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Alimentary Production of Gallstones in Hamsters

11. Relation between diet and composition of the bladder bile 1

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With 13 tables and 2 figures

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In an early period of the hamster's life, cholesterol gallstones can be produced with great regularity by raising the animals on a fat-free diet containing a large amount of an easily absorbable carbohydrate, such as glucose (1, 2).

A small amount of a highly unsaturated fat, e. g., 2% of cod liver oil, has been found to abolish the tendency to formation of cholesterol gallstones, even when the carbohydrate was to a large extent supplied in the form of glucose (62.3% glucose + 12.0% rice starch) (1).

Under the same conditions a small amount of fat of low unsaturation, e. g., 2% of lard, was found to counteract formation of cholesterol gallstones to some extent (1).

When in a diet with 2% of lard the carbohydrate component consisted entirely of rice starch or lactose, formation of cholesterol gallstones was completely suppressed (3).

Later experience has shown that rice starch and lactose almost eliminate the development of cholesterol gallstones even when no fat is incorporated into the diet.

Amorphous pigmented gallstones (containing high amounts of calcium, phosphorus and bile acids (4), can also be produced in hamsters by dietary means (5), and, as later experience has shown, throughout the animal's entire life time. This type of gallstones is favored by dietary fat (1), especially by fat of a high degree of unsaturation (1); sucrose seems to favor it more than glucose (3, and general experience in our laboratory). Further, the diet used for our stock colony of hamsters (1) tends to produce amorphous pigmented gallstones, when it is given over a long period of time.

Dissolution of cholesterol gallstones already formed has been accomplished by means of a diet containing 10% lard, 20% casein, 36% dried brewer's yeast, 28.3% ground polished rice, and 5% of a salt mixture supplemented with Cu, plus the usual supply of vitamins (6).

This diet is referred to in the following as "the curative diet"[1]). Recent experience has shown that, given prophylactically, this diet prevents formation of gallstones of any type.

The present communication describes some initial stages in the elucidation of the mechanisms mediating the dietary causation and inhibition of gallstone formation in young hamsters, with special attention to cholesterol stones.

[1]) This designation does not necessarily infer that a diet of simpler composition cannot be used in a curative experiment.

To this end we have examined the composition of the bladder bile with respect to cholesterol, bile acids, lipid soluble phosphorus and pH in hamsters reared on "fat-free" diets with glucose, rice starch and lactose as the carbohydrate component, and in hamsters reared on the above-mentioned "curative diet".

The influence of dietary fats on the composition of the bladder bile as well as the influence of diet on constituents of the bile other than those mentioned above will be dealt with in later communications.

Experimental

The animals were golden hamsters from our stock colony. The experimental diets are listed in table 1[1]). Before the animals received these diets they had access to the stock diet (1) and to water and milk (1:1), in one case also to small pieces of lettuce and carrots. (Two groups transferred to the glucose diet at the age of 107–111 days had water instead of water:milk during the last 77–80 days before the transfer.)

Table 1. Composition of the experimental diets

	Glucose diet %	"Curative" diet %	Rice starch diet %	Lactose diet %
Glucose	74.3			
Rice starch			74.3	
Lactose				74.3
Casein, "Vitamin Test"[1])	20.0		20.0	20.0
Casein, crude[2])		20.0		
Salt mixture, U.S.P. XIII, No. 2	5.0		5.0	5.0
Salt mixture[3])		5.0		
Vitamin mixture[4])	0.5	0.5	0.5	0.5
Choline chloride	0.2	0.2	0.2	0.2
Lard		10.0		
Ground polished white rice		28.3		
Dry yeast, Fleischmann Type 2019		36.0		

[1]) Genatosan Ltd., Loughborough, England.

[2]) "Dairinex", from A/S Dansk Mejeri Industri & Export Kompagni, Stege, Denmark.

[3]) U.S.P. XIII, No. 2, supplement with 0.131% $CuSO_4 \cdot 5\,H_2O$ per 100 g.

[4]) Biotin, 0.050 g; folic acid, 0.050 g; ascorbic acid, 5.000 g; thiamine hydrochloride, 5.000 g; pyridoxine hydrochloride, 5.000 g; calcium pantothenate, 5.000 g; nicotinic acid, 8.000 g; inositol, 15.000 g; p-aminobenzoic acid, 35.000 g; vitamin K ("Synkavit", Roche), 1.000 g; dl-α-tocopheryl acetate ("Ephynal", Roche), 5.000 g; and sugar up to 500 g.

Vitamins A and D_3 were given as an aqueous solution, containing 2000 I.U. vitamin A and 200 I.U. vitamin D_3 per ml. 0.5 ml of this solution was given twice a week to each animal, corresponding to 59 I.U. vitamin A and 5.8 I.U. vitamin D_3 per animal per day (cf. reference 1).

The age of the animals at the beginning of the experimental feeding is mentioned in the tables for each group.

[1]) The diets and tap water were available ad libitum.

The last 1 to 2 hours before the animals were sacrificed (with chloroform) they had no accecs to food and water but could run in a cylindrical cage, rotable on a horizontal spindle.

Immediately after sacrifice, laparotomy was performed and bile was collected by suction through a glass tube drawn out to a capillary and inserted into the gallbladder. In most cases the total bile from two or more animals had to be pooled in order to get enough for analysis. The collected bile was weighed in the tube, blown out, and aliquots were measured out for analysis with Carlsberg pipettes (constriction pipettes). In those cases where gallstones were present their type was identified as usual by observation under dissecting and polarizing microscopes.

For determination of cholesterol and phospholipids 5 microliters of bile were heated with 300 microliters of a mixture of absolute ethanol and acetone (1:1) in a small (4.5 ml) centrifuge tube with polyethylene stopper in a water bath at 70–80 °C for 5 minutes. After violent shaking in a shaking apparatus [1]) and centrifugation the supernatant was transferred into a 2-ml measuring flask by a CARLSBERG pipette. The residue was reextracted twice with 100 microliters of ethanol-acetone and filled up to 2 ml in the measuring flask.

For determination of *phospholipids,* 400 microliters of the content of the measuring flask (corresponding to 1 microliter of bile) were brought into a Pyrex test tube, evaporated in a stream of nitrogen and incinerated with 50 microliters of perchloric acid (70–72%) over a microburner for about 5 minutes until the brown color has disappeared. Thereafter the phosphorus content was determined by means of ammonium molybdate and aminonaphthol-sulfonate according to the method of W. M. SPERRY (7), using one tenth of the quantity of reagent indicated in the original method. After 10 minutes at room temperature the absorbance at 330 millimicrons was read (in semimicrocuvettes) in the BECKMAN spectrophotometer against the reagents plus water. A solution of sodium phosphate in water containing 0.204 micrograms of P in 300 microliters served as standard.

For determination of *cholesterol,* the rest of the content of the measuring flask (1.6 ml) corresponding to 4 microliters of bile was transferred quantitatively into a centrifuge tube and evaporated at 70 °C in a stream of nitrogen. 500 microliters of chloroform were added and the mixture shaken violently in the shaking apparatus. After centrifugation the supernatant was transferred into a conical centrifuge tube, and the residue reextracted 3 times with 200 microliters of chloroform. The combined extracts were evaporated under nitrogen, taken up in chloroform and chromatographed (ascending) on paper as described earlier (8). Cholesterol was finally determined in the eluate by a modification of ZLATKIS' reaction (8).

