low resolution power (large receptive fields), while only a few cortical fibers are distributed to cells with high resolution power (small receptive fields). Therefore, the question arises whether the function of the cortical feedback might be related to the localizing resolution power of this sensory system.

Summary. The distribution of the cortical feedback fibers in the nuclei cuneatus and gracilis has been compared with the cyto-architecture and the dendritic architecture of these nuclei. This comparison revealed that the cortical fibers distribute primarily to those parts of the nuclei containing multipolar, triangular, and fusiform cells maintaining long, sparsely ramifying dendrites. The cells with frequently ramifying dendrites, on the other hand, receive only few fibers. Furthermore, preliminary evidence suggests that some of the former cells maintain more collaterals than the latter.

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Effect of Fat-Free Diets and Lipid Unsaturation on Rat Tissue Cholesterol Levels.† (27020)

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The degree of unsaturation of dietary fats and oils has been postulated as a factor which may influence cholesterol metabolism(1). Variations in degree of unsaturation have been commonly obtained by either partial hydrogenation of a given lipid or by the combination of lipids from different sources. Although such manipulation yeilds a lipid with a specific degree of unsaturation as defined by iodine value, the effect of positional and geometrical isomers produced by partial hydrogenation, and of short-chain fatty acid triglycerides, cannot be evaluated. Thus the effect on liver and blood cholesterol levels produced by a lipid from a single source, but differing in degree of unsaturation, is of interest. Three degrees of unsaturation were obtained by use of unhydrogenated oil, an aliquot of the same oil completely hydrogenated, and a simple mixture of these in equal proportion. Data for both corn oil and safflower oil are presented.

Methods. An experimental group of 8 male rats* each weighing ca. 100 g was housed 2 rats per metal, screen-bottom cage. Rats were allowed access to experimental diet and water *ad libitum*. Composition of the basal diet is given in Table I. Addition of 5% lipid and/or 2% cholesterol was made at the expense of potato starch. Lipids with different degrees of unsaturation, as determined by iodine number, were obtained by use of (a) commercially

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TABLE I. Composition of Basal Diet.

Component	%
Lipid[1]	0
Cholesterol	0
Casein, vitamin-free[2]	20.0
Potato starch	37.0
Sucrose	28.0
Cellulose, powdered	10.0
Salt mixture[3]	4.4
p-aminobenzoic acid	.1
Inositol	.4
Choline	.1
Vitamin mixture[4]	+

[1] Dietary lipids were those described in Methods.
[2] Borden Co., Chicago.
[3] Hawk-Oser salt mixture(5).
[4] The vitamin mixture supplied the following in mg/100 g of diet: riboflavin, .04; pyridoxine·HCl, .02; niacin, .64; folic acid, .002; biotin, .0016; vit K diphosphate, .04; α-tocopherol, .80; ascorbic acid, .50; calciferol, .036; vit A, .443.

available oil, (b) the same oil, but completely hydrogenated**, and (c) 1:1 mixture of a and b. By this method iodine numbers(2) of 130, 1.5, and 61 for corn oil***, and 137, 1.5, and 57 for safflower oil**** were obtained. The hydrogenated lipid was found to be free of *trans*-isomers by the method of Holmes, Ener, and Edmondson(3). Animals were sacrified after 8 weeks on experimental diets. Terminal blood was obtained by cardiac puncture and was heparinized to obtain plasma; also, the liver was removed. Liver and plasma were frozen and stored at −15°C in tightly sealed bottles until analyzed. Hepatic free and total cholesterol and plasma total cholesterol were determined by the method of Sperry and Webb(4).

Results. Plasma total cholesterol levels were lowest and were independent of the cholesterol content of the diet when rats were fed a lipid-free diet (Table II). However, addition of 5% lipid to the diet increased plasma cholesterol levels. The greatest increase in total cholesterol was observed when 2% cholesterol was added to lipid-containing diets. There was no apparent correlation between plasma cholesterol levels and degree of unsaturation in corn oil-fed rats. Plasma cholesterol levels obtained with saturated safflower oil, without or with 2% cholesterol, were not different from levels observed in corresponding groups fed saturated corn oil. However, plasma cholesterol levels were higher using either unsaturated safflower oil without cholesterol or the 1:1 mixture and unsaturated safflower oil with cholesterol than in the respective corn oil-fed rats.

