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## Alimentary Production of Gallstones in Hamsters

17. Influence of butter fat and the fat of a dietetic margarine rich in linoleic acid on gallstone formation and composition of the bladder bile\*)

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With 3 figures and 5 tables

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Previous work from our laboratory (1) has shown that fats counteract the development of cholesterol gallstones in young hamsters fed a diet containing a high level of glucose. When the fats were given in low amounts, it could be shown that soybean oil and cod liver oil, i. e. fats rich in polyunsaturated fatty acids, are more efficient than lard in counteracting the development of this type of gallstones.

The present work concerns the development of gallstones under the influence of two different fats used in human nutrition, viz. butter fat and the fat of a dietetic margarine having a high content of linoleic acid.

### Experimental

The hamsters (*Mesocricetus auratus auratus*) were young from out stock colony, about one month old at the beginning of the experiment. They were caged individually, and each of them received 0.1 ml of a 0.5% solution of Mepacrine hydrochloride (3-Chloro-7-methoxy-9-(1-methyl-4-diethylaminobutylamino)acridine dihydrochloride) by mouth on 3 consecutive days before the experimental feeding started, as a measure to prevent spreading of a protozoal intestinal infection.

The results were based only on animals living through the entire experimental period of 6 to 7 weeks and not having diarrhea.

At the end of each experiment, the animals were killed with chloroform and autopsied immediately thereafter. Examination for the presence of gallstones and determination of the type of stones found were carried out as described earlier (1).

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In one of the experimental series (G 117), bile was collected from the gallbladder at autopsy for quantitative determination of cholesterol, bile acids and lipid soluble phosphorus as described in an earlier communication (2). It was not possible to obtain bile from all the animals in this series, and in several cases it was necessary to pool bile from 2 or 3 animals in order to get enough material for the determinations.

The composition of the fat-free basal diet is shown in table 1. Vitamins A and D<sub>3</sub> were included in the vitamin mixture instead of being given separately as in most of our previous studies. Further, the salt mixture contained added trace elements as shown in the footnote to table 1.

Table 1. Composition of the fat-free basal diet

Casein <sup>1)</sup> .....	20.0 g
Glucose .....	62.3 g
Rice starch .....	12.0 g
Salt mixture <sup>2)</sup> .....	5.0 g
Vitamin mixture <sup>3)</sup> .....	0.5 g
Choline chloride .....	0.2 g
	100.0 g

<sup>1)</sup> "Vitamin Test Casein" from Genatosan Ltd., Loughborough, England.

<sup>2)</sup> Sodium chloride, 0.3 g; magnesium subcarbonate, 0.25 g; potassium chloride, 0.35 g; dipotassium phosphate, 0.85 g; monosodium phosphate (2 aq.), 0.5 g; monocalcium phosphate (1 aq.), 0.85 g; calcium lactate (approx. 5 aq.), 1.8 g; ferric citrate (16.7% Fe), 0.1 g; potassium iodate, 0.25 mg; zinc carbonate, basic, (56% Zn), 3.6 mg; manganese carbonate (47.8% Mn), 2.1 mg; cupric carbonate (50-55% Cu), 0.95 mg; sodium fluoride, 2.0 mg; sodium molybdate (2 aq.), 0.25 mg; chromium sulfate (15 aq.), 0.065 mg; selenium dioxide, 0.016 mg; total 5.009 g.

<sup>3)</sup> Biotin, 0.05 mg; folic acid, 0.2 mg; ascorbic acid, 10 mg; thiamine hydrochloride, 1.5 mg; riboflavin, 1.5 mg; pyridoxine hydrochloride, 1.5 mg; calcium pantothenate, 5 mg; nicotinic acid amide, 5 mg; inositol, 5 mg; p-aminobenzoic acid, 1 mg; menadiol diphosphate tetrasodium salt (6 aq.) ("Synkavit", Roche), 0.5 mg;  $\alpha$ -tocopherol acetate ("Ephynal", Roche), 5 mg; cyanocobalamin, 0.003 mg (furnished in the form of "Bendogen", GEA); vitamin A, 1000 I. U., and vitamin D<sub>3</sub>, 100 I. U. (furnished in the form of "Rovimix 50/5", Roche, 20 mg); sucrose to make a total of 500 mg.

The whole amount of butter fat and margarine fat necessary for one experiment was prepared in advance by melting and separation from non-lipid material. The fats so prepared were stored in several 0.5 liter plastic containers at minus 20 °C until use.

