Plasma and Liver Cholesterol Levels in Chicks Fed Medium Chain Triglycerides (MCT) and Cholestyramine. (29761)

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Medium chain triglycerides (MCT) consisting mainly of C_8 and C_{10} fatty acids, have been shown to lower plasma cholesterol and phospholipid levels when substituted for butter fat in a formula diet fed to humans(1). Kaunitz *et al*(2) have shown that rats fed an MCT-containing diet had lower plasma cholesterol levels than those fed the same diet containing lard. Unpublished work in this laboratory has also shown that rats fed a diet containing MCT had lower plasma and liver cholesterol levels, and lower body fat levels than those fed diets containing lard or corn oil.

The feeding of cholestyramine, an anion exchange resin which binds bile acids in the intestine, thereby promoting their excretion, results in increased oxidation of cholesterol and lowered plasma cholesterol levels in man (3,4) and in experimental animals(5).

The present work was conducted to determine the effect of MCT on cholesterol levels in chicks, and to determine whether cholestyramine has a hypocholesteremic effect in the chicks when fed an MCT-containing diet.

Procedure. Day-old White Leghorn cockerels were fed a 15% coconut oil diet (Table I) for a week, after which 3 groups of 30 each were selected on the basis of body weight. One group was continued on the coconut oil diet, and the other groups received this diet with 14.7% MCT and 0.3% safflower oil or with 15% corn oil replacing the coconut oil. The safflower oil was added with the MCT to supply adequate essential fatty acids and to supply approximately the same level of linoleic acid as was provided by the coconut oil. Body weight gain and food consumption were recorded. Plasma cholesterol was determined weekly(6).

After 2 weeks on the latter diets each group was divided into 2 subgroups of equal average body weight. One per cent cholestyramine was added to the diet of one subgroup on each regimen. Plasma cholesterol was measured weekly for 2 weeks, and the chicks were sacrificed at the end of the third week. Livers were assayed for cholesterol(6) and total lipids(7).

TABLE I. Basal Diet.

Ingredient	% of diet
Soybean oil meal (50% protein)	46.2
Corn, yellow, ground	26
Fat*	15
Amidex (corn starch)	5
Steamed bone meal	3.5
Alfalfa meal	3
Iodized salt	.4
Vitamin mix†	.55
Methionine-hydroxy-analogue‡	.35
Manganese sulfate	.02

* See text for dietary fats.
† Supplied the following per kg diet: 4000 I.U. vit A, 400 I.C.U. vit D_3, 2g choline, 1g inositol, 50 mg niacin, 20 mg dl-α-tocopheryl acetate, 20 mg p-aminobenzoic acid, 15 mg Ca pantothenate, 6 mg riboflavin, 5 mg pyridoxine-HCl, 4 mg thiamine-HCl, 4 mg folic acid, 750 μg menadione, 200 μg biotin, and 20 μg vit B_{12}.
‡ Calcium DL-2-hydroxy-4-methyl thiobutyrate, generously supplied by Monsanto Chemical Co., St. Louis, Mo.

Results. Plasma cholesterol was elevated in chicks fed coconut oil and lowered in those fed corn oil (Table II). The addition of MCT to the diet resulted in lower plasma cholesterol levels than did coconut oil, but not as low as those found with corn oil. MCT also gave slightly lower liver cholesterol levels than were obtained with either coconut oil or corn oil. Liver fat content was a little lower in chicks fed MCT or corn oil than in those fed coconut oil. Chicks fed the corn oil diet gained more weight than those fed coconut oil, while those fed the MCT diet gained least. Kaunitz *et al*(2) have reported that rats fed MCT gain less weight than those fed lard.

Addition of 1% cholestyramine to the coconut oil diet resulted in reductions in plasma cholesterol levels of 24 and 15% in the first and second weeks respectively. With

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TABLE II. Plasma Cholesterol, Body Weight Gain, and Liver Fat and Cholesterol Levels of Chicks Fed Coconut Oil, MCT, or Corn Oil with and without Cholestyramine.**

Group No.††	Dietary fat	Cholestyramine in diet (3rd-5th wk)	Plasma cholesterol, mg/100 ml 1st wk	2nd wk	3rd wk	4th wk	Body wt gain, g 2 wk	4 wk	Liver analyses Cholesterol	Fat
		(%)							(mg/g)	(%)
1A	15%	0	192 ± 26	191 ± 24	191 ± 21	178 ± 16	173 ± 11	399 ± 28	3.6 ± .17	4.7 ± .33
1B	Coconut oil	1			145* ± 22	151* ± 24		394 ± 25	3.4* ± .22	4.7 ± .40
2A	14.7% MCT	0	149* ± 19	161* ± 12	157* ± 12	152* ± 18	148* ± 19	357* ± 37	3.4* ± .20	4.4* ± .18
2B	.3% safflower oil	1			128† ± 13	120† ± 13		372 ± 40	3.1† ± .24	4.2† ± .25
3A	15% corn oil	0	131*‡ ± 19	130*† ± 15	127*† ± 7	127*† ± 9	187*† ± 18	441*† ± 34	3.6‡ ± .35	4.4* ± .41
3B		1			96∥ ± 11	104∥ ± 19		433 ± 56	3.4§ ± .21	4.4 ± .24

* P <.01 compared with Group 1A.
† P <.01 " " " 2A.
‡ P <.05 " " " 2A.
§ P <.05 " " " 3A.
∥ P <.01 " " " 3A.

