet Causing Formation of Cholesterol Gallstones in Young Hamsters *)

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With 2 tables

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A fat-free diet with glucose as the carbohydrate component causes formation of cholesterol gallstones in young hamsters (1, 2). The bladder bile of young hamsters reared on such a diet has been analyzed with respect to cholesterol, lipid phosphorus, bile acids and pH. The results were compared with those obtained with bladder bile from hamsters reared on diets affording complete and partial protection against gallstone formation in this species (2).

White mice reared on the „fat-free glucose diet" do not develop gallstones. It was, therefore, of interest to examine the composition of bladder bile of mice reared on this diet.

Experimental

The mice used in the present experiment were young from our stock colony of white mice, which was kept on the same diet and water: milk, as our hamster colony (3). Until the beginning of the feeding experiment the young mice had access to the stock diet and water: milk.

Three groups of mice (about equal numbers of males and females in each group) were used. They were housed in metal cages with wire screen bottom and given the „fat-free glucose diet" (1, 2) for 48 to 56 days. In group 8 the experimental feeding began when the mice were 31-33 days old, in group 9 when the animals were 20—22 days old, and in group 15 when they were 22 to 24 days of age. Food and tap water were available *ad libitum*. Other experimental details were as in the corresponding experiment with hamsters (2), except that the chromatographic separation of bile acids was limited to the taurine conjugates.

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Table 1.
Length of experimental feeding period, initial and final weights

Group no. 8					Group no. 9					Group no. 15				
Mouse no.	Sex	Experim. feeding period, days	Weight, g initial	Weight, g final	Mouse no.	Sex	Experim. feeding period, days	Weight, g initial	Weight, g final	Mouse no.	Sex	Experim. feeding period, days	Weight, g initial	Weight, g final
1	m	56	37	43	6	m	31	16	30	72	m	48	16	28
3	m	56	36	42	14	m	34	16	25	85	m	48	13	30
6	m	56	38	53	15	m	50	16	27	92	m	48	13	25
7	m	56	33	42	24	m	30	12	23	96	m	48	13	27
8	m	56	34	41	53	m	49	12	33	70	f	48	15	25
11	m	56	29	41	1	f	34	16	28	82	f	48	15	23
12	m	56	31	39	2	f	30	16	27	83	f	48	14	22
16	m	56	27	33	28	f	49	12	26	104	f	48	11	19
17	m	56	27	33	45	f	50	9	19	109	f	48	9	19
55	m	56	28	38	56	f	31	15	30	110	f	48	12	25
2	f	56	31	35										
4*	f	56	34	40										
9	f	56	30	34										
10	f	56	30	33										
13	f	56	27	29										
14	f	56	32	36										
15	f	56	30	30										
18	f	56	24	22										
19	f	56	27	27										
20	f	56	29	28										

*) The bile of this animal contained a small body of birefringent material.

Table 2.
Analytical data of the bladder bile (millimolarities)

Group no.	Mice nos.	Days on diet	pH	Cholesterol	Lipid phosphorus	Total bile acids	Tauro-cholic acid	Taurine conjugated dihydroxy-cholanic acids	Ratio dihydroxy: trihydroxy cholanic acids	Ratio total bile acids: cholesterol	Ratio lipid phosphorus: cholesterol
8	1+ 3+ 6+ 7+ 8	56	7.8	3.1	37.4	83.0	63.2	19.8	0.31	26.6	12.0
8	16+ 17+ 55	56	—	2.6	—	53.0	43.4	9.6	0.21	20.1	—
8	2+ 4+ 9+ 10+ 13+ 20+	56	7.4	4.3	16.9	111.0	101.8	9.2	0.09	25.9	3.9
8	14+ 15+ 18+ 19	56	—	4.9	41.0	125.1	111.5	13.6	0.18	25.5	8.4
15	70+ 104+ 109	48	—	3.3	27.6	71.3	66.0	5.3	0.08	21.9	8.5
9 15	15+ 45+ 72+ 85+ 92+ 96+ 110	50 48	—	5.3	42.8	107.6	88.4	19.2	0.21	20.2	8.1
Average				3.9	33.1	91.8	79.1	12.8	0.18	23.4	8.2

Results and discussion

Table 1 shows the length of the feeding period and the initial and final weights of the individual animals in the three groups.