The fats were incorporated into the basal diet instead of an equal amount by weight of glucose. Two kg of diet lasting for 4-5 days were prepared at a time and stored at 4 °C when not in use.

The dietetic margarine was of the brand "MIFU" which is commonly used in Denmark. It contains 40% or more of linoleic acid in the fat which according to information obtained from the manufacturer consists of cottonseed oil, 82.7%; hydrogenated palm oil, 17%; and sesame oil, 0.3%; plus the prescribed addition of vitamins A and D\*).

In two experimental series (G 112 and G 117), the effect of this margarine fat was compared with that of butter fat at the dietary level of 10%. In a third experimental series (G 113), the effect of the fats were compared at the 3% dietary level.

The fatty acid composition of the fats used in each of the experimental series was determined by gas liquid chromatography of the methyl esters. The results of these determinations are shown in table 2.

<sup>4)</sup> In Denmark, margarine shall contain 14 i.u. preformed vitamin A, 6 i.u. vitamin A in the form of carotene, and 0.5 i.u. vitamin D per g.

Table 2. Fatty acid composition of the fats used.

Per cent of the methyl esters of the individual fatty acids in the methyl esters of the total fatty acids from each fat

Fatty acid <sup>1)</sup> (Number of carbon atoms and double bonds)	Butter fat			Margarine fat "MIFU"		
	G 112	G 113	G 117	G 112	G 113	G 117
4:0	0.8	0.9	t			
6:0	0.9	0.7	t			
8:0	0.8	1.1	0.3			
10:0	1.7	2.4	2.2			
11:0	0.6	0.8	0.2			
12:0	2.9	3.2	4.0	0.3	0.2	0.4
13:0	0.6	0.8	0.8			
14:0	8.8	9.3	15.3	0.7	0.7	0.9
14:1	3.2	2.3		3.6		
15:0	2.2	2.0				
16:0 br.? <sup>2)</sup>	0.8	0.6	0.4			
16:0	22.9	26.4	38.2	24.4	22.4	30.3
16:1	5.2	6.6	6.6	2.5	2.7	1.1
17:0	2.1	1.3	0.9			
18:0 br.? <sup>2)</sup>	0.5	0.5	t			
18:0	11.3	10.6	6.7	3.1	3.2	3.6
18:1	27.7	25.6	17.5	26.6	26.4	21.0
18:2	3.8	3.0	1.9	41.1	43.3	40.0
18:3	2.5	2.0	0.8	1.0	0.9	2.6
20:1	0.7	t	t			
22:1				0.3	0.3	t

<sup>1)</sup> The amounts of fatty acids of 8:0 and lower are undoubtedly low because of high volatility of esters of these acids.

<sup>2)</sup> br. = branched.

### Results and Discussion

The incidences of the various types of gallstones are shown in table 3.

The results of the analyses of bladder bile from animals in the experimental series G 117 are shown in tables 4 and 5 and in figs. 1, 2, and 3.

In each of the two experimental series (G 112 and G 117), in which the fats of butter and dietetic margarine were compared at the 10% level, the incidence of cholesterol gallstones was much less with the margarine fat than with butter fat. For each sex this difference is significant with a probability of more than 99% [the method for evaluating the significance was that described by KOLLER (3)].

In the experimental series (G 113) in which the two fats were compared at the 3% level, the incidence of cholesterol gallstones was also less with the margarine fat than with the butter fat, but the significance of the difference was lower, viz. 95% for the females, and also for the two sexes considered together.

The incidences of amorphous pigmented gallstones and of "mixed gallstones" were low in each of the experimental series of the present study.

The growth of the animals was about the same with the two fats and faster at the 10% than at the 3% fat level.

The cause of the lower incidence of cholesterol gallstones obtained with the fat of the dietetic margarine as compared with butter fat is, apparently, the much higher content of linoleic acid in the margarine fat.

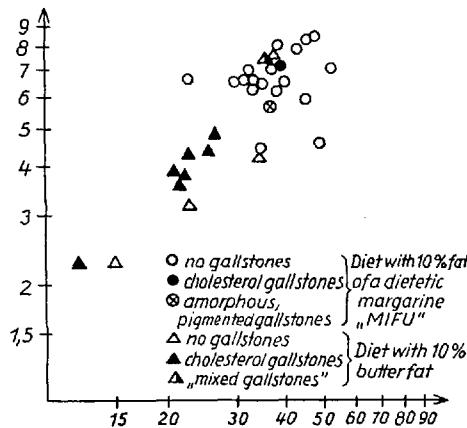


Fig. 1. Molar ratios bile acids/cholesterol (horizontal) and lipid-soluble phosphorus/cholesterol (vertical) in bladder bile of hamsters from Experimental Series G 117. Logarithmic scale.

