durante 4 semanas). Dosis diarias de 27.3 g/kg de peso corporal se revelaron manifiestamente tóxicas. Con esta dosificación, la tasa de mortalidad fue del 77% en el curso de 4 semanas. Basándose en estos ensayos, puede aceptarse como límite máximo de tolerancia para una administración continua, el de 10 g de ácido ascórbico por kg de peso. Según esto, la dosis diaria de 75 mg, que se estima indicada para el hombre, tiene un margen de seguridad de aproximadamente 1 : 10000. El aumento que, en la ingestión de ácido ascórbico, por el organismo, puede significar el uso de dicha sustancia en la preparación de artículos alimenticios a fin de conseguir determinados efectos técnicos, carece de importancia en vista de su amplio margen de seguridad. Se darán a conocer los cálculos pertinentes. Con la dosis diaria de 1 g de ácido ascórbico, que a veces se aplica con fines terapéuticos, el margen de seguridad es todavía de aproximadamente 1 : 700.

Por cosiguiente, el ácido ascórbico, incluso cuando se administra en forma continua, a dosis diarias muy superiores a los requerimientos normales, es una sustancia completamente inocua.

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Alimentary Production of Gallstones in Hamsters.
12. Studies with Rice Starch Diets with and without Antibiotics*)

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With 6 tables

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Young hamsters reared on a fat-free diet or a diet sufficiently low in fat have a marked tendency to development of cholesterol gallstones when the dietary carbohydrate is glucose, but a very low tendency to development of such gallstones when the dietary carbohydrate is rice starch (1, 2) (or potato starch).

The cholesterol content is lower and the content of bile acids higher in the bladder bile of hamsters on the rice starch diet than in bladder bile of hamsters on the glucose diet (2).

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The starch diet favors a lactic acid flora and produces a much more voluminous content of the intestine of the hamsters than does the glucose diet.

Therefore, it could be thought that the low incidence of cholesterol gallstones among the hamsters on the starch diet in some way is due to the increased lactic acid flora.

In order to test this possibility we have examined the incidence of gallstones and the intestinal flora of hamsters reared on the glucose and rice starch diets used in some of our previous studies (2) and on rice starch diets to which antibiotics and other antimicrobial agents were added.

Many trials with diets of the last mentioned type have been carried out. In no case did the experiments lead to an increase of the incidence of gallstones, but in most cases in which drastic changes of the intestinal flora were obtained the animals died within a too short time to permit any conclusions as to the cause of the absence of cholesterol gallstones.

However, in two experiments did we succeed in drastically altering the lactic acid flora in the colon of the hamsters on the rice starch diet and yet keeping several of the animals alive. These experiments are reported in the following.

Experimental

The hamsters were young individuals from our stock colony. They were shifted from the stock diet (3) to the experimental diets at the age of 28–46 days, the two sexes being housed separately in wire screen cages as in our previous studies. Diet and water were available *ad libitum.*

The experimental diets used were the following:

Diet No. 1: A fat-free diet with glucose as carbohydrate component as described in our previous paper (2).

Diet No. 2: A fat-free[1]) diet with rice starch as carbohydrate component as described in our previous paper (2).

Diet No. 3: A diet as no. 2 with the addition of 0.75% Sulfaguanidine.

Diet No. 4: A diet as no. 2 with the addition of 0.25% Terramycin, 0.25% Phthalylsulfathiazole, and 0.1% Vioform.

Diet No. 5: A diet as no. 2 with the addition of 0.25% Terramycin, 0.25% Phthalylsulfathiazole, 0.1% Vioform, 0.2% Neomycin, and 250,000 units of Mycostatin per 100 g diet.

At the end of the experimental feeding period the animals were sacrificed with chloroform, autopsied and examined for gallstones as usual (3). Colonic content was taken out and its microbial population examined as indicated below. The p_H of the colonic content was determined by means of a micro glass electrode. As a further indication of the activity of the intestinal flora, the bladder bile was examined qualitatively for the presence of glycodeoxycholic acid by paper chromatography according to SJÖVALL (4, 5).

