content was 29.8 and 54.6% of the baseline value after one and two weeks respectively. The corresponding mean decrease was 15.6 and 31.7% in body weight. No significant changes in urinary creatinine excretion occurred. 3. In a separate group of rabbits, tissue analyses for radiopotassium and water concentration after one week of starvation revealed no significant changes when compared with control animals, continued on a constant diet. 4. The decrease in total body potassium content, as measured by the exchange of isotopic potassium, as well as the loss in the urine during starvation could be accounted for on the basis of tissue catabolism without postulating an intracellular deficiency of this cation in the remaining tissues. A functional abnormality in potassium metabolism may be detectable by the radioisotope method prior to its manifestation by the external balance method.

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Cholic Acid: An Adequate Stimulus for Hypercholesteremia in the Normal Fasting Rat.* (19128)

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Recent studies(1,2) in this laboratory have indicated that the administration of sodium cholate to a rat with biliary obstruction markedly increases the degree of hypercholesteremia ordinarily occurring after obstruction. This effect of cholate could be obtained as well in the starved as in the fed animal. Moreover, parenteral injection of cholate was as effective as oral administration of the drug.

These facts suggested to us the possibility that perhaps intravenous administration of cholate to the normal, intact, starved rat might in itself produce hypercholesteremia. The present report indicates the results of such administration of cholate.

Methods. Male rats (Long Evans) approximately 10 weeks of age, were operated upon under ether anesthesia. One end of a flexible polyethylene cannula (diameter: 0.011 inch) was inserted into the inferior vena cava of each animal via a lumbar tributary. The other end of the cannula was attached to a syringe whose piston was gear driven in a special apparatus† at such a rate as to deliver 0.3 ml of fluid per hour. The abdominal incision was then closed and the rats were placed in individual Bollman cages(3). In this manner, a preparation was obtained which allowed the *continuous* intravenous injection of fluid into unanesthetized rats. Six of the animals were given sodium cholate in Tyrode's solution at a rate equivalent to 25 mg of cholic acid per hour. The remaining eight rats received Tyrode's solution, alone, thus serving as controls. Each of the experimental rats received approximately 500 mg of cholate per day. The rats were starved for 24 hours before operation and during the experiment. Blood samples taken before and 24 hours after the beginning of the injection were analyzed for bile acids and cholesterol in plasma according to previously described methods(4,5).

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† The entire apparatus was constructed for us by Charles Calvert, Pacific Industrial Electronics Co., San Francisco, Calif.

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TABLE I. Effect of Intravenous Cholate on Plasma Cholesterol of Normal Rat.

Wt, g	Amt cholic acid given (mg/24 hr)	Cholesterol (mg/100 cc) Before inj.	Cholesterol (mg/100 cc) 24 hr after inj.	Bile acid (mg/100 cc) Before inj.	Bile acid (mg/100 cc) 24 hr after inj.
		(Rats given cholate)			
320	570	57	133	6.3	17.8
226	500	70	140	6	29
202	500	73	107	3	18
207	500	54	140	1	—
279	503	46	91	3	23
220	500	48	96	5.4	32
Avg 241		58	118	4.1	24
		(Control rats)			
191	—	56	60	8	7
168	—	58	88	2	5
211	—	82	55	1	3
238	—	71	74	4	4
192	—	64	85	4	4
200	—	48	56	—	—
210	—	41	53	—	—
205	—	40	49	—	—
Avg 201		58	65	3.8	4.6

Results. As Table I indicates, experimental elevation of the plasma bile acid was followed by elevation of the plasma cholesterol. The average content of bile acid increased from 4.1 mg to 24.0 mg per 100 cc during the injection period. The average plasma cholesterol increased from 55 mg to 118 mg per 100 cc. No significant changes occurred in the cholesterol content of the control rats which had not received cholate.

Discussion. The rats given cholate became hypercholesteremic despite the fact that they were *starved* and the substance was given *parenterally*. These facts make it clear that the cholate effect could not have been due to some theoretical alteration in the intestinal absorption of steroids. Moreover, we found in a previous study(2) that cholate alone, of 4 different bile acids examined, exerted this hypercholesteremic effect in the rat with biliary obstruction. It seems, therefore, most likely that the action of cholate is a specific one.

The experimental production of hypercholesteremia by *prior* injection of cholate is important because it suggests that hypercholesteremic conditions, if accompanied by an excess of plasma cholate, may have their origin in the accumulation of plasma cholate. In other words, various hypercholesteremic states heretofore considered primary or idiopathic may be instead, secondary to an *initial* derangement of cholate metabolism. Certainly it seems important to re-investigate hypercholesteremic conditions with this possibility in mind.

Summary. Experimental hypercholesteremia was produced by intravenous injection of sodium cholate into normal fasting rats. The implications of this finding were discussed.

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