Linoleic acid, however, is not the only polyenoic fatty acid capable of keeping the incidence of cholesterol gallstones low, since in previous experiments drastic reduction of the formation of cholesterol gallstones has been obtained also with cod liver oil (1), cod liver oil freed from vitamin A, and with ethyl esters of the fatty acids from menhaden oil (4).

The analyses of the bladder bile from animals receiving butter fat and margarine fat, resp., at the 10% dietary level (tables 4 and 5 and figs. 1, 2, and 3) show the following:

The ratios bile acids/cholesterol and -lipid P/cholesterol are particularly scattered in the butter fat group. In more than half of the cases in the butter fat group, these ratios are lower than the lowest value obtained in the margarine fat group (fig. 1).

The concentrations of cholesterol are also particularly scattered in the butter fat group, but in more than half of the cases higher than the highest cholesterol concentration found in the margarine fat group (figs. 2 and 3).

Furthermore, in the butter fat group there is a general trend for the values of the two ratios to decline with increasing concentrations of cholesterol (figs. 2 and 3).

The data recorded in figs. 1, 2, and 3 may represent part of the explanation why the occurrence of cholesterol gallstones is much more frequent in the 10% butter fat groups than in the 10% margarine fat groups. The validity of an explanation based on these data is, of course, dependent upon the correctness of the assumption that low values of the two ratios together with high cholesterol concentration *within the ranges observed* are incompatible with keeping

Table 3. Incidence of gallstones and other data for the three experimental series

Exp. Series	Age of animals at beginning of feeding, days	Duration of feeding period, days	Diet characteristics	Sex and number of animals	Number of animals having			Percentage of animals having gallstones	Mean weight gain during first 42 days, g	Range
					Cholesterol gallstones, %	Mixed gallstones, %	Amorphous gallstones, %			
G 112	29-37	42-43	10% butter fat	m	22	13	0	9	59.2	22-62
				f	23	14	0	8	60.9	16-48
				m + f	45	27	0	17	60.0	
			10% margarine fat (MIFU)	m	19	0	0	19	0	
				f	25	2	0	22	8.0	
				m + f	44	2	0	41	4.6	
G 113	34-37	43-45	3% butter fat	m	21	19	0	2	90.5	2-54
				f	32	25	0	7	78.2	1-36
				m + f	53	44	0	9	83.0	
			3% margarine fat (MIFU)	m	22	16	0	6	77.7	
				f	25	12	0	13	48.0	
				m + f	47	28	0	19	59.6	
G 117	27-33	48-50	10% butter fat	m	15	13	0	2	86.7	
				f	19	12	2	0	63.2	
				m + f	34	25	2	7	73.5	
			10% margarine fat (MIFU)	m	20	2	0	1	10.0	
				f	18	2	0	1	11.1	
				m + f	38	4	0	2	10.5	

Two figures connected with a solid vertical line on their right-hand side are considered to be different with a probability of more than 99%.  
 Two figures connected with a dotted vertical line on their right-hand side are considered to be different with a probability of 95%.

Table 4. Data for bladder bile of hamsters (Experimental series G 117) on the diet with 10% butterfat from the age of 27-33 days.  
All concentrations are given as millimolarities