** Means given with standard deviations.
†† Thirty chicks per group, first 2 weeks on each fat, 15 chicks per group thereafter.

MCT and corn oil diets, cholestyramine lowered plasma cholesterol levels from 18 to 24% (Table II). With each dietary fat, liver cholesterol was slightly, but significantly reduced by the addition of cholestyramine to the diets. In the MCT-fed chicks, liver fat was also lower with cholestyramine. Dietary cholestyramine did not significantly affect body weight gains with any of the three diets.

Discussion. The plasma cholesterol levels of chicks fed a diet containing 14.7% MCT and 0.3% safflower oil were significantly lower than those of chicks fed a similar diet containing 15% coconut oil. This difference is not due to the level of polyunsaturated fatty acids, since these diets contained similar adequate levels of linoleic acid. Corn oil, which contains over half of its fatty acids as linoleic acid, gave significantly lower plasma cholesterol levels than did MCT. These results are quite similar to those reported in man and other animals(1,2). Much apparently remains to be learned as to the mechanism by which MCT lowers plasma and liver cholesterol.

Fisher and Kaunitz(8) have recently reported that chicks fed saturated long chain triglycerides, C_{12} to C_{18}, (LCT), had lower plasma cholesterol levels than did those fed MCT, C_6 to C_{10} triglycerides. This is the reverse of their observation in the rat, and also does not appear to be consistent with the present finding in the chick that plasma cholesterol levels were lower with MCT than with coconut oil. (Approximately three-quarters of the fatty acids of coconut oil consist of C_{12} to C_{18}.) This difference between findings in the chick studies may be related to the levels of linoleic acid in the test diets used, since LCT may increase the dietary requirement of linoleic acid(9).

The type of fat in the diet had no effect on the hypocholesteremic response to dietary cholestyramine. The magnitude of the reduction was similar with each of the 3 dietary fat sources. In unpublished work from this laboratory, cholestyramine has also been shown to have a hypocholesteremic effect in chicks receiving a cholesterol-containing diet with coconut oil, corn oil, partially hydrogenated soybean oil, a commercial vegetable shortening, or safflower oil as the source of dietary fat.

Summary. Substitution of medium chain triglycerides (MCT) for coconut oil in a 15% fat diet fed to young chicks resulted in lower plasma and liver cholesterol levels, lower liver fat levels, and less body weight gain than were observed in chicks continued on the coconut oil diet. Plasma cholesterol was lower with corn oil than with MCT, but liver cholesterol was lower with MCT. Addition of cholestyramine to these diets reduced plasma and liver cholesterol levels with each of the dietary fats, but reduced liver fat only with the diet containing MCT. Cholestyramine did not significantly affect body weight gains.

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Patterns of Reconstitution of Neonatally Thymectomized Mice by Injections of Isolated Lymphopoietic and Hematopoietic Cells. (29762)

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Recent investigations have led to a better understanding of thymic function in neonatal mice. In these animals, the thymus is an active site of lymphopoiesis, and plays a critical role in establishing the integrity of the lymphoid system(1). Thymectomy in the newborn results in a striking decline in lymphocyte number in the peripheral blood, and in a marked atrophy of lymphoid tissues (2). As a consequence, a serious impairment of immunologic capacity develops, evidenced by a pronounced deficiency in the production of circulating antibodies following primary stimulation with several antigens, *e.g.*, sheep erythrocytes, Salmonella H antigen, killed influenza virus, and bovine albumin(2-4). In addition, neonatal thymectomy has been shown to be an effective means of protecting Swiss mice from the lethal effect of infection with lymphocytic choriomeningitis virus, by depressing normal hypersensitivity to this agent(5). The immunologic defect has moreover been demonstrated by using skin homografts and grafts of foreign cells, both normal and neoplastic(3,6-11). Neonatal thymectomy is also followed by a generalized wasting syndrome, characterized by progressive loss of weight, cachexia, lethargy, ruffled fur and diarrhoea, time of onset and extent of these symptoms and signs depending on the strain of mice(2,6,12).

Subcutaneous grafting of newborn or adult syngeneic or allogeneic thymus in neonatally thymectomized mice at 1 to 3 weeks of age reversed the changes in lymphopoietic tissues, abolished immunologic unresponsiveness, and prevented wasting disease(2,13). Thymic grafting as late as 3 to 4 weeks, but not at 6 to 7 weeks, has been found effective in preventing or reversing these changes(14).

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