Glycine conjugated cholic, chenodeoxycholic and deoxycholic acids were determined in 3 microliters of bile by descending chromatography on Whatman 3 MM paper using 70% acetic acid as the stationary phase and ethylenechloride:heptane (50:50) as the mobile phase, according to SJÖVALL (9, 10).

Taurocholic acid and (taurochenodeoxycholic + taurodeoxycholic) acid were determined in 3 microliters of bile by ascending chromatography on Whatman 3 MM paper using 70% formic acid as the stationary phase and isoamylacetate:heptane (85:15) as the mobile phase, as described by SJÖVALL (9).

pH *of the bile* was measured on approximately 10 microliter samples using McINNES micro-glass electrodes and pH-meter 22 from Radiometer, Copenhagen.

Results and Discussion

The results are shown in tables 2–13 and figures 1 and 2.

The data in the tables show no great difference between the two sexes, although by and large the concentrations of lipid phosphorus and bile acids are somewhat higher in the males than in the females. In the figures the values are plotted without markation of the sex.

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[1]) Microid Flask Shaker, Griffin & George Ltd., England.

Table 2. Incidence of gallstones in all the hamsters in the various groups.

Diet		Age at transfer, days	Total no. of animals	Animals with: cholesterol gallstones only		Animals with: amorphous pigmented gallstones only		Animals with: cholesterol and amorphous pigmented gallstones		Animals without gallstones	
				No.	%	No.	%	No.	%	No.	%
Glucose	group 1	41–44	70	57	81.4	1	1.9	0	0	12	17.1
Glucose	group 2	31–35	30	27	90	0	0	1	3.7	2	6.7
Glucose	group 3	31–35	69	63	92.3	0	0	1	1.5	5	7.2
Curative	group 1	41–46	40	0	0	0	0	0	0	40	100
Curative	group 2	32–35	10	0	0	0	0	0	0	10	100
Rice starch	group 1	41–44	20	1	5	0	0	0	0	19	95
Rice starch	group 2	30–34	49	0	0	3	6.1	0	0	46	94
Lactose	group 1	41–46	20	2	10	0	0	0	0	18	90
Lactose	group 2	30–34	36	5	13.9	0	0	0	0	31	86.1
Glucose	group 4	107–111	28	0	0	13	46.5	0	0	15	53.5
Glucose	group 5	107–111	25	0	0	13	52	0	0	12	48

Table 3. Incidence of gallstones in the hamsters used for bile analysis.

Diet		Age at transfer, days	No. of animals	Animals with: cholesterol gallstones only		Animals with: amorphous pigmented gallstones only		Animals with: cholesterol and amorphous pigmented gallstones		Animals without gallstones	
				No.	%	No.	%	No.	%	No.	%
Glucose	group 1	41–44	17	13	76.5	0	0	0	0	4	23.6
Glucose	group 2	31–35	13	11	84.5	0	0	0	0	2	15.4
Glucose	group 3	31–35	15	14	93.5	0	0	1	6.7	0	0
Curative	group 1	41–46	38	0	0	0	0	0	0	38	100
Curative	group 2	32–35	10	0	0	0	0	0	0	10	100
Rice starch	group 1	41–44	17	0	0	0	0	0	0	17	100
Rice starch	group 2	30–34	41	0	0	2	4.9	0	0	39	95.5
Lactose	group 1	41–46	12	0	0	0	0	0	0	12	100
Lactose	group 2	30–34	17	1	5.9	0	0	0	0	16	94
Glucose	group 4	107–111	16	0	0	9	56.2	0	0	7	43.8
Glucose	group 5	107–111	17	0	0	10	59	0	0	7	41

Table 4. Data for bladder bile of female hamsters reared on the *glucose diet* from the age of 31–44 days. All concentrations are given as millimolarities.

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	102	c	65	—	—	—	9.9	5.4	3.6	1.9	2.9	23.7	18.9	4.8	11.8	11.9	3.9	1.0	—	—
	133	o	72	—	2.7	3.4	11.5	11.9	11.9	1.6	1.4	38.3	35.3	3.0	13.1	25.2	11.8	1.9	14.2	1.3
	32	o	72	—	4.9	4.4	29.6	7.0	4.8	4.9	3.3	49.6	41.4	8.2	34.5	15.1	5.1	0.4	10.2	0.9
	104+ 8	c o	72	—	5.0	11.1	21.9	8.8	13.6	1.8	4.4	50.5	44.3	6.2	23.7	26.8	7.2	1.1	10.1	2.2
	53	o	72	—	2.7	7.5	29.4	9.6	14.3	3.5	3.5	60.3	53,3	7.0	32.9	27.4	7.6	0.8	22.4	2.8
2	7	c	48	—	6.1	11.2	43.0	10.9	35.3	3.1	4.4	96.7	89.2	7.5	46.1	50.6	11.9	1.1	15.8	1.8
	19	c	48	—	5.7	4.7	5.5	0.8	6.7	0.6	5.9	19.5	13.0	6.5	6.2	13.4	2.0	2.2	3.4	0.8
	55	o	49	—	3.0	7.0	29.5	7.6	4.3	2.7	2.9	47.0	41.4	5.6	32.2	14.7	7.3	0.5	15.6	2.4
	89	c	49	—	5.7	6.5	13.7	6.3	14.5	2.1	1.0	37.6	34.5	3.1	15.8	21.8	11.0	1.4	6.6	1.1
	40	c	49	—	7.6	8.5	17.7	4.3	19.0	2.1	3.3	46.4	41.0	5.4	19.8	26.6	7.6	1.3	6.2	1.1
	4	o	49	—	3.8	3.6	14.8	3.1	2.2	3.1	1.6	24.8	20.1	4.7	17.9	6.9	4.3	0.4	6.6	0.9
	8+ 106	c c	55	—	2.6	4.8	9.9	3.1	7.1	1.8	1.1	23.0	20.1	2.9	11.7	11.3	6.9	1.0	8.9	1.9
3	19+ 49	c, a c	55	7.8	3.3	4.9	17.9	16.2	7.7	4.4	7.2	53.4	41.8	11.6	22.3	31.1	3.6	1.4	16.0	1.5
	41+ 74	c c	55	7.6	3.3	10.6	28.0	13.7	3.6	3.5	3.4	52.2	45.3	6.9	31.5	20.7	6.6	0.7	15.7	3.2
	72+ 69	c c	99	7.2	3.1	8.6	33,5	4.8	3.9	5.2	5.0	52.4	42.2	10.2	38.7	13.7	4.1	0.4	16.9	2.8
Average				7.5	4.3	6.9	21.1	7.6	10.2	2.8	3.4	45.1	38.7	6.2	23.6	21.1	6.7	1.0	11.4	1.6

GC = Glycocholic acid
GCD = Glycochenodeoxycholic acid
GD = Glycodeoxycholic acid
TC = Taurocholic acid
TCD + TD = Taurochenodeoxycholic acid + taurodeoxycholic acid

c = cholesterol gallstones
a = amorphous pigmented gallstones
c, a = c and a occurring together in the same animal
o = no gallstones

G = Glycine conjugated bile acids
T = Taurine conjugated bile acids
Tri = Trihydroxycholanic acids = Glycocholic acid + Taurocholic acid
Di = Dihydroxycholanic acids = glycochenodeoxycholic acid + glycodeoxycholic acid + taurochenodeoxycholic acid + taurodeoxycholic acid.