Group no./ hamster no.	Type of stones	Days on diet	Chole- sterol	Lipid phos- phorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	G/T	DI/TD	Total bile acids/ cholest.	Lipid- phos- phor/ cholest.
<i>females:</i>																		
1226/2	C	48	6.1	17.0														2.8
1226/19	C	48	5.8	—	63.1	51.2	14.5	12.8	25.9	167.5	128.8	38.7	75.9	91.6	3.3	1.2	28.9	—
1226/30	C	48	8.0	18.6	28.3	57.8	8.5	7.6	17.1	119.3	94.6	24.7	35.9	83.4	3.8	2.3	14.9	2.3
1226/68	C	50	4.9	15.5	61.6	18.9	14.6	8.7	8.4	112.2	95.1	17.1	70.3	41.9	5.6	1.6	22.9	3.2
1226/17	O	50	8.0	18.3	40.1	29.3	14.7	8.1	4.2	96.4	84.1	12.3	48.2	48.2	6.8	1.0	12.1	2.3
1227/39	O	50	4.3	20.6	25.1	57.4	8.8	8.4	16.4	116.1	91.3	24.8	33.5	82.6	3.7	2.5	27.0	4.8
1227/94	C	50	3.1	11.6	22.9	29.8	6.5	3.8	5.4	68.4	59.2	9.2	26.7	41.7	6.4	1.6	22.1	3.8
1227/83	C	50	2.4	18.3	37.4	9.3	20.6	9.5	11.5	88.3	67.3	21.0	46.9	41.4	3.2	0.9	36.8	7.6
1227/86	C	50	2.7	20.1	38.4	23.4	13.6	7.3	14.4	97.1	75.4	21.7	45.7	51.4	3.5	1.1	36.0	7.4
1228/13	C	50	2.0	8.3	12.2	44.3	3.5	1.9	7.1	69.0	60.0	9.0	14.1	54.9	6.7	3.9	34.5	4.2
1228/41	O	50	3.1	11.6	22.9	29.8	6.5	3.8	5.4	68.4	59.2	9.2	26.7	41.7	6.4	1.6	22.1	3.8
1228/97	O	50	5.0	18.3	37.4	9.3	20.6	9.5	11.5	88.3	67.3	21.0	46.9	41.4	3.2	0.9	36.8	7.6
1228/47	C	50	2.7	20.1	38.4	23.4	13.6	7.3	14.4	97.1	75.4	21.7	45.7	51.4	3.5	1.1	36.0	7.4
1229/21	O	50	5.7	25.3	31.9	67.4	11.9	10.0	25.5	146.7	111.2	35.5	41.9	104.8	3.1	2.5	25.7	4.4
1229/90	M	50	5.7	25.3	31.9	67.4	11.9	10.0	25.5	146.7	111.2	35.5	41.9	104.8	3.1	2.5	25.7	4.4
<i>males:</i>																		
1226/22	C	48	7.1	26.3														3.7
1226/10	C	48	8.3	27.6														3.3
1226/58	C	48	8.1	20.4														2.5
1226/40	O	48	8.4	33.0	50.0	69.2	11.5	19.1	29.2	179.0	130.7	48.3	69.1	109.9	2.7	1.6	21.3	3.9
1227/23	C	49	6.3	22.7	25.7	60.3	13.9	8.2	30.0	138.1	99.9	38.2	33.9	104.2	2.6	3.1	21.9	3.6
1227/49	C	49	7.9	33.8	67.0	49.8	9.7	17.3	36.6	180.4	126.5	53.9	84.3	96.1	2.3	1.1	22.8	4.3
1228/12	C	49	7.9	33.8	67.0	49.8	9.7	17.3	36.6	180.4	126.5	53.9	84.3	96.1	2.3	1.1	22.8	4.3
1228/33	C	49	6.3	22.7	25.7	60.3	13.9	8.2	30.0	138.1	99.9	38.2	33.9	104.2	2.6	3.1	21.9	3.6
1228/80	C	49	7.9	33.8	67.0	49.8	9.7	17.3	36.6	180.4	126.5	53.9	84.3	96.1	2.3	1.1	22.8	4.3
1229/15	C	49	7.9	33.8	67.0	49.8	9.7	17.3	36.6	180.4	126.5	53.9	84.3	96.1	2.3	1.1	22.8	4.3
1229/57	C	50	5.7	25.3	31.9	67.4	11.9	10.0	25.5	146.7	111.2	35.5	41.9	104.8	3.1	2.5	25.7	4.4
1229/91	C	50	5.7	25.3	31.9	67.4	11.9	10.0	25.5	146.7	111.2	35.5	41.9	104.8	3.1	2.5	25.7	4.4

C = cholesterol gallstones. M = mixed gallstones. O = no gallstones.

Table 5. Data for bladder bile of hamsters (Experimental series G 117) on the diet with 10% margarine fat (MIFU) from the age of 27-33 days.