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1) The small amount of fat contained in the rice starch being left out of consideration.

For the bacteriological examination the following substrates were used:

1. *Tomato-agar*, p_H 6.9, containing per liter:

Casein-peptone (1% N)	400 ml
Yeast autolysate (1% N)	400 ml
Peptone, Witte	5 g
Tomato purée	50 g
Bacto-agar, Difco	15 g
Glucose	10 g
Cysteine hydrochloride	2 g

2. *Thioglycollate medium*, Difco, of p_H 7.1, containing per liter:

Bacto-Casitone	15 g
Bacto-Yeast extract	5 g
Bacto Dextrose (glucose)	5 g
Sodium chloride	2.5 g
L-Cystine, Difco	0.5 g
Thioglycollic acid	0.3 ml
Bacto-agar	0.75 g
Resazurin, certified	1 mg

3. *Tomato agar with soidum azide:*

   Substrate 1 with the addition of 0.025% sodium azide (NaN_3)

4. *Eosine-methylene blue agar* containing per liter:

Potassium phosphate, dibasic (K_2HPO_4)	2 g
Peptone, Witte	10 g
Bacto-agar, Difco	15 g
Lactose	10 g
Eosine, yellowish	0.4 g
Methylene blue	0.1 g

The colonic content was weighed and diluted 10 times with sterile saline (0.85% NaCl) by grinding in a mortar. Therefrom dilutions $1:10^2, 1:10^3 \ldots 1:10^{10}$ (in proportion to the colonic content) were prepared.

Substrate 1 (tomato-agar in tubes) was inoculated with the dilutions $1:10^7$, $1:10^8$, $1:10^9$ and $1:10^{10}$.

Substrate 2 (thioglycollate medium in tubes) was inoculated with the same dilutions.

Substrate 3 (tomato-agar with sodium azide in tubes) was inoculated with the dilutions $1:10^6$, $1:10^7$, $1:10^8$, and $1:10^9$.

Substrate 4 (eosine-methylene blue-agar plate) was inoculated with the dilutions $1:10^3$, $1:10^4$, and $1:10^5$.

Substrate 1 is well suited for the counting of Lactobacillus bifidus, but most intestinal bacteria, aerobe as well as anaerobe, grow well in it.

Substrate 2 is commonly used for tests of sterility of biological materials. It is well suited for growth of aerobe and anaerobe bacteria.

Evolution of gas is easily observed with substrates 1 and 2.

The highest count obtained with either of the two substrates 1 or 2 is considered as the total number of bacteria in the colonic content.

Substrate 3 was used for the counting of gram-positive bacteria.

Substrate 4 was used for the counting of Escherichia coli and Aerobacter aerogenes.

Yeast will grow on the surface of substrates 1, 2, and 4.

Results and Discussion

Tables 1 and 2 present an introductory orientation of the microbial population of the colon of hamsters receiving the glucose- and the rice starch-diets, respectively. This part of the study was carried out before the experiment in which the influence of antibiotics as examined.

In the rice starch group, nine out of the 10 animals had no gallstones, one animal had cholesterol stones.

In the glucose group, only one out of the 20 animals had no gallstones, the other 19 had cholesterol gallstones.

The p_H of the colonic content was lower in the rice starch group (average $p_H = 5.6$) than in the glucose group (average $p_H = 6.7$)[1]).

The total number of bacteria per g of colonic content was of the same order of magnitude (10^9) in both groups.

Lactobacillus bifidus was present in an amount of about 10^9 per g in the rice starch group. In the glucose group, this bacteria was present in one case in the amount of 10^7; in the other 19 cases in amounts lower than 10^7. More concentrated inocula than 10^{-7} were not tested. It is therefore possible that in these cases L. bifidus was not present at all.

In the rice starch group, *gram-positive rods* (lactic acid rods) occur in 7 cases in amounts of 10^9, in the 3 other cases in amounts of 10^8. In the glucose group, these bacteria occur in amounts of 10^8 in 8 cases; in the other 12 cases in amounts of 10^7 or less (10^{-7} is the most concentrated inoculum tested).