Table 5. Data for bladder bile of male hamsters reared on the *glucose diet* from the age of 31–44 days. All concentrations are given as millimolarities.

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	91	c	64	—	—	—	21.3	11.8	23.2	1.9	3.5	61.7	56.3	5.4	23.2	38.5	10.4	1.7	—	—
	37+, 111	c, c	65	—	—	—	21.4	10.7	10.4	3.1	4.1	49.7	42.5	7.2	24.5	25.2	5.9	1.0	—	—
	59	c	70	—	2.2	—	16.1	8.4	19.8	2.6	4.2	51.1	44.3	6.8	18.7	32.4	6.5	1.7	23.2	—
	92+, 109	c, c	70	—	3.5	—	20.6	9.0	4.7	4.9	5.0	44.2	34.3	9.9	25.5	18.7	3.4	0.7	12.6	—
	81+, 95	c, c	70	—	2.7	—	22.1	8.9	11.2	4.4	4.7	51.3	42.2	9.1	26.5	24.8	4.7	0.9	19.0	—
	20+, 41	c, c	70	—	2.8	—	17.4	4.8	10.3	3.6	3.6	39.7	32.5	7.2	21.0	18.7	4.6	0.9	14.2	—
	130	c	71	—	3.9	4.2	13.6	3.8	2.3	2.9	1.5	24.1	19.7	4.4	16.5	7.6	4.4	0.5	6.2	1.1
2	29+, 96	c, c	48	—	5.7	9.8	27.9	7.1	9.2	4.0	3.8	52.0	44.2	7.8	31.9	20.1	5.7	0.6	9.3	1.7
	45+, 47+, 102	c, c, c	48	—	6.6	7.8	16.0	2.9	14.3	2.8	2.5	38.5	33.2	5.3	18.8	19.7	6.3	1.1	5.8	1.2
3	4+, 24	c, c	50	7.5	4.8	13.9	34.4	23.3	15.1	5.2	6.6	84.6	72.8	11.8	39.6	45.0	6.2	1.1	17.7	2.9
	60+, 73	c, c	55	7.0	6.6	11.1	35.0	18.0	14.1	17.1	17.4	101.6	67.1	34.5	52.1	49.5	1.9	0.9	15.4	1.7
	23+, 34	c, c	55	7.6	3.4	6.1	32.4	14.0	10.2	7.5	5.8	69.9	56.6	13.3	39.9	30.0	4.3	0.8	20.7	1.8
	77+, 22	c, c	55	7.6	4.7	8.8	37.9	18.6	9.9	7.3	7.6	81.3	66.4	14.9	45.2	36.1	4.5	0.8	17.4	1.9
	70	c	55	7.8	2.6	14.8	22.1	11.4	20.2	1.7	3.8	59.2	53.7	5.5	23.8	35.4	9.7	1.5	22.4	5,6
Average				7.6	4.1	9.6	24.2	10.9	12.5	4.9	5.3	57.8	47.6	10.2	29.1	28.7	5.6	1.0	15.3	2.2

Table 6. Data for bladder bile of female hamsters reared on the "*curative*" *diet* from the age of 32–46 days. All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio *total* bile acids/ cholest.	Ratio lipid phos./ cholest.
1	23	o	63	—	—	25.7	22.4	24.6	3.4	9.6	85.7	72.7	13.0	29.1	56.6	5.6	1.9	—	—
	53	o	63	—	—	27.3	24.9	27.3	4.0	10.8	94.3	79.5	14.8	31.3	63.0	5.4	2.0	—	—
	76	o	63	—	—	22.6	23.8	20.3	3.1	5.8	75.6	66.7	8.9	25.7	49.9	7.5	1.9	—	—
	100+ 85	o o	76	1.0	5.9	15.4	9.6	6.9	5.9	8.4	46.2	31.9	14.3	21.3	24.9	2.2	1.7	46.2	5.9
	86	o	91	1.1	15.0	27.9	18.2	12.7	5.3	7.6	71.7	58.8	12.9	33.2	38.5	4.5	1.2	65.1	13.6
	47	o	91	1.6	10.3	35.3	12.7	15.5	8.4	8.8	80.7	63.5	17.2	43.7	37.0	3.7	0.9	50.5	6.4
	2	o	91	2.4	17.1	59.5	21.6	31.5	11.5	13.9	138.0	112.6	25.4	71.0	67.0	4.4	0.9	57.5	7.2
	48	o	91	1.9	14.3	33.7	15.4	21.6	6.5	8.2	85.4	70.7	14.7	40.2	45.2	4.8	1.1	44.9	7.5
	116	o	91	1.1	17.7	30.7	12.1	17.2	7.8	8.2	76.0	60.0	16.0	38.5	37.5	3.7	1.0	69.1	16.1
	64	o	91	2.5	22.7	51.5	17.4	31.0	11.7	14.1	125.7	99.9	26.1	63.2	62.5	3.8	1.0	50.1	9.1
	65+ 71	o o	101	1.6	14.6	36.0	22.9	24.6	6.3	9.7	99.5	83.5	16.0	42.3	57.2	5.2	1.4	62.2	9.1
	28	o	101	1.0	9.3	21.6	16.2	7.1	5.8	7.6	58.3	44.9	13.4	27.4	30.9	3.4	1.1	58.3	9.3
	56+ 118	o o	101	1.2	11.3	22.2	13.0	10.2	8.3	9.7	63.4	45.4	18.0	30.5	32.9	2.5	1.1	52.8	9.4
	126	o	105	1.3	9.9	42.8	17.8	21.6	12.9	12.4	107.5	82.2	25.3	55.7	51.8	3.3	0.9	82.5	7.6
	43	o	105	1.7	16.5	76.9	19.8	18.5	29.4	13.5	152.3	114.4	42.8	106.3	51.0	2.7	0.5	92.5	9.7
	38+ 54	o o	105	—	—	44.2	14.9	24.6	9.7	11.5	104.9	83.7	21.2	53.9	51.0	3.9	1.0	—	—
	59	o	112	1.2	14.8	49.5	11.4	29.5	7.3	9.0	106.7	90.4	16.3	56.8	49.9	5.5	0.9	88.9	12.4
	57	o	112	1.2	11.5	37.7	15.8	22.4	4.5	5.8	86.2	75.9	10.3	42.2	44.0	7.4	1.0	71.9	9.6
	97	o	112	1.6	13.7	39.5	4.2	29.2	22.2	31.4	126.5	72.9	53.6	61.7	64.8	1.3	1.1	79.0	8.5
Average				1.5	13.6	36.8	16.5	20.9	9.2	10.9	94.1	74.2	20.1	46.0	48.2	4,3	1.2	65.5	9.6