All concentrations are given as millimolarities

Group no./ hamster no.	Type of stones	Days on diet	Chole- sterol	Lipid phos- phorus	GC	GCD	GD	TC	TCD + TD	Total bile acids	G	T	Tri	Di	G/T	Di/Tri	Total bile acids/ cholest.	Lipid phos- phor./ cholest.
<i>females:</i>																		
1230/67	0	48	2.6	21.4	32.9	54.9	7.3	7.7	120.5	95.1	25.4	40.6	79.9	3.7	2.0	46.3	8.2	
1230/18	0	48	3.8	17.2	60.1	41.5	24.5	14.6	148	155.5	126.1	29.4	74.7	80.8	4.3	1.1	40.9	4.5
1230/32	0	48	5.0	19.1	49.1	35.8	18.9	8.8	17.8	130.4	103.8	26.6	57.9	72.5	3.9	1.3	37.3	5.5
1230/78	0	50	3.5	11.6	7.2	65.1	4.4	3.7	10.8	91.2	76.7	14.5	10.9	80.3	5.3	7.4	45.6	5.8
1230/89	A	50	2.0	19.9	59.3	40.6	14.9	12.6	25.1	152.5	114.8	37.7	71.9	80.6	3.0	1.1	52.6	6.9
1231/45	0	50	2.9	19.9	59.3	40.6	14.9	12.6	25.1	152.5	114.8	37.7	71.9	80.6	3.0	1.1	52.6	6.9
1231/37	0	50	2.4	16.3	17.4	38.6	8.5	4.0	8.9	77.4	64.5	12.9	21.4	56.0	5.0	2.6	32.3	6.8
1231/85	0	50	2.4	11.6	6.5	21.8	28.9	0.9	2.8	60.9	57.2	3.7	7.4	53.5	15.5	7.2	33.8	6.4
1233/16	0	50	1.8	11.6	7.2	37.8	13.3	5.4	10.9	74.6	58.3	16.3	12.6	62.0	3.6	4.9	29.8	6.4
1233/29	0	50	2.5	16.0	7.2	37.8	13.3	5.4	10.9	74.6	58.3	16.3	12.6	62.0	3.6	4.9	29.8	6.4
1233/52	0	50	2.9	18.8	8.6	26.5	15.7	5.0	11.4	67.2	50.8	16.4	13.6	53.6	3.1	3.9	23.2	6.5
1233/191	0	50	2.5	16.0	7.2	37.8	13.3	5.4	10.9	74.6	58.3	16.3	12.6	62.0	3.6	4.9	29.8	6.4
1232/46	0	50	2.9	18.8	8.6	26.5	15.7	5.0	11.4	67.2	50.8	16.4	13.6	53.6	3.1	3.9	23.2	6.5
1233/84	0	50	2.9	18.8	8.6	26.5	15.7	5.0	11.4	67.2	50.8	16.4	13.6	53.6	3.1	3.9	23.2	6.5
<i>males:</i>																		
1230/75	0	48	3.7	30.7	49.4	35.5	16.2	34.9	36.5	172.5	101.1	71.4	84.3	88.2	1.4	1.0	46.6	8.3
1230/76	0	48	4.3	27.4	39.3	51.4	26.2	21.6	9.5	148.0	116.9	31.1	60.9	87.1	3.8	1.4	34.4	6.4
1230/20	0	48	3.9	25.0	38.0	44.3	18.3	9.2	12.6	122.4	100.6	21.8	47.2	75.2	4.6	1.6	31.4	6.4
1230/69	0	49	3.4	21.2	27.7	49.8	10.0	8.9	15.8	112.2	87.5	24.7	36.6	75.6	3.5	2.1	33.0	6.2
1231/26	0	49	3.8	29.4	62.1	43.2	11.7	23.7	22.1	162.8	117.0	45.8	85.8	77.0	2.6	0.9	42.8	7.7
1232/5	0	49	1.7	13.4	26.8	16.3	8.5	6.1	7.5	65.2	51.6	13.6	32.9	32.3	3.8	0.9	38.4	7.9
1232/24	0	49	2.9	18.5	39.3	31.1	29.1	6.3	10.6	116.4	99.5	16.9	45.6	70.8	5.9	1.6	40.1	6.4
1232/8	0	49	4.2	25.8	32.0	35.6	6.1	42.9	42.6	159.2	73.7	85.5	74.9	84.3	0.9	1.1	37.9	6.1
1232/59	0	49	4.2	13.4	26.8	16.3	8.5	6.1	7.5	65.2	51.6	13.6	32.9	32.3	3.8	0.9	38.4	7.9
1233/11	0	49	2.9	18.5	39.3	31.1	29.1	6.3	10.6	116.4	99.5	16.9	45.6	70.8	5.9	1.6	40.1	6.4
1233/35	0	50	3.8	16.8	44.5	38.4	12.4	15.0	22.0	132.3	95.3	37.0	59.5	72.8	2.6	1.2	34.8	4.4
1233/73	0	50	3.1	21.9	35.2	46.7	13.6	8.4	14.4	118.3	95.5	22.8	43.6	74.7	4.2	1.7	38.2	7.1

C = cholesterol gallstones. A = amorphous pigmented gallstones. O = no gallstones

cholesterol in solution in the bile. An exact settlement of this question will require suitable *in vitro* solubilization experiments.