In the rice starch group, *E. coli* and *A. aerogenes* are present in amounts of 10^3 or less in 7 out of the 10 animals. In one case the number of E. coli is exceptionally high, about 10^7. In the glucose group, E. coli is present in amounts of about 10^5 or less, with the exception of one case in which the number is of the order of 10^6. The highest number of A. aerogenes in the glucose group is about 10^5. It is evident that E. coli and A. aerogenes represent only a small fraction of the total number of bacteria in both groups (roughly 10^{-6} in the rice starch group and 10^{-4} in the glucose group).

Yeast was not found in any of the two groups.

Because only small amounts of E. coli and A. aerogenes were found in the preliminary study, these bacteria were not counted in the following part of the experiment.

In an experiment (the details of which are not reported here), lactose was given instead of rice starch to a group of 10 hamsters. Gallstones did not occur and p_H and bacterial counts of the colonic content were essentially the same as in the rice starch group (table 2), but the growth rates of the lactose-fed hamsters were not as good as the growth rates of the hamsters in the rice starch group.

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[1]) "Average p_H" is calculated as the negative logarithm of the average hydrogen ion concentration.

Table 1. Data for hamsters on the fat-free glucose diet.
(Age of the animals at the beginning of the experiment: 41–44 days)

Animal no.	Sex	Days on diet	Gain in weight g	Occurrence of gallstones*	pH of colonic content	Microbial counts per g of colonic content: Total number of bacteria $\times 10^9$	Lactobacillus bifidus $\times 10^9$	Gram-positive rods $\times 10^9$	Escherichia coli $\times 10^3$	Aerobacter aerogenes $\times 10^3$	Other bacteria present in amounts above 10^7	Yeast $\times 10^3$
745/127	f	59	— 21	C	7.2	5.0	< 0.01	0.01	340	50	gas producing bacteria (10^8)	< 1
745/99	f	59	12	C	6.7	1.8	< 0.01	0.01	180	30	gas producing bacteria	< 1
746/10	m	57	0	C	6.7	7.5	< 0.01	0.1	190	< 1		< 1
746/83	m	58	19	C	6.7	7.0	< 0.01	0.1	20	1–10		< 1
746/90	m	58	16	C	6.5	5.0	< 0.01	0.1	6	80		< 1
746/102	m	70	— 19	C	6.8	0.8	< 0.01	0.1	< 1	< 1		< 1
746/59	m	70	1	C	6.6	0.8	< 0.01	< 0.01	2	72		< 1
746/104	f	72	0	C	6.9	3.2	0.01	< 0.01	280	23	bacteroides	< 1
748/111	m	65	12	C	6.6	7.0	< 0.01	< 0.01	4	110	streptococci	< 1
748/33	m	65	17	C	6.6	2.9	< 0.01	< 0.01	< 1	40	streptococci	< 1
748/29	f	65	24	C	6.6	1.7	< 0.01	< 0.01	9	140	streptococci	< 1
748/49	f	65	— 6	0	6.6	4.6	< 0.01	< 0.01	4000	30	streptococci, gas producing bacteria	< 1
748/50	f	65	17	C	6.6	2.5	< 0.01	< 0.01	1	10	streptococci?	< 1
749/92	m	70	20	C	6.7	2.3	< 0.01	0.1	9	6	streptococci?	< 1
749/13	m	70	25	C	6.8	2.5	< 0.01	< 0.01	30	90	streptococci?	< 1
749/109	m	70	19	C	6.6	2.2	< 0.01	0.1	6	28	streptococci?	< 1
749/76	m	70	8	C	6.7	2.5	< 0.01	< 0.01	400	3		< 1
750/81	m	70	7	C	6.6	2.5	< 0.01	< 0.01	40	80	micrococci	< 1
750/27	f	72	11	C	6.8	4.5	< 0.01	0.1	1	53	short rods or cocci in chains, bacteroides	< 1
750/78	f	72	2	C	7.1	1.1	< 0.01	0.1	5	40	streptococci	< 1
Average					6.7							

*) C = cholesterol gallstones; 0 = no gallstones.