Table 7. Data for bladder bile of male hamsters reared on the "*curative*" *diet* from the age of 32–46 days. All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	101+, 32	o, o	57	—	—	—	29.6	10.0	8.4	16.6	14.6	79.2	48.0	31.2	46.2	33.0	1.5	0.7	—	—
	1+, 49+, 70+, 102	o, o, o, o	63	—	3.3	—	47.2	31.6	29.6	8.2	18.1	134.7	108.4	26.3	55.4	79.3	4.1	1.4	40.7	—
	117	o	70	—	3.0	14.6	52.6	15.3	20.1	16.4	15.7	120.1	88.0	32.1	69.0	51.1	2.7	0.7	40.0	4.8
	90+, 113	o, o	70	—	1.8	15.6	49.4	21.1	19.7	10.6	12.2	113.0	90.2	22.8	60.0	53.0	9.9	0.9	62.6	8.7
	82	o	70	—	1.7	19.5	71.0	44.5	13.3	32.4	19.2	180.4	128.8	51.6	103.4	77.0	2.5	0.7	106.0	11.5
	15+, 105	o, o	70	—	4.2	16.4	36.3	16.0	15.3	10.9	12.1	90.6	67.6	23.0	47.2	43.4	2.9	0.9	21.6	3.9
	42	o	101	—	1.6	13.2	31.8	9.9	31.8	5.3	9.9	88.7	73.5	15.2	37.1	51.6	4.8	1.4	55.4	8.3
	91	o	101	—	1.4	12.8	26.8	11.4	16.1	7.9	7.9	70.1	54.3	15.8	34.7	35.4	3.5	1.0	50.1	9.2
	95	o	105	—	1.5	14.2	49.5	13.9	24.6	22.1	17.4	127.5	88.0	39.5	71.6	55.9	2.2	0.8	85.0	9.5
2	16+, 58	o, o	46	7.1	3.0	20.9	—	—	—	—	—	—	—	—	—	—	—	—	—	6.9
	9+, 13	o, o	46	7.4	2.7	16.4	69.0	24.9	30.4	11.9	12.8	149.0	124.3	24.7	80.9	68.1	5.1	0.8	55.2	6.1
	6+, 10+, 15	o, o, o	46	7.3	1.7	16.4	64.8	19.7	26.0	18.7	13.7	142.9	110.5	32.4	83.5	59.4	3.4	0.7	83.9	9.6
	75+, 79	o, o	55	7.0	2.7	18.4	81.7	36.8	22.9	18.4	16.7	176.5	141.4	35.1	100.1	76.4	4.0	0.8	65.3	6.8
	67	o	55	7.3	1.7	11.4	43.7	16.5	15.9	6.6	5.2	87.9	76.1	11.8	50.3	37.6	6.4	0.8	51.6	6.7
Average				7,3	2.3	15.8	50.3	20.9	21.1	14.3	13.5	120.3	92.2	27.8	64.6	55.5	3.6	0.9	51.8	7.7

Table 8. Data for bladder bile of female hamsters reared on the *rice starch diet* from the age of 30–44 days. All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	16+ 73	o o	72	—	1.0	5.4	28.6	8.2	7.5	4.8	3.8	52.9	44.3	8.6	33.4	19.5	5.1	0.6	52.9	5.4
	107	o	72	—	1.8	3.8	10.5	4.2	10.2	3.2	5.1	33.2	24.9	8.3	13.7	19.5	3.0	1.4	18.4	2.1
	8	o	72	—	2.1	4.3	18.3	4.4	19.4	3.2	6.6	51.9	42.1	9.8	21.5	30.4	4.3	1.4	24.8	2.1
	21	o	72	—	1.2	2.3	21.0	3.6	8.4	4.4	3.6	41.0	33.0	8.0	25.4	15.6	4.1	0.6	34.2	1.9
	6	o	84	—	1.0	3.8	27.4	2.4	13.3	5.0	4.7	52.8	43.1	9.7	32.4	20.4	4.4	0.6	52.8	3.8
	15+ 123	o o	84	—	2.1	7.0	51.8	7.7	22.2	12.8	11.1	105.6	81.7	23.9	64.6	51.0	3.4	0.8	50.4	3.3
	98	o	84	—	2.4	7.0	44.7	3.8	17.3	10.3	8.8	84.9	65.8	19.1	55.0	29.9	3.5	0.5	35.4	2.9
2	18+ 60+ 82	o o o	47	7.0	3.7	10.8	54.4	12.2	16.4	16.3	10.7	110.0	83.0	27.0	70.7	39.3	3.1	0.6	29.7	2.9
	71+ 86	o o	47	7.4	2.9	6.3	35.2	12.0	18.9	6.2	5.8	78.1	66.1	12.0	41.4	36.7	5.5	0.9	27.0	2.2
	34+ 43+ 56	o o o	47	7.4	4.0	7.7	47.3	14.1	16.4	9.5	8.8	96.1	77.8	18.3	56.8	39.3	4.3	0.7	24.0	1.9
	61+ 23	o o	56	7.3	2.2	10.1	31.2	7.9	11.5	12.5	9.5	72.6	50.6	22.0	43.7	28.9	2.3	0.7	33.0	4.6
	24+ 85	o o	56	7.2	1.4	10.2	39.6	7.1	21.8	10.1	9.9	88.5	68.5	20.0	49.7	38.8	3.4	0.8	63.2	7.3
	1+ 7	o o	56	—	1.0	8.5	54.4	19.0	20.9	17.3	17.3	128.9	94.3	34.6	71.7	57.2	2.7	0.8	128.9	8.5
	50+ 53	a a	103	7.2	2.6	13.4	55.3	12.5	29.0	5.9	6.2	108.9	96.8	12.1	61.2	47.7	8.0	0.8	42.0	5.2
	32+ 36	o o	103	6.8	2.2	15.7	66.5	18.0	44.6	15.1	17.7	161.9	129.1	32.8	81.6	80.3	3.9	1.0	73.6	7.1
	63	o	103	7.3	2.6	7.3	51.0	11.9	11.6	6.4	6.5	87.4	74.5	12.9	57.4	30.0	5.8	0.5	33.6	2.8
	55	o	103	—	—	10.2	27.2	8.8	21.0	8.7	7.3	73.0	57.0	16.0	35.9	37.1	3.5	1.0	—	—
Average				7,25	2.1	7.9	39.1	9.3	18.3	8.9	8.4	84.0	66.6	17.2	48.0	36.8	4.1	0.8	42.8	4.0