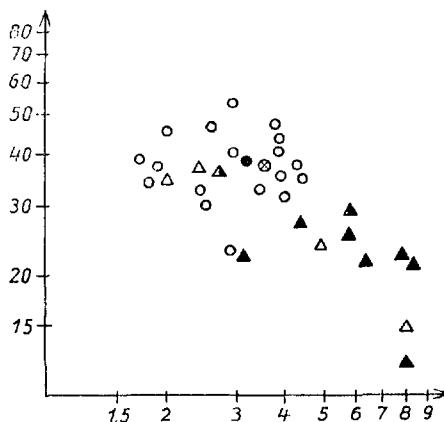


Fig. 2. Molar ratios bile acids/cholesterol (vertical) and millimolar concentrations of cholesterol (horizontal), of bladder bile of hamsters from Exp. Series G 117. Logarithmic scale. Symbols as for fig. 1

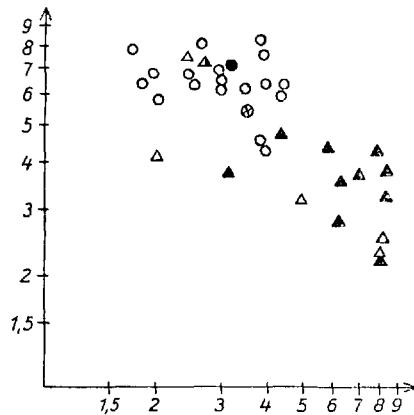


Fig. 3. Molar ratios lipid-soluble phosphorus/cholesterol (vertical) and millimolar concentration of cholesterol (horizontal) of bladder bile of hamsters from Exp. Series G 117. Logarithmic scale. Symbols as for fig. 1

From the figs. it is evident, that in the butter fat group there is not in every case correlation between the trend of the analytical data and the occurrence or absence of cholesterol gallstones. The absence of cholesterol gallstones in some of the cases having high cholesterol concentrations and low ratios bile acids/cholesterol and lipid-P/cholesterol is, however, not surprising since precipitated cholesterol or small gallstones may have passed out of the gallbladder. More interesting is the occurrence of cholesterol gallstones in one or two cases in the butter fat group having data within or close to the range of the corresponding data in the margarine fat group. Further, there is even

one case of cholesterol gallstones in the margarine fat group. This suggests that other features besides those hitherto considered may play a role in determining the occurrence of cholesterol gallstones.

In a previous series of experiments (5), young hamsters received diets with 10% butter fat and with 10% of the fat from a high linoleic acid margarine of the same brand and essentially the same fatty acid composition as that used in the present experiments. (The fat-free basal diet was one that did not greatly favor the occurrence of cholesterol gallstones.) It was then found that the bile lecithin of the animals receiving the margarine fat contained much more linoleic acid and correspondingly less oleic acid than did the bile lecithin from the animals receiving butter fat.

The fatty acid compositions of the bile phosphatides of the butter and margarine fat groups in the present experiment were not examined, but there can hardly be any doubt that they have had differences similar to those found in the earlier study.

The question therefore arises whether the bile phosphatides characteristic of the margarine fat group are more efficient in preventing formation of cholesterol gallstones than are the bile phosphatides characteristic of the butter fat group.

Attempts to decide this question must be made in future studies, i. a. by comparing the solubilization properties of phosphatides with different fatty acid patterns, towards cholesterol in the presence of bile acids.

### *Summary*

Young hamsters were reared on diets containing butter fat and fat of a high linoleic acid margarine, respectively.

The basal diet without the fat had previously been shown to produce a very high incidence of cholesterol gallstones in young hamsters.

In two trials, in which the fats were compared at the 10% dietary level, the incidence of cholesterol gallstones was much less with the diets containing margarine fat than with the diets containing butter fat. The difference was significant with a probability of more than 99%.