Table 2. Data for hamsters on the fat-free rice starch diet.
(Age of the animals at the beginning of the experiment: 41–46 days)

Animal no.	Sex	Days on diet	Gain in weight g	Occurrence of gallstones*	pH of colonic content	Microbial counts per g of colonic content: Total number of bacteria $\times 10^9$	Lactobacillus bifidus $\times 10^9$	Gram-positive rods $\times 10^9$	Escherichia coli $\times 10^3$	Aerobacter aerogenes $\times 10^3$	Other bacteria present in numbers above 10^7	Yeast $\times 10^3$
757/113	m	57	26	0	5.9	2.4	1	1	< 1	< 1	gas producing bacteria	< 1
757/68	m	59	10	0	5.4	6.0	1	1	< 1	4	streptococci?	< 1
757/84	m	59	31	C	5.4	2.8	1	1	< 1	< 1	streptococci?	< 1
757/31	m	59	25	0	5.5	1.8	0.1	1	< 1	3	streptococci?, gas producing bacteria	< 1
757/43	m	77	25	0	5.5	7.0	1	1	< 1	< 1	streptococci, bacteroides fusiformis	< 1
758/107	f	72	30	0	5.4	4.0	1	1	1	< 1	bacteroides fusiformis	< 1
758/73	f	72	27	0	5.8	8.6	1	0.1	30500	3	short rods in chains, veillonella, bacteroides, gas producing bacteria (10^8)	< 1
758/21	f	72	36	0	5.9	1.0	0.1	0.1	20	< 1	gas producing bacteria	< 1
758/16	f	72	32	0	6.1	2.0	1	1	1	1		< 1
758/8	f	72	23	0	5.6	1.4	1	0.1	21	1	streptococci?, gas producing bacteria	< 1
Average					5.56							

*) C = cholesterol gallstones; 0 = no gallstones.

Table 3. Data for hamsters on the fat-free rice starch diet.
(Age of the animals at the beginning of the experiment: 28–32 days)

Animal no.	Sex	Days on diet	Gain in weight g	Occurrence of gallstones[1]	GD[2]	pH of colonic content	Microbial counts per g of colonic content: Total number of bacteria $\times 10^9$	Lactobacillus bifidus $\times 10^9$	Gram-positive rods $\times 10^9$	Gram-positive streptococci $\times 10^9$	Other bacteria present in numbers above 10^7	Yeast $\times 10^9$	Remarks
801/55	f	41	27	0	+	5.5	5	2	< 0.01	< 0.01	rods in chains	< 0.01	
801/8	f	42	24	0	+	6.7	30	30	0.03	< 0.01		< 0.01	almost only bifidus
801/44	f	42	10	0	+	6.1	7	7	< 0.01	< 0.01		< 0.01	only bifidus
801/5	f	42	23	0	+	6.8	25	25	< 0.01	< 0.01		< 0.01	only bifidus
801/64	f	42	24	0	+	5.6	7	ca. 7	ca. 0.1	< 0.01		< 0.01	98.6% bifidus
801/2	m	44	33	0	+	5.5	20	20	< 0.01	< 0.01		< 0.01	only bifidus
801/32	m	44	31	0	+	5.4	25	ca. 25	+	+		< 0.01	Lbc. acidophilus (3×10^9)
801/78	m	44	30	0	+	5.8	15	7	2	1		< 0.01	
801/58	f	44	21	0	+	5.7	5	4	ca.0.1**)	ca. 1	bacteroides?	< 0.01	**) threads
Average						5.71							

[1]) 0 = no gallstones.

[2]) Presence of glycodeoxycholic acid in bladder bile.