Table 9. Data for bladder bile of male hamsters reared on the *rice starch diet* from the age of 30–44 days. All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	68+ 31	o o	59	—	—	—	93.5	27.1	28.1	3.5	3.4	155.6	148.7	6.9	97.0	58.6	21.5	0.6	—	—
	43	o	77	—	1.5	4.7	25.7	4.2	10.6	4.7	6.4	51.6	40.5	11.1	30.4	21.2	3.6	0.7	34.5	3.1
	41	o	76	—	1.4	4.2	36.2	10.3	11.0	7.6	5.6	70.7	57.5	13.2	43.8	26.9	4.4	0.6	50.5	3.0
	1+ 14	o o	83	—	3.2	8.9	80.4	11.1	23.7	12.2	5.6	133.0	115.2	17.8	92.6	40.4	6.5	0.4	41.5	2.8
	74+ 27	o o	112	—	2.5	5.2	22.5	22.7	12.0	3.9	6.4	67.5	57.2	10.3	26.4	41.1	5.6	1.6	27.0	2.1
2	22+ 29	o o	46	7.4	2.0	6.8	74.6	7.5	28.4	14.5	12.5	137.5	110.5	27.0	89.1	48.4	4.1	0,5	68.7	3.4
	58+ 62+ 66	o o o	46	7.5	1.5	7.2	55.4	13.7	12.7	11.0	5.5.	98.3	81.8	16.5	66.4	31.9	5.0	0.5	65.5	4.8
	25+ 42+ 59+ 65	o o o o	46	7.2	2.9	8.5	56.5	16.8	27. 3	10.3	8.3	119.2	100.6	18.6	66.8	52.4	5.4	0.8	41.0	2.9
	72+ 84	o o	56	7.5	1.8	4.0	32,3	12.4	17.2	8.8	11.8	82.5	61.9	20.6	41.1	41.4	3.0	1.0	45.7	2.2
	69+ 80+ 2	o o o	56	7.6	2.6	7.7	32.1	9.7	25.8	6.4	7.8	81.8	67.6	14.2	38.5	43.3	4.8	1.1	31.4	3.0
	67+ 33	o o	56	7.4	2.7	9.3	46.0	13.9	18.1	10.0	10.1	98.1	78.0	20.1	56.0	42.1	3.9	0.8	36.2	3.4
	11+ 21	o o	103	6.9	2.6	17.2	48.5	18.9	24.2	9.3	11.5	112.4	91.6	20.8	57.8	54.6	4.4	0.9	43.0	6.6
	45+ 75+ 79	o o o	106	7.3	2.5	16.0	73.7	20.3	19.4	11.8	11.6	136.8	113.4	23.4	85.5	51.3	4.9	0.6	54.5	6.4
Average				7,4	2.3	8.3	48.7	13.5	19.2	9.2	8.6	99.1	81.3	17.8	57.9	41.3	4.6	0.8	45,0	3.6

Table 10. Data for bladder bile of female hamsters reared on the *lactose diet* from the age af 30–46 days. All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	7+	o	65	—	—	—	10.4	18.2	1.8	3.8	6.0	40.2	30.4	9.8	14.2	26.0	3.1	1.9	—	—
	129	o																		
	10+	o	76	—	4.3	8.1	21.7	12.7	1.3	5.4	13.7	54.8	35.7	19.1	27.1	27.7	1.9	1.0	12.7	1.9
	115	o																		
2	12+	o	48	7.6	5.4	8.5	30.2	50.6	3.2	9,0	13.9	106.9	84.0	22.9	39.2	67.7	3.7	1.7	19.7	1.6
	83+	c																		
	88	o																		
	19+	o	48	6.6	4.3	11.6	—	—	—	—	—	—	—	—	—	—	—	—	—	2.7
	5+	o																		
	46+	o																		
	74+	o																		
	87+	o																		
	90	o																		
Average					4.7	9.4	20.8	27.2	2.1	6.0	11.2	67.3	50.1	17.2	26.8	40.4	2.9	1.5	16.2	2.1

Table 11. Data for bladder bile of male hamsters reared on the *lactose diet* from the age of 30–46 days. All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
1	51+, 22	o, o	65	—	4.7	—	30.4	33.8	5.7	5.1	7.9	82.9	69.9	13.0	35.5	47.4	5.3	1.3	17.7	—
	45	o	65	—	3.1	—	31.5	21.4	5.2	4.9	5.5	68.5	58.1	10.4	36.4	32.1	5.6	0.9	22.1	—
	25+, 67	o, o	65	—	—	—	41.2	22.4	8.1	6.7	7.6	86.0	71.7	14.3	47.9	38.1	5.0	0.8	—	—
	83+, 26	o, o	105	—	5.4	10.1	38.4	28.2	12.5	12.0	15.9	107.0	79.1	27.9	50.4	56.6	2.8	1.1	19.7	1.9
	66	o	105	—	3.9	9.4	29.7	20.7	15.0	10.1	8.5	84.0	65.4	18.6	39.8	44.2	3.6	1.1	21.5	2.4
2	4+, 8+, 13+, 15	o, o, o, o	47	7.5	—	11.6	43.4	44.8	6.2	10.4	10.9	115.7	94.4	21.3	53.8	61.9	4.4	1.2	—	—
	16+, 39+, 48+, 78	o, o, o, o	47	7.6	3.1	6.5	19.2	20.8	2.6	6.7	8.1	57.4	42.6	14.8	25.9	31.5	2.9	1.2	18.6	2.1
Average					4.0	9.4	33.4	27.4	7.9	8.0	9.2	85.9	68.7	17.2	41.4	44.5	4.2	1.1	19.9	2.1

Table 12. Data for bladder bile of female hamsters reared on the *glucose diet from the age of 107–111 days.* All concentrations are given as millimolarities

Group no.	Hamster no.	Type of stone	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
4	88	o	61	7.1	1.3	6.3	4.9	3.8	4.1	2.0	1.7	16.5	12.8	3.7	6.9	9.6	3.5	1.4	12.7	4.9
	72+, 95+, 104	a, a, a	61	7.2	1.9	11.0	31.8	11.7	17.2	4.2	12.4	77.3	60.7	16.6	36.0	41.3	3.7	1.1	38.6	5.8
	40+, 105	a, a	63	6.5	2.8	13.9	31.9	18.8	16.2	5.8	6.6	79.3	66.9	12.4	37.7	41.6	5.4	1.1	28.2	4.9
	60+, 79	o, a	63	7.0	—	10.8	23.2	7.7	7.7	13.6	15.0	67.2	38.6	28.6	36.8	30.4	1.4	0.9	—	—
5	48	a	62	7.2	2.5	12.1	21.5	7.5	8.6	4.0	8.0	49.6	37.6	12.0	25.5	24.1	3.1	0.9	19.7	4.8
	15	a	62	7.7	0.5	8.7	9.5	7.5	11.4	2.4	3.5	34.3	28.4	5.9	11.9	22.4	4.9	1.9	68.6	17.4
	69+, 121+, 74	a, a, a	62	7.6	1.1	6.9	13.8	8.5	7.3	3.6	4.9	38.1	29.6	8.5	17.4	20.7	3.5	1.2	34.6	6.3
	59+, 58	o, o	62	6.7	2.2	13.9	28.5	23.8	9.9	14.4	13.3	89,9	62.2	27.7	42.9	47.0	2.2	1.1	40.8	6.3
	38	a	62	7.1	0.6	5.8	9.5	5.9	2.9	4.4	3.9	26.6	18.3	8.3	13.9	12.7	2.0	0.9	44.3	9.7
	23+, 109	a, o	63	7.7	2.1	7.0	11.9	12.9	3.1	5.2	4.9	38.0	27.9	10.1	17.1	20.9	2.8	1.2	18.1	3.3
	76	o	63	7.4	—	5.8	4.9	8.3	2.4	2.9	5.5	24.0	15.6	8.4	7.8	16.2	1.9	2.1	—	—
Average				7,2	1.7	9.2	17.4	10.6	8.3	5.7	7.2	49.2	36.2	12.9	23.1	26.1	2.9	1.3	33.9	7.0