TABLE II. Effect of Dietary Additions on Plasma Cholesterol Levels.[1]

Dietary Lipid	Without Cholesterol	With 2% Cholesterol
	w/o Lipid	
—	44 ± 5.5	43 ± 2.6
	w/Corn oil	
Sat.	56 ± 2.7	88 ± 10.5
1:1	68 ± 3.7	77 ± 6.4
Unsat.	61 ± 3.8	80 ± 3.6
	w/Safflower oil	
Sat.	52 ± 3.2	80 ± 9.9
1:1	66 ± 4.3	125 ± 11.0
Unsat.	87 ± 4.6	99 ± 5.8

[1] Data expressed as mg/100 cc plasma ± stand. error.

When a cholesterol-free diet was fed, hepatic free and total cholesterol concentrations were not affected by either the concentration or characteristics of the dietary lipid (Table III). However, when 2% cholesterol was added to a diet which was either lipid-free or contained 5% lipid in the diet, free and total cholesterol concentration was increased. Hepatic free cholesterol concentration was independent of amount and degree of unsaturation of dietary lipid when cholesterol was fed. However, total hepatic cholesterol level was determined by amount and degree of unsaturation of the dietary lipid. In rats fed 2% cholesterol in the diet, the smallest increase in hepatic cholesterol was observed with a lipid-free diet. Highest cholesterol concentrations were observed in rats which were fed diets containing 5% lipid and 2% cholesterol. In addition, total cholesterol concentration was dependent upon degree of unsaturation of dietary lipids. An increase in esterified cholesterol characterized the increase of total hepatic cholesterol concentration. The esterified cholesterol fraction was dependent upon the amount and degree of

** Hydrogenation was carried out in a stainless steel hydrogenator in presence of Rainey nickel. The reaction was essentially complete at the end of 3 hours; however, it was allowed to proceed until pressure within the reaction vessel had equilibrated at 500 p.s.i. The product was discharged and filtered at 100°C.

*** Mazola Oil, Corn Products Co., Argo, Ill.

**** Holmes, Welch & Clark Co., New York.

TABLE III. Effect of Dietary Additions on Hepatic Cholesterol Levels.[1]

Dietary Lipid	Without Cholesterol FC[2]	Without Cholesterol TC[2]	With 2% Cholesterol FC	With 2% Cholesterol TC
		w/o Lipid		
—	1.77 ± .07	1.99 ± .04	2.53 ± .18	3.30 ± .25
		Corn Oil		
Sat.	1.86 ± .06	2.04 ± .07	2.49 ± .11	5.07 ± 1.13
1:1	1.72 ± .25	1.88 ± .05	2.55 ± .08	11.70 ± 2.19
Unsat.	1.90 ± .09	2.17 ± .10	2.56 ± .15	12.90 ± 2.60
		Safflower Oil		
Sat.	1.90 ± .08	2.22 ± .04	2.72 ± .07	4.66 ± .59
1:1	1.55 ± .08	2.23 ± .06	2.73 ± .08	14.77 ± 2.97
Unsat.	1.99 ± .10	2.35 ± .13	2.28 ± .09	21.10 ± 3.15

[1] mg/g ± standard error.
[2] FC and TC are free and total cholesterol respectively.

saturation of the dietary lipid.

Discussion. In this study greater tissue cholesterol concentrations were seen when cholesterol was fed, indicating a greater rate of absorption than of excretion of the sterol nucleus in attainment of the steady state. Hepatic cholesterol responded more sensitively than did plasma cholesterol to qualitative and quantitative changes of dietary lipid. These data support the hypothesis that in the rat, liver reflects changes of cholesterol metabolism more sensitively than does the plasma(6). The increase in hepatic cholesterol was primarily confined to esterified cholesterol which accumulates with an excess of either exogenous or endogenous cholesterol in the animal body(7,8,9). In either rabbit or chicken a greater increase of the free cholesterol fraction is observed than in the rat.