Table 4. Data for hamsters on the fat-free rice starch diet + 0.75% sulfaguanidine.
(Age of the animals at the beginning of the experiment: 28–32 days)

Animal no.	Sex	Days on diet	Gain in weight g	Occurrence of gallstones[1]	GD[2]	pH of colonic content	Microbial counts per g of colonic content: Total number of bacteria $\times 10^9$	Lactobacillus bifidus $\times 10^9$	Gram-positive rods $\times 10^9$	Gram-positive streptococci $\times 10^9$	Other bacteria present in numbers above 10^7	Yeast $\times 10^9$	Remarks
802/80	f	42	16	0	+	6.5	17	> 1	?	0.1	rods and threads	< 0.01	
802/6	f	42	24	0	+	6.0	3	ca. 3	ca. 0.01	ca. 0.1		< 0.01	97% bifidus
802/52	f	42	27	0	+	6.6	5	2	0.2*)	< 0.01	short or ovod rods	< 0.01	*) long threads
802/86	f	42	28	0	+	6.0	6	ca. 5	0.01	< 0.01	long and short rods	< 0.01	
802/92	f	42	26	0	+	6.2	2.5	2	0.02*)	< 0.01		< 0.01	*) threads + acidophilus
802/4	m	44	26	0	+	6.7	1.5	ca. 1	ca. 0.1*)	< 0.01		< 0.01	*) acidophilus
802/30	m	44	21	0	+	5.6	ca. 10	ca. 7	ca. 0.02	ca. 2		< 0.01	
802/45	m	44	31	0	+	5.4	ca. 10	2	ca. 0.1*)	< 0.01		< 0.01	*) acidophilus
802/94	m	44	30	0	+	5.9	8	4	2	< 0.01		< 0.01	
902/13	f	44	30	0	+	5.8	4	3	< 0.01	0.1		< 0.01	
Average						5.79							

[1]) 0 = no gallstones.

[2]) Presence of glycodeoxycholic acid in bladder bile.

Table 5. Data for hamsters on the fat-free rice starch diet + 0.25% Terramycin, 0,25% Phthalylsulfathiazole and 0.1% Vioform

(Age of the hamsters at the beginning of the experiment: 28–32 days)

Animal no.	Sex	Days on diet	Gain in weight g	Occurrence of gallstones[2]	GD[1]	pH of colonic content	Microbial counts per g of colonic content: Total number of bacteria $\times 10^9$	Lactobacillus bifidus $\times 10^9$	Gram-positive rods $\times 10^9$	Gram-positive streptococci $\times 10^9$	Other bacteria present in numbers above 10^7	Yeast $\times 10^9$	Remarks
805/72	m	41	11	A	0	5.3	1.7	< 0.01	< 0.01	1.3	gas producing bacteria (10^9)	< 0.01	
805/38	m	41	9	A	0	5.25	3	< 0.01	< 0.01	1.4	bacteroides and gas producing bacteria	1	
805/10	m	41	13	0	0	6.0	2	< 0.01	< 0.01	0.7	gas producing bacteria (10^8), ovoid organisms, bacteroides	< 0.01	butyric acid smell
805/57	f	41	—5	0	0	5.3	4	< 0.01	< 0.01	1.3	gas producing bacteria (10^8), short rods, ovoid organisms, bacteroides	1	
805/79	f	43	4	0	0	6.8	3	< 0.01	< 0.01	1.5	gas producing bacteria (10^9), rods with translucent spots	< 0.01	
805/50	f	43	17	0	0	5.4	6	< 0.01	< 0.01	1.5	gas producing bacteria, bacteroides, ovoid organisms, short and slender rods	1	
806/71	m	43	5	0	0	5.3	1.1	< 0.01	< 0.01	+	gas producing bacteria (10^9), bacteroides, rods, ovoid organisms	1	
806/53	m	43	12	0	0	5.9	5	< 0.01	< 0.01	0.7	rods (10^9), gas producing bacteria	1	
806/9	m	43	15	0	0	6.1	1.7	< 0.01	< 0.01	+	gas producing bacteria (10^9), streptococci (10^9), bacteroides, ovoid organisms, granular rods	ca. 10	
806/3	f	43	—1	0	0	5.9	65	< 0.01	< 0.01	65	gas producing bacteria (10^{10})	< 0.01	
Average						5.54							

[1]) A = amorphous pigmented gallstones; 0 = no gallstones. [2]) Presence of glycodeoxycholic acid in bladder bile.