Table 13. Data for bladder bile of male hamsters reared on the *glucose diet from the age of 107–111 days.* All concentrations are given as millimolarities

Group no.	Hamster *no.*	Type of *stone*	Days on diet	pH	Cholesterol	Lipid phosphorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	Ratio G/T	Ratio Di/Tri	Ratio total bile acids/cholest.	Ratio lipid phos./cholest.
4	78+	a	60	7.4	2.1	19.0	30.7	33.3	13.9	8.9	14.3	101.1	77.9	23.2	39.6	61.5	3.4	1.6	47.7	9.1
	111	a																		
	39+	o	60	7.2	3.3	18.7	21.7	20.2	9.1	9.7	10.5	71.2	51.0	20.2	31.4	39.8	2.5	1.3	21.5	5.7
	66+	o																		
	71+	o																		
	36	o																		
	41+	o	60	7.2	3.4	18.7	27.4	19.1	14.1	8.5	10.7	79.8	60.6	19.2	35.9	43.9	3.2	1.2	23.4	5.5
	92	a																		
5	28+	o	61	7.1	2.5	15.9	44.2	20.8	12.3	12.8	13.8	103.9	77.3	26.6	57.0	46.9	2.9	0.8	41.5	6.4
	43+	a																		
	63+	o																		
	14	o																		
	100	a	61	8.0	2.4	22.7	33.0	16.9	14.4	4.9	6.8	76.0	64.3	11.7	37.9	38.1	5.5	1.1	31.6	9.6
	93	a	61	7.7	—	—	32.1	13.5	17.0	6.5	7.3	76.4	62.5	13.8	38.6	37.8	4.5	0.9	—	—
Average				7.3	2.7	19.0	31.5	20.6	13.5	8.5	10.5	84.7	65.7	19.1	40.1	44.6	3.7	1.2	33.1	7.3

For practical reasons the animals could not be sacrificed within a narrow interval of time, and it was difficult to extend the feeding period in the glucose groups as long as in the other groups.

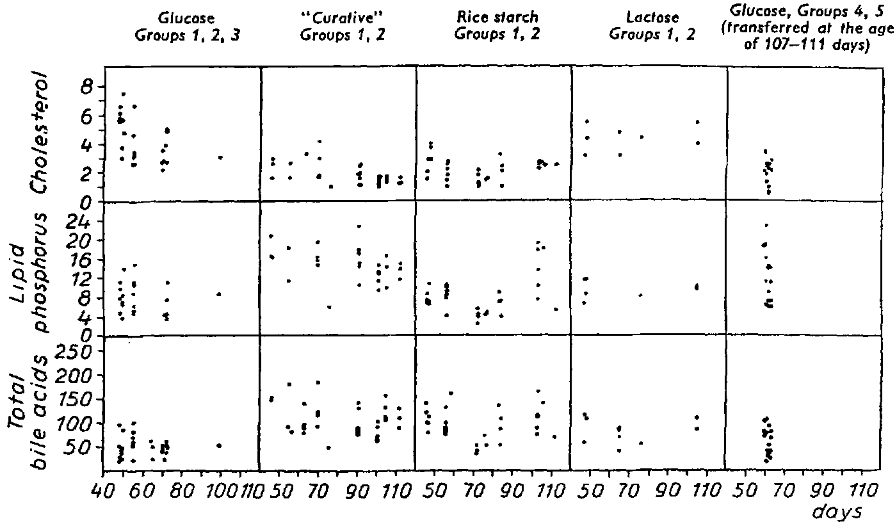

Fig. 1. *Ordinates* Concentrations (millimol): Cholesterol; Lipid phosphorus; Total bile acids. *Abscissae*: Days on experimental diets.

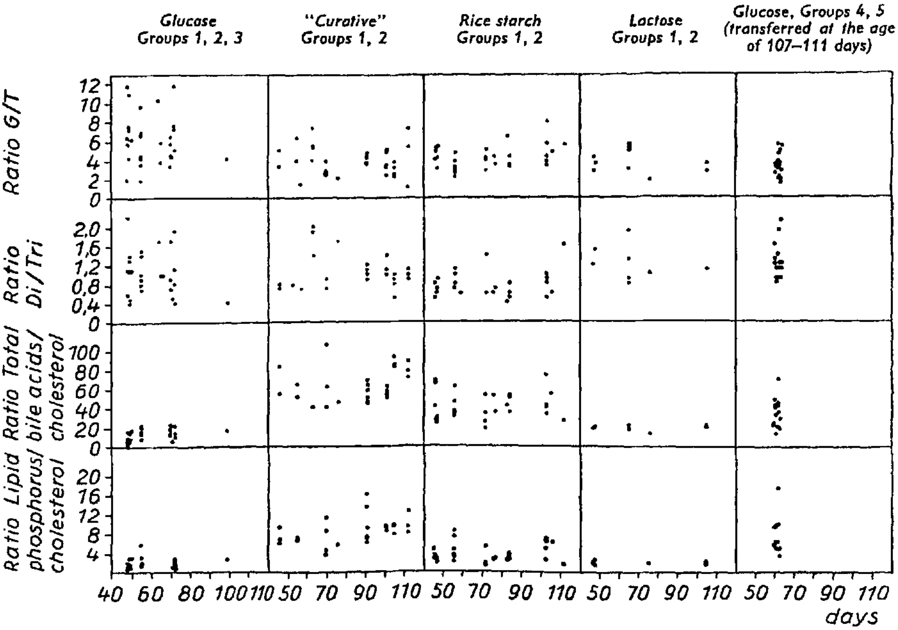

Fig. 2. *Ordinates*: Ratios (millimol./millimol.): Glycine conjugated bile acids/taurine conjugated acids (G/T); Dihydroxycholanic acids/trihydroxycholanic acids (Di/Tri); Total bile acids/cholesterol; Lipid phosphorus/cholesterol. *Abscissae*: Days on experimental diet.

In spite of this and of the scattering of the values within each group, the following conclusions can be drawn:

1. *The hamsters transferred from the stock diet to the experimental diets at the age of 30 to 46 days.*

In those cases where the pH *of the bladder bile* was determined, these values were essentially the same in the various groups. It is, therefore, unlikely that pH is the factor determining whether cholesterol gallstones occur or not.

The figures for *bladder bile cholesterol* tend to be higher in the glucose groups than in the groups receiving the rice starch diet and the "curative" diet.

The values for cholesterol in the glucose groups seem to be particularly high in the early part of the experiment. This may, however, be merely due to the fact that the range of the values for the glucose-fed animals in the later part of the feeding period could not be assessed.

Total bile acids tend to be lower in the glucose groups than in the groups fed the rice starch diet and the "curative" diet.

The figures for *lipid phosphorus* tend to be lower in the glucose and rice starch groups than in the group fed the "curative" diet.

In the rice starch groups there is a tendency for the lipid phosphorus values to rise after about 100 days of feeding. The reason for this is not clear. In the same interval there are no data for the glucose-groups available for comparison.