Dietary lipid has been deemed necessary for absorption of cholesterol(10). The results reported here indicate that dietary lipid was not obligatory for cholesterol absorption. Inasmuch as hepatic cholesterol levels were greatly increased upon addition of lipid to the diet, endogenous lipids in the intestine were not present in sufficient concentrations for maximal cholesterol absorption. Similar observations have been made for the rat(11,12) and the chicken(13,14,15).

There have been many reports on the effect of unsaturation of dietary lipids on tissue cholesterol levels(1). Generally it has been concluded that a cholesterol-lowering effect of lipids was dependent upon either unsaturation or certain essential fatty acids. However, we observed lowest hepatic cholesterol levels when a completely hydrogenated lipid was fed. Hepatic cholesterol levels were directly related to increased unsaturation of the dietary fat. Likewise, Dam *et al.*(13,15) reported that chickens had higher cholesterol levels when fed unsaturated, rather than partially saturated, peanut oil. Later, this group(14) found no difference in hepatic cholesterol content of chickens when they were fed either hydrogenated or unhydrogenated peanut oil with cholesterol. Beare *et al.*(16) found that rabbit hepatic cholesterol concentrations were directly related to unsaturation of dietary lipid. Although there was no obvious correlation between total unsaturation and plasma cholesterol, plasma cholesterol levels were higher in safflower-oil-fed rats than in corn oil-fed rats.

It is interesting that safflower oil is richer in linoleic acid than is corn oil. That a dietary fat rich in linoleic acid increased serum and hepatic cholesterol levels in the rat is in agreement with results of Funch(17) and of Klein (9). In addition Gerson et al.(18) found that total body cholesterol of the rat was significantly greater with linoleic acid than when beef fat was fed.

Since corn oil and safflower oil consist almost entirely of triglycerides containing saturated and unsaturated fatty acids with 18 carbon atoms, the completely hydrogenated lipids are composed primarily of stearic acid triglycerides. Inasmuch as the highest hepatic cholesterol levels were observed when cholesterol was fed with unsaturated lipid, it may be concluded that unsaturated fats increase rate of cholesterol absorption. Mattson(19) has demonstrated that absorbability of a fat

was directly proportional to its content of triglycerides composed of unsaturated fatty acids with a chain length of 18 carbon atoms or more. Absorption of dietary cholesterol may be dependent upon fatty acid composition of the dietary lipid because constituent fatty acids affect digestibility of the dietary lipid.

Fatty acids may affect cholesterol absorption by some mechanism other than by altering lipid digestibility. Cholesterol absorption has been associated with pancreatic cholesterol esterase, which catalyzes the esterification of cholesterol with fatty acids(20). The esterification of cholesterol *in vitro* proceeds at a much greater rate with unsaturated acids(21); the same relative rates presumably would hold *in vivo*. Indeed it has been shown that feeding stearic acid resulted in very poor cholesterol absorption(22,23,24). Funch *et al.*(17) observed that rats fed margarines containing hydrogenated whale oil have lower endogenous blood cholesterol levels than rats fed butter.

Summary and Conclusion. 1. Rats were fed diets which were either fat-free or contained 5% lipid and either without or with 2% cholesterol. Dietary lipids with 3 degrees of unsaturation were obtained by use of unhydrogenated oil, completely hydrogenated oil, and a 1:1 mixture of the two. 2. A dissociation of plasma and hepatic cholesterol was observed. Liver reflected changes in cholesterol metabolism more sensitively than did plasma. 3. Hepatic cholesterol concentrations were directly related to degree of unsaturation of dietary lipid when cholesterol was fed. The increase in hepatic cholesterol was confined to esterified cholesterol. 4. Dietary lipid was not obligatory for cholesterol absorption. However, absorption appeared to be dependent upon digestibility and fatty acid composition of dietary lipid.

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