Table 6. Data for hamsters on the fat-free rice starch diet + 0.25% Terramycin, 0,25% Phthalylsulfathiazole, 0,1% Vivoform, 0.2% Neomycin, and 250,000 units of Myocstatin per 100 g diet.
(Age of the hamsters at the beginning of the experiment: 28–32 days)

Animal no.	Sex	Days on diet	Gain in weight g	Occurrence of gallstones[1]	GD[2]	pH of colonic content	Microbial counts per g of colonic content: Total number of bacteria $\times 10^9$	Lactobacillus bifidus $\times 10^9$	Gram-positive rods $\times 10^9$	Gram-positive streptococci $\times 10^9$	Other bacteria present in numbers above 10^7	Yeast $\times 10^9$	Remarks
807/60	m	41	3	A	0	6.6	0.3	< 0.01	< 0.01	0.005	bacteroides (0.3 × 10^9), large colonies surrounded by small colonies	< 0.01	
807/21	f	43	—2	0	0	6.0	1.9	< 0.01	< 0.01	< 0.01	pseudomonas, bacteroides (0,5 × 10^9)	< 0.01	
807/66	m	41	9	A	0	6.5	4.0	< 0.01	< 0.01	0.3	bacteroides	< 0.01	
808/34	m	41	1	0	0	6.9	1.4	< 0.01	< 0.01	ca. 1	pseudomonas and rods (ca. 10^9)	< 0.01	
808/59	m	41	2	0	0	5.8	0.5	< 0.01	< 0.01	0.2	pseudomonas and big granular rods	< 0.01	
Average						6.18							

[1]) A = amorphous pigmented gallstones; 0 = no gallstones.

[2]) Presence of glycodeoxycholic acid in bladder bile.

In the rice starch group of the following part of the experiment (table 3), none of the 9 animals had gallstones. p_H of the colonic content was on the average 5.7. Glycodeoxycholic acid (together with glycocholic and glycochenodeoxycholic acids) was present in all cases as could be expected from previous experiments (2). The total numbers of bacteria and of L. bifidus were somewhat higher than in the rice starch groups of the preliminary experiment (tables 1 and 2). The number of gram-positive rods was lower. The weight gain of the animals was fairly good.

In the group receiving 0.75% sulfaguanidine in the rice starch diet (table 4), the data are approximately as in the group without sulfaguanidine. The total number of bacteria is slightly reduced. The figures suggest a slight reduction of L. bifidus and a slight increase of the number of gram-positive rods, but the flora is still greatly dominated by lactic acid bacteria. In fact, the data in table 4 could very well be considered as an extension of table 3.

In the group receiving 0.25% Terramycin, 0.25% Phthalylsulfathiazole, and 0.1% Vioform (table 5), 12 out of the original 22 animals died during the experiment with diarrhea (they had no gallstones). Table 5 presents the data of the 10 animals that survived more than 40 days. Eight out of these animals had no gallstones, 2 had amorphous pigmented stones. Glycodeoxycholic acid was absent (but glycocholic and glycochenodeoxycholic acids were present). The p_H of the colonic content was on the average 5.5. The total number of bacteria is of the same order of magnitude as in the corresponding rice starch group (table 3) (in most cases somewhat lower), but L. bifidus is greatly reduced (less than 10^7 per g) and gram-positive streptococci greatly increased (10^9 per g). Gas producing bacteria and bacteroides and in some cases yeast appear. The gain in weight of the animals during the experimental period is not as good as in the rice starch group without antibiotics. In two cases the weight gain is negative.

