liver total cholesterol of the 9 species of laboratory animals studied. The collection of bile from pigeons was not successful because of the extremely small size of the gall bladder. The significance of the high serum and liver total cholesterol of this species is not known. Recently, it was reported that certain breeds of pigeons have a high incidence of spontaneous atheromatous lesions in the aorta that are strikingly similar to those found in man(2).

Total cholesterol concentration in the liver of the amphibian varies with the 4 species studied. These concentrations do not differ greatly from those of the 9 species of laboratory animals. Serum total cholesterol concentrations of both species of toads are higher than those of both species of frogs. Both species of frogs excrete significant amounts of total cholesterol in the bile. Collection of bile from toads was not successful.

Summary. 1. Serum, bile, and liver total cholesterol levels of 9 species of laboratory animals and 4 species of amphibians are reported. 2. Dogs, monkeys, hamsters, and mice have relatively higher serum total cholesterol concentration than cats, rats, rabbits, and guinea pigs. 3. Total cholesterol concentration in liver varies only slightly among these species. 4. Gall-bladder bile of monkeys contains large amounts of total cholesterol. Guinea pigs excrete very small amounts of total cholesterol in bile. 5. Serum and liver total cholesterol concentrations of the pigeon are very high. 6. Total cholesterol concentration in liver varies slightly among the 4 species of amphibians used. Frogs excrete significant amounts of cholesterol in bile. 7. Serum total cholesterol concentrations of both species of toads are higher than those of both species of frogs.

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Plasma Cholesterol Levels in Rats Fed "Infarct-Producing Diets."* (25313)

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Hypercholesterolemia and experimental atherosclerosis have been produced by Wissler, by Fillios and Stare, and others, in rats fed diets containing cholesterol, thiouracil and bile salts(1,2). Only rarely has this atherosclerosis been complicated by coronary thrombosis and myocardial infarction. Recently, Hartroft, Thomas and O'Neal produced thromboses and infarcts in a large percentage of rats fed such diets modified by addition of 40% fat(3,4,5). More recently, Wilgram has also produced myocardial infarcts in rats by a somewhat similar regimen(6). This report presents results of studies of levels of plasma total cholesterol in animals given various modifications of our infarct-producing diet. Details of experiments and anatomic features of the disease have been described (3,4,5).

Method. Groups of 10 to 30 rats (Wistar albino males; 80-130 g initial weights) were housed in individual wire-bottom cages in air-conditioned animal room and given water *ad lib.* Semisynthetic diets were prepared according to Table I ("basal ingredients" with partial replacement of sucrose by various fats). Diets were refrigerated and kept no longer than 2 weeks. All rats were offered more food than they would eat, left-overs and scatter weighed, and daily records of food consumption of each animal kept. They were weighed weekly during experiment. Blood specimens were obtained by clipping tails at intervals of 2 weeks, and total cholesterol content in plasma was determined by the method of Pearson, Stern and McGavack(7).

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TABLE I. Characteristics of the Infarct-Producing Diet and Plasma Cholesterol Levels in 5 Experiments.

No. exp.	Group	Dietary fat and other variations*	No. rats sampled	Plasma cholesterol (mg %)	p values for diff. in values of cholesterol
I	A	Butter 40%	11	2,570	<.005
	B	Crisco "	11	1,611	"
	C	Corn oil "	20	717	"
II	D	Butter "	10	1,396	>.30
	E	Butter-oil "	16	1,327	>.35
	F	Lard "	14	1,446	>.30
III	G	Butter "	11	2,570	<.005
	H	Butter " (no cholesterol)	30	764	
IV	I	Butter "	34	2,248	"
	J	Corn oil 10% (no other fat)	32	1,106	
V	K	Butter 40%	13	1,641	"
	L	Butter " (salt mix 12%)	6	3,315	

* Non-fat portions of diet (basal ingredients) which do not appear in the Table but make up remainder of diet consist of cholesterol 5%, propyl-thiouracil 0.3%, sodium cholate 2%, choline chloride 0.2%, salt mix 4%, vitamin mix 2%, Alphacel 6%, casein 20% and sucrose 20.5%, in % by wt of final diet. The salt mix is Wesson modification of Osborne & Mendels—*Science*, 1932, v175, 339. The vitamin mix is Nutritional Biochemicals' "Diet Fortification Mixture" without choline chloride. Changes in the diet noted in parentheses under "other variations" were compensated for by the addition or removal of sucrose in basal ingredients.