In a third trial, in which the fats were compared at the 3% dietary level, the incidence of cholesterol gallstones was also less with margarine fat than with butter fat. Here the difference was significant with a probability of more than 95% but less than 99%.

The superior effect of the margarine fat in counteracting the development of cholesterol gallstones is ascribed to its high content (about 40%) of linoleic acid.

In one of the trials in which the two fats were given at the 10% dietary level the bladder bile was analyzed for cholesterol, bile acids and lipid soluble phosphorus, with the following results:

For the animals receiving the butter fat the concentrations of cholesterol were found to be more scattered and, in more than half of the cases, higher than for animals receiving margarine fat.

The ratios between the molar concentrations of bile acids and cholesterol and between the molar concentrations of lipid soluble phosphorus and cholesterol were also more scattered for animals receiving the butter fat diet, but in more than half of the cases in the butter fat group these ratios were lower than in the margarine fat group.

In the butter fat group the values for the two aforementioned ratios tended to decrease with increasing concentrations of cholesterol.

A more exact correlation of the composition of the bladder bile with the occurrence of gallstones must take into account not only the analytical data summarized above, but,

probably, also a previous finding according to which the bile lecithin from hamsters receiving a diet with 10% of the high linoleic acid margarine fat contained much more linoleic acid and correspondingly less oleic acid than did the bile lecithin from hamsters receiving a diet with 10% butter fat.

### Zusammenfassung

Junge Hamster wurden mit Nahrungen, die Butterfett bzw. das Fett einer linolsäure-reichen Diätmargarine enthielten, gefüttert.

Frühere Versuche hatten gezeigt, daß die fettfreie Basal-Nahrung eine hohe Incidenz von Cholesterin-Gallensteinen in jungen Hamstern hervorruft.

In zwei Versuchen, in welchen die zwei Fette in der Höhe von 10% der Nahrung gegeben wurden, war die Incidenz von Cholesterin-Gallensteinen viel niedriger in den mit Margarinefett gefütterten Gruppen als in den mit Butterfett gefütterten Gruppen von Tieren. Die Differenz war mit mehr als 99% Sicherheit signifikant.

In einem dritten Versuch, in welchem die Fette in der Höhe von 3% gegeben wurden, war die Incidenz von Cholesterin-Gallensteinen auch niedriger in der mit Margarinefett gefütterten Gruppe als in der mit Butterfett gefütterten. Die Differenz war signifikant mit 95% aber nicht mit 99% Sicherheit.

Die Überlegenheit des Margarinefettes in bezug auf die Unterdrückung der Cholesterin-Gallensteinbildung wird dem hohen Linolsäuregehalt (ungefähr 40%) dieses Fetts zugeschrieben.

In einem der Versuche, in welchem die Fette in der Höhe von 10% gegeben wurden, wurde die Blasengalle auf Cholesterin, Gallensäuren und lipid-löslichem Phosphor analysiert. Die Hauptergebnisse waren die folgenden:

In der Butterfett-Gruppe waren die Einzelwerte der Konzentrationen des Cholesterins besonders zerstreut und, in mehr als der Hälfte der Fälle höher als in der Margarinefett-Gruppe.

Die Einzelwerte der Verhältnisse der molären Konzentrationen von Gallensäuren zu Cholesterin und von lipid-löslichem Phosphor zu Cholesterin waren auch besonders zerstreut in der mit Butterfett gefütterten Gruppe. In mehr als der Hälfte der Fälle in der Butterfett-Gruppe waren diese Verhältnisse niedriger als in der Margarinefett-Gruppe.

In der Butterfett-Gruppe zeigten die beiden Verhältnisse eine Neigung zur Abnahme mit zunehmenden Cholesterin-Konzentrationen.

Eine genauere Korrelation der Zusammensetzung der Blasengalle mit dem Vorkommen von Gallensteinen in den zwei Gruppen muß neben den obenerwähnten analytischen Befunden wahrscheinlich auch die in früheren Untersuchungen gefundene verschiedene Fettsäurezusammensetzung der Gallenphosphatide in Betracht ziehen. Nach diesen Untersuchungen enthielt das Gallenlecithin der mit 10% linolsäurereicher Diätmargarine gefütterten Hamster viel mehr Linolsäure und entsprechend weniger Ölsäure als das Gallenlecithin der mit 10% Butterfett gefütterten Hamster.

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