In the group receiving 0.2% Neomycin and 250,000 units of Mycostatin in addition to the antibiotics given in the foregoing group, most of the original 23 animals died early (they had no gallstones). Table 6 presents the data of the 5 animals that survived more than 40 days.

Two out of these 5 animals had amorphous pigmented gallstones, the other 3 had no gallstones. Glycodeoxycholic acid was not present in the bladder bile (but glycocholic and glycochenodeoxycholic acids occurred). The p_H of the colonic content was on the average 6.2, i. e., higher than in the foregoing groups although not quite as high as in the glucose group in the preliminary experiment.

The total number of bacteria is somewhat reduced. L. bifidus and gram-positive rods are reduced as in the foregoing group. Gram-positive streptococci are further reduced. The population of the colon is changed in the direction of a gram-negative flora consisting of bacteroides and pseudomonas, but there are still some gram-positive streptococci (probably Sc. faecalis which is very resistant). Yeast is suppressed. The growth of the animals is poor.

The general conclusion of the experiments is that in hamsters on the rice starch diet, the tendency to formation of cholesterol gallstones is not increased when L. bifidus, gram-positive lactic acid bacteria, and the yet unknown bacteria responsible for the formation of deoxycholic acid are suppressed.

The final solution of the question whether some inhabitants of the intestine may influence the formation of gallstones must await the rearing of hamsters under germ-free conditions.

Summary

An orientation of the microflora of the colon of hamsters reared on fat-free diets with glucose or with rice starch as the carbohydrate components is presented in tables 1 and 2. The predominance of the lactic acid flora (Lactobacillus bifidus and gram-positive rods) in the rice starch group is evident. Escherichia coli and Aerobacter aerogenes are present in irregular but low amounts in proportion to the total count of bacteria. As usual, the incidence of cholesterol gallstones is very high in the glucose group and very low in the rice starch group.

The following part of the experiment was carried out with groups of hamsters reared on rice starch diets with and without addition of anti-microbial agents. E. coli and A. aerogenes were not counted but, as a further indication of the microbial activity, the bladder bile was examined for the presence of glycodeoxycholic acid. The results are presented in tables 3 to 6. By suitable combinations of anti-microbial agents (tables 5 and 6) the yet unknown bacteria responsible for the formation of deoxycholic acid could be suppressed together with L. bifidus and gram-positive lactic acid bacteria without introducing a tendency to formation of cholesterol gallstones.

Zusammenfassung

Die Tabellen 1 und 2 geben eine Orientierung über die Mikroflora des Dickdarms von Hamstern, die mit synthetischen, fettfreien Nahrungen, deren Kohlenhydrat-Komponente entweder aus Glucose oder Reisstärke bestand, gefüttert wurden. Die Dominanz der Milchsäureflora (Lactobacillus bifidus und Gram-positiver Stäbchen) in der Reisstärke-Gruppe ist evident. Die Zahlen für Escherichia coli und Aerobacter aerogenes sind unregelmäßig aber gering im Verhältnis zu der Gesamtzahl der Bakterien. Die Inzidenz von Cholesterin-Gallensteinen ist – wie gewöhnlich – groß in der Glucosegruppe und sehr niedrig in der Reisstärke-Gruppe.

Der folgende Teil des Experiments (Tabellen 3–6) umfaßt Gruppen von Hamstern auf Reisstärke-Nahrungen mit oder ohne Zusatz von antimikrobiellen Substanzen. E. coli und A. aerogenes wurden nicht gezählt. Dagegen wurde als weitere Indikation der mikrobiellen Aktivität die Blasen-Galle auf Anwesenheit von Glycodeoxycholsäure geprüft. Gewisse Kombinationen von stark wirksamen antimikrobiellen Substanzen (Tabellen 5 und 6) unterdrückten die (bis jetzt noch unbekannten) Bakterien, welche für die Umwandlung von Cholsäure in Deoxycholsäure verantwortlich sind, zusammen mit L. bifidus und Gram-positiven Milchsäurebakterien, ohne eine Neigung zu Cholesterin-Gallensteinbildung herbeizuführen.

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