After 18 weeks all survivors were killed and autopsied.

Results. Plasma cholesterol levels (Table I) represent an average of values obtained between 8 and 18 weeks of the experiment. For rats in Group C, fed basal ingredients plus 40% corn oil, the average of plasma cholesterol levels was 717 mg%, compared with 1,611 mg% in rats of Group B, fed 40% hydrogenated vegetable fat (Crisco), and with 2,570 mg% in those of Group A, fed 40% butter. The difference between any 2 of the 3 groups is highly significant statistically. No significant difference was observed between any 2 of the 3 groups in Exp. II, offered basal ingredients plus 40% butter, 40% butter-oil or 40% lard. Cholesterol levels of rats in Group H, fed basal ingredients without addition of exogenous cholesterol to the 40% butter, averaged 764 mg%, compared with 2,570 mg% for those of Group G, fed regular basal ingredients containing 5% cholesterol plus 40% butter; a highly significant difference. Cholesterol levels of animals in Group J, fed basal ingredients plus 10% corn oil, were 1,106 mg%, significantly lower than the level of 2,248 mg% obtained in Group I, fed basal ingredients plus 40% butter. The amount of salt mix in the diet fed rats of Group L was increased to 12% (with 40% butter) and the average of their cholesterol levels was 3,315 mg%, compared to 1,641 mg% in Group K receiving only 4% of the salt mix with 40% butter.

Fig. 1 is a graph of plasma cholesterol levels of 30 rats of one group fed basal ingredients plus 40% butter during a 4 month experimental period. Levels started to rise within a few days after initiation of the dietary regimen, and reached almost 3,000 mg% at the end of 4 months. Six out of 30 rats in this group developed either single or multiple infarcts of heart or kidneys. The solid line represents levels in rats that developed infarcts, and the dotted line, levels in rats without infarcts. No significant difference was observed between those two ($p = 0.5$).

Discussion. Atherosclerosis develops in rats fed low fat diets supplemented with cholesterol (5%), thiouracil (0.3%) and bile salts (2%)(2), but complications of atherosclerosis, such as thromboses and infarcts, are rare. Addition of 40% saturated fat to those diets produces a high incidence of myocardial and renal infarcts(3,4,5). Plasma cholesterol levels of rats fed these infarct-producing diets

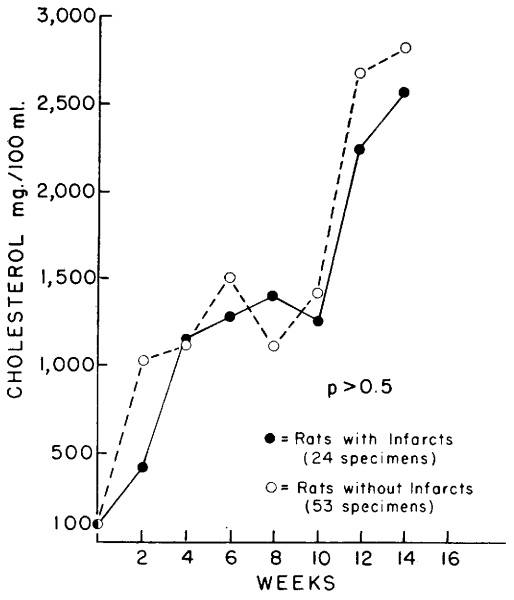

FIG. 1. Plasma cholesterol levels from *one group* of rats with and without infarcts, fed a butter-cholesterolemic diet.

vary from group to group, depending on kind and amount of added fat. It has been established in human and animal experiments that diets containing a large amount of saturated fatty acids tend to cause elevation of blood cholesterol levels(8,9,10). In our studies the basal ingredients plus highly saturated animal fat such as butter or lard, produced the highest plasma cholesterol levels; cholesterol levels were much lower in rats fed basal ingredients plus corn oil, a highly unsaturated fat. The absolute level of plasma cholesterol in the group fed basal ingredients plus 10% corn oil (1,106 mg%) was higher than that of the group fed 40% corn oil (717 mg%), and even those offered only 10% corn oil had significantly lower levels than the comparable group fed 40% butter. Infarcts have not been encountered in rats fed 10% corn oil as sole source of dietary fat except in instances where the dietary supplement of choline chloride was raised from 0.2% to 1.0%. In the latter group, levels of plasma cholesterol were also raised (2,430 mg%) and infarcts occurred(4).