The analyses of the bladder bile are presented in table 2.

Generally, the mice grew better and more uniformly on the experimental diet than hamsters and had no tendency to diarrhea. None of them had gallstones, but in one individual the bile contained a small body of birefringent material.

The bile acids of mice (and rats) are almost entirely present as taurine conjugates (4). In a few cases we have chromatographed the bile of mice for glycine conjugated bile acids, but with the amounts of bile available none could be found.

The major bile acids in mice are cholic and chenodeoxycholic acids, since in mice (as in rats) deoxycholic acid formed by the action of intestinal bacteria on cholic acid is hydroxylated to cholic acid after absorption (4). The amount of chenodeoxycholic acid is relatively small in proportion to the amount of cholic acid. Other bile acids (3α, 6β, 7α-hydroxycholanic acid and 3α, 6β, 7β-hydroxycholanic acid) occur in trace amounts only (4) and were, therefore, not taken into account in the present study. The system used for the paper chromatographic separation of the taurine conjugated bile acids gives one spot for taurocholic acid and another for taurochenodeoxycholic plus taurodeoxycholic if the latter were present. It cannot separate these two dihydroxycholanic acids from each other. However, in the present case this is of no importance.

The results listed in table 2 are to be compared with the data for hamsters reared on the „fat-free glucose diet" under corresponding conditions. These data are contained in tables 4 and 5 in our previous communication (2).

The comparison shows that:

None of the mice have gallstones, whereas almost all the hamsters have cholesterol gallstones.

The cholesterol content of the bladder bile is about the same for mice as for hamsters.

The values for lipid phosphorus and the ratio lipid phosphorus: cholesterol are higher for mice than for hamsters.

Whereas the mice have only taurine conjugated bile acids, the hamsters have several times as much glycine conjugated as taurine conjugated bile acids.

The values for total bile acids and the ratio total bile acids: cholesterol are, generally, somewhat higher for mice than for hamsters.

In the cases where pH was determined, the figures were about the same for mice and for hamsters.

When the data are compared with those for hamsters on the „curative diet" which affords complete protection against gallstone formation (tables 6 and 7 in our previous communication (2)), it is seen that the ratio lipid phosphorus: cholesterol for the mice on the „fat-free glucose diet" reaches about the same level as that for the hamsters on the „curative diet", whereas the ratio total bile acids: cholesterol is somewhat lower for the mice on the „fat-free glucose diet" than for the hamsters on the „curative diet".

Even though other factors in addition to those examined may play a role in gallstone formation it is clear that the somewhat higher ratio total bile acids:

cholesterol and, especially, the much higher ratio lipid phosphorus: cholesterol found for the mice are in agreement with the difference between the two species with respect to formation of cholesterol gallstones. Further, the higher values for dihydroxy:trihydroxy cholanic acids found in hamster bile are not sufficient to prevent formation of cholesterol gallstones in this species.

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Summary

Young white mice did not develop gallstones when they were reared on a diet which causes cholesterol gallstones in young hamsters, viz. a fat-free diet with glucose as the carbohydrate component.

The cholesterol content and pH of the bladder bile of the mice was about the same as previously found for hamsters, but the ratio total bile acids : cholesterol was somewhat higher and the ratio lipid phosphorus : cholesterol much higher in the mice than in the hamsters. The ratio dihydroxy:trihydroxy cholanic acids was much lower in the mice.

Zusammenfassung

Junge weiße Mäuse entwickelten keine Gallensteine, wenn sie mit einer Nahrung gefüttert wurden, welche in jungen Hamstern Cholesteringallenstein-Bildung hervorruft. Die verwendete Nahrung war fettfrei und hatte Glucose als Kohlenhydrat-Komponente.

Die Konzentration von Cholesterin und auch das pH der Blasengalle waren ungefähr gleich in Mäusen und Hamstern. Das Verhältnis Gesamt-Gallensäuren: Cholesterin war etwas höher und das Verhältnis Lipid-Phosphor: Cholesterin viel höher bei Mäusen als bei Hamstern. Das Verhältnis Dihydroxycholansäure: Trihydroxycholansäure war viel niedriger bei den Mäusen.

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