When the ratio *total bile acids/cholesterol* is considered, the difference between the glucose groups on the one side and the rice starch and "curative" diet groups on the other is marked. This ratio is lower for the glucose groups (within which cholesterol gallstones occur abundantly) than for the rice starch groups (within which cholesterol gallstones are rare), and for the "curative" diet groups (within which cholesterol gallstones do not occur at all).

The ratio *lipid phosphorus/cholesterol* is, generally, highest for the "curative" diet groups and tends to be higher for the rice starch groups than for the glucose groups. The overlapping of the figures for the latter two groups is marked and the difference is due to the lower values for cholesterol in the rice starch groups.

The general trend of the results mentioned is in accordance with current concepts, according to which bile acids and lecithin are important factors in keeping cholesterol in solution in the bile (11, 12).

The ratios bile acids/cholesterol and lipid phosphorus/cholesterol may not, however, be the only factors involved. In the *lactose group* (transferred from the stock diet to the lactose diet at the age of 30–46 days), these figures, as well as the figures for cholesterol, bile acids and lipid phosphorus *per se*, were near the range of the figures found in the glucose groups, and yet cholesterol gallstones are rare in hamsters receiving the lactose diet and appeared only in one of the lactose-fed animals used for the analyses.

In future experiments, therefore, it will be desirable to examine also the content of other constituents of the bile, e. g., the mucine or the mucopolysaccharides and the possible presence of unesterified fatty acids.

The dihydroxycholanic acids deoxycholic- and chenodeoxycholic acids are more potent as solubilizing agents than cholic acid (12). There is, however, no apparent difference with respect to the ratios dihydroxy/trihydroxycholanic acids in the various groups. Therefore, the absence of cholesterol gallstones in the "curative" group and the rare occurrence of cholesterol stones in the rice starch groups are not due to an increase of dihydroxycholanic acids in proportion to trihydroxycholanic acid.

The highest figures for the ratio *glycine-conjugated/taurine-conjugated bile acids* (G/T value) are found in the glucose groups, but within the glucose groups there is no correlation between the G/T values and the occurrence or absence of cholesterol gallstones.

The observation that the ratio total bile acids/cholesterol is higher in the rice starch groups than in the glucose groups recalls the finding of PORTMAN et al. (13) that in rats the daily excretion of bile acids is higher when the carbohydrate component of the diet is starch than when it is sucrose. But in rats it is not possible to relate this finding to cholesterol gallstone formation.

The mechanism by which rice starch increases the ratio total bile acids/cholesterol and counteracts formation of cholesterol gallstones has not been elucidated. Observations made during the present and similar experiments show that the volume of the intestinal content is much larger in the animals fed rice starch diets than in animals fed glucose diets. The bulk of the intestinal content is also large in animals fed lactose diets. Further, the p_H of the coecum and the large intestine is lower in the animals fed rice starch and lactose diets than in animals on the glucose diet. It is possible that the volume of the intestinal content has some influence on the composition of the bladder bile. PORTMAN et al. (13) found that increase of the amount of roughage in the diet enhanced the excretion of bile acids in rats. The factors determining the concentrations of the constituents of bladder bile may not all be strictly biochemical. Also physiological factors may play a role.

The possible role of the intestinal flora favored by the diets used in the present experiment will be the subject of separate studies.

The fact that lipid phosphorus was higher in the group fed the "curative" diet than in the groups fed the glucose and rice starch diets (with exception of the last days in the rice starch group) may be due to the presence of 10% lard in the "curative" diet. The other two diets are very low in fat (the glucose diet contains 0.2% fat derived entirely from the casein; the rice starch diet contains in addition thereto 0.22% fat from the rice starch, one third of which is linoleic acid).

An increased content of lecithin in the total solids of bladder bile of calves reared on whole milk instead of on skim milk and grass has been reported by ISAKSSON (12).

In the glucose groups, 6 out of the 45 animals for which analyses are presented had no cholesterol gallstones. There was, however, no obvious difference between the analytical data of these animals and those of the other animals in the same groups.

The scattering of the data within each group makes it seem likely that variations in the composition of the bladder bile of an animal may occur in the course of the day or during the experimental period. Thus, in animals having cholesterol stones concentrations favoring precipitation of cholesterol need not necessarily exist at all times.

2. The hamsters transferred to the glucose diet at the age of 107–111 days.

These hamsters did not develop cholesterol gallstones but had a marked tendency to formation of amorphous pigmented gallstones (such gallstones occurred in 26 out of all 53 animals in these groups and in 18 out of the 33 animals whose bile was analyzed).

There was no apparent difference in the development of amorphous pigmented gallstones as to whether or not the animals received lettuce and carrots in addition to the stock diet before they were transferred to the glucose diet.

In these groups the data for bladder bile constituents show the following relation to those found for animals transferred to the glucose diet at the age of 30–46 days:

p_H is essentially the same; cholesterol tends to be lower; lipid phosphorus tends to be higher; whereas total bile acids are largely within the same range. Thus, the ratios total bile acids/cholesterol and, especially, lipid phosphorus/cholesterol tend to be higher.

This may have minimized the tendency to formation of cholesterol gallstones in these animals.

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Summary

The composition of bladder bile with respect to p_H, cholesterol, lipid phosphorus, glycine conjugated cholic, chenodeoxycholic and deoxycholic acids, and of taurine conjugated cholic and chenodeoxycholic plus deoxycholic acids was analyzed in young hamsters reared from the age of 30–46 days for various lengths of time on

1) a fat-free diet with glucose as the carbohydrate component, producing cholesterol gallstones in young hamsters,
2) a fat-free with rice starch as the carbohydrate component which, largely, prevents the formation of cholesterol gallstones.
3) a fat-free diet with lactose as the carbohydrate component which also counteracts the formation of cholesterol gallstones,
4) a diet of more complicated composition, containing 10% of lard, 20% of casein, 36% of dried brewer's yeast, 28.3% of ground polished rice, and with Cu added to the salt mixture. This "curative diet" completely prevents the formation of cholesterol and amorphous pigmented gallstones and causes already formed cholesterol stones to dissolve.

The bladder bile of hamsters transferred from the stock colony diet to the glucose diet at the age of 107–111 days was analyzed similarly.

The p_H was essentially the same in all groups.

The abundance of cholesterol gallstones among the hamsters fed the fat-free glucose diet from 30–46 days of age paralleled a tendency to higher levels of cholesterol and lower levels of total bile acids – and, therefore, generally lower levels of the ratio total bile acids/cholesterol than in the groups fed the rice starch diet and the "curative diet".

In the glucose groups and in the rice starch groups the levels of lipid phosphorus were within the same range and lower than in the groups fed the "curative diet". However, in the rice starch groups the values for lipid phosphorus increased after about 100 days of feeding.

In the lactose fed groups, the values for cholesterol, bile acids and lipid phosphorus were almost within the same range as in the glucose groups, suggesting that other factors than those analyzed may be responsible for the rare occurrence of cholesterol gallstones in lactose fed hamsters.

