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Effect of Diet on Biliary Cholesterol.

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It has been shown by us that the actual cholesterol content in bile is not as important in gall stone formation as the ratio of cholesterol to the substance which holds it in solution, namely, the bile salts. In these studies, however, we are mainly concerned with the cholesterol factor of this ratio and the effects produced on it by the administration of fats and lipoids.

Our experiments were performed on 3 dogs, using the Rous 2-way fistula. This method prevents the interruption of the entero-hepatic circulation of bile and also minimizes infection of the liver. The administration, by mouth, of olive oil, butter and cream did not increase bile cholesterol. Meat, regarded by some as a precursor of cholesterol, also had no effect, throughout our series. Large amounts of bile acids were also fed by mouth and these produced no effect on either the cholesterol or bile acid content of the bile.

Further observations were made on a diabetic with a common duct tube, from which all the bile was drained for 19 days. The diabetes was mild and well controlled before the operation. For the first few days following the operation she had a slight glycosuria and some acidosis, but she rapidly returned to normal. While no blood cholesterol studies were made, one would expect somewhat of a lipemia in such a case. However, if this was present it was not reflected in an increased bile cholesterol. From the 4th postoperative day to the 12th she was receiving 130 gm