Of interest was the observation of significantly different cholesterol levels between 2 groups of rats given 4% and 12% salt mix in each basal ingredient plus 40% butter. We have no evidence as to the reason for this difference; it may be due to changes in rate of absorption of lipids from the intestinal tract, in transport of absorbed lipids, or in their metabolism.

Of particular interest was the finding that levels of plasma cholesterol in rats that developed infarcts did not rise significantly higher or more rapidly than did those of animals fed the same diet, that failed to develop infarcts. Comparing the various groups of rats, those with higher levels of plasma total cholesterol developed more infarcts than those with lower average levels. But the level of cholesterol at any point in the experiment gave no indication whether an individual rat was or was not more likely to develop an infarct than another rat in the same experimental group. In this regard cholesterol determinations in these experimental models had a somewhat analogous prognostic role to similar determinations in man *i.e.*, they provide a guide to the likelihood of infarction for large groups but not for individuals.

Summary. Levels of total cholesterol in plasma of rats fed several variations of a basal infarct-producing diet containing 40% butter, butter-oil or lard were higher than in rats of other groups fed vegetable fat (corn oil or Crisco). Levels of rats in group offered a diet not containing exogenous cholesterol were far lower than those of the control group. A significantly high level was observed when the amount of salt mix in the diet was increased 3-fold to 12%. In a group of 30 rats fed the basal diet, cholesterol in plasma of those that developed infarcts rose neither more rapidly nor to significantly higher levels than did cholesterol in plasma of rats in the same group that did not develop infarcts within experimental period of 4 months.

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Metabolism of Radioactive Cholografin in Normal Controls and in Patients with Known Liver Disease. (25314)

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It was shown(1) that concentration of radioactivity by liver following injection of cholografin tagged with iodine 131 was less in dogs with altered liver physiology than in normal dogs. Differences were also noted in clearance rate of radioactivity from blood and excretion of radioactivity in urine. The present study was undertaken to determine whether or not similar results would be obtained with normal controls and patients with known liver diseases.

Procedure. Twenty-five μcuries of sodium cholografin‡ tagged with iodine 131 were administered intravenously to normal controls and to patients in whom liver disease had been proven either by needle biopsy or by laboratory studies. The tagged cholografin was diluted to a volume of 1 ml/40 lb body weight with untagged sodium cholografin. This study was also performed on one patient with abdominal enlargement but negative liver function tests and needle biopsy. Individuals were fasted 12 hours preceding the test. Following intravenous injection of tagged cholografin, concentration of radioactivity over liver and bladder was determined by scintillation detectors, ratemeters, and strip chart recorders. Blood samples were drawn at intervals to determine clearance of radioactivity from blood. Two hours after injection of tagged cholografin the subjects were given 5 ounces of water. One hour later urine specimens were collected and percentage of injected radioactivity excreted in these specimens was determined in a deep-well scintillation detector and scaler. Urine and fecal specimens were collected from controls until insignificant radioactivity was present. Urine was collected from patients for 24 hours and feces for 48 hours. The percentage of original radioactivity excreted in urine and feces was calculated for these periods. Controls were 4 young healthy adults with no history or signs of liver disease and on whom serum bilirubin levels were normal.

Results. In normal subjects the level of radioactivity over the liver increased at least 30% above equilibrium level recorded immediately after complete mixing of injected cholografin in blood volume. In patients with proven liver disease there was no concentration of cholografin by the liver and in several cases there was a decrease of 60% of radioactivity over the liver in 30 minutes. Representative curves are illustrated in Fig. 1.

Concentration of radioactivity in bladders of normal subjects increased slightly over a 30 minute interval with a maximum increment of approximately 15%. In a similar period of time 3 of 5 patients with proven liver

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