The hamsters in the groups transferred to the glucose diet at 107–111 days of age did not get cholesterol stones but had a marked tendency to formation of amorphous pigmented stones. This condition corresponded to a tendency to higher values of the ratios total bile acids/cholesterol, and, especially, lipid phosphorus/cholesterol than in the groups transferred to the glucose diet at the age of 30–46 days.

Zusammenfassung

Die Blasengalle von Hamstern wurde auf p_H, Cholesterin, Lipid-Phosphor, Glycin-konjugierte Cholsäure, Chenodesoxycholsäure und Desoxycholsäure, sowie Taurin-konjugierte Cholsäure und Chenodesoxy- plus Desoxycholsäure analysiert.

Ein Teil der Tiere wurde von einem Alter von 30 bis 46 Tagen an während Zeiträumen verschiedener Länge mit den unten angeführten Nahrungen gefüttert:

1. Eine fettfreie Nahrung mit Glucose als Kohlenhydrat-Komponente, die an jungen Hamstern Cholesterin-Gallensteine hervorruft.
2. Eine fettfreie Nahrung mit Reisstärke als Kohlenhydrat-Komponente, welche die Bildung von Cholesterin-Gallensteinen fast aufhebt.
3. Eine fettfreie Nahrung mit Lactose als Kohlenhydrat-Komponente, welche ebenfalls die Bildung von Cholesterin-Gallensteinen stark herabsetzt.
4. Eine Nahrung komplizierterer Zusammensetzung, enthaltend u. a. 10% Schweineschmalz, 20% Casein, 36% Trockenhefe, 28,3% gemahlenen, polierten Reis und ein Salzgemisch mit Zusatz von Cu („Kurative Nahrung"), welche die Bildung von Cholesterin- und amorphen pigmentierten Gallensteinen vollkommen aufhebt, und schon gebildete Cholesterin-Gallensteine in Lösung bringen kann.

Ein anderer Teil der Tiere wurde im Alter von 107–111 Tagen von der „Stock diet" bzw. von der „Stock diet" mit einer mäßigen Zulage von Salat und Möhren zu der fettfreien Nahrung 1. überführt.

Die Ergebnisse waren:

Das p_H war hauptsächlich dasselbe in allen Gruppen.

Das reichliche Vorkommen von Cholesterin-Gallensteinen in den Gruppen, welche vom Alter von 30 bis 46 Tagen an mit der fettfreien Glucosenahrung gefüttert wurden, entsprach im allgemeinen einem höheren Cholesteringehalt und niedrigeren Gehältern an Gesamtgallensäuren und deswegen einem niedrigeren Verhältnis von Gesamtgallensäuren zu Cholesterin als in den Gruppen, welche die Reisstärke, bzw. die „kurative" Nahrung erhielten.

In den erwähnten Glucosegruppen und in den Reisstärke-Gruppen war der Gehalt an Lipidphosphor ungefähr gleich und niedriger als in der Gruppe, welche mit der „kurativen" Nahrung gefüttert wurde. Jedoch trat nach ungefähr 100 Tagen ein Ansteigen der Lipid-Phosphor-Werte in der Reisstärke-Gruppe ein.

In den Lactosegruppen lagen die Werte für Cholesterin, Gesamtgallensäuren und Lipidphosphor in der Nähe der entsprechenden Werte der Glucosegruppen, was darauf hindeutet, daß das verhältnismäßig seltene Vorkommen von Cholesterin-Gallensteinen bei Lactose-gefütterten Hamstern teilweise durch andere Faktoren bedingt sein kann.

Die Hamster, welche erst im Alter von 107–111 Tagen zu der Glucosenahrung überführt wurden, bekamen keine Cholesterin-Gallensteine, hatten aber eine ausgesprochene Neigung zur Bildung von amorphen, pigmentierten Gallensteinen (unabhängig davon, ob vorher eine mäßige Zulage von Salat und Möhren gegeben wurde.) Diesem Zustand entsprachen eine Neigung zu höheren Werten des Verhältnisses Gesamtgallensäuren zu Cholesterin, und, besonders eine Neigung zu höheren Werten des Verhältnisses, Lipidphosphor zu Cholesterin verglichen mit den Gruppen, welche im Alter von 30 bis 46 Tagen zu der Glucosenahrung überführt wurden.

References

1. DAM, H. and F. CHRISTENSEN, Z. Ernährungswiss. 2, 36 (1961). — 2. DAM, H. and F. CHRISTENSEN, Z. Ernährungswiss. 2, 154 (1962). — 3. DAM, H. and F. CHRISTENSEN, Z. Ernährungswiss. 2, 91 (1961). — 4. PRANGE, I., F. CHRISTENSEN and H. DAM, 5. Int. Congr. Biochem. Moskva 1961. Abstr. of Communications 12. 58. 1859. — 5. DAM, H. and F. CHRISTENSEN, Acta pathol. microbiol. Scand. 30, 236 (1952). — 6. CHRISTENSEN, F., H. DAM and G. KRISTENSEN, Acta physiol. Scand. 36, 329 (1956). — 7. SPERRY, W. M., Ind. Eng. Chem., Analyt. Edit. 14, 88 (1942). — 8. HANSEN, P. W. and H. DAM, Acta Chem. Scand. *11*, 1658 (1957). — 9. SJÖVALL, J., Acta chem. Scand. 10, 1051 (1956). — 10. SJÖVALL, J., Arkiv Kemi 8, 317 (1955). — 11. SPANNER, G. O. and L. BAUMAN, J. Biol. Chem. 98, 181 (1932). — 12. ISAKSSON, B., On the Lipids and Bile Acids in Normal and Pathological Bladder Bile. Dissertation (Lund 1954). — 13. PORTMAN, O. W., G. V. MANN and A. P. WYSOCKI, Arch. Biochem. Biophys. 59, 224 (1955).

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Zur Provenienz der in die Bundesrepublik Deutschland importierten Nährstoffe nach Produkten und Regionen

Von WILLI WIRTHS

Mit 13 Abbildungen und 5 Tabellen

(Eingegangen am 3. Juli 1962)

Die Bundesrepublik Deutschland hat in den letzten Jahren in zunehmendem Maße ernährungswirtschaftliche Güter aus einer großen Zahl von Ländern importiert. Seit 1950/51 zeigt sich volumenmäßig mehr als eine Verdopplung; wertmäßig nahezu eine Verdopplung (1950/51 = 5,591 Mrd. DM, 1959/60 = 11,337 Mrd. DM) (1). Wenngleich auch alkoholische Getränke und weitere Genußmittel sowie direkte Futtermittel bei ernährungswirtschaftlichen Einfuhren einzuordnen sind, so bilden doch Nahrungsmittel und solche Produkte, die *auch* für die menschliche Ernährung verwendet werden, den weitaus größten Anteil.

Bei einer Betrachtung der eingeführten Produkte im ernährungsphysiologischen Blickpunkt interessiert zunächst, welche Nahrungsmittel aus welchen Ländern bzw. Regionen stammen. Dabei sind im allgemeinen die Mengen und/oder die dafür aufgewandten Preise zu erfahren. Insgesamt betrug die inländische Nahrungsmittelproduktion 1959/60 einschließlich Erzeugung aus Auslandsfutter 66 v.H. (1958/59 sowie 1960/61 jeweils 70 v.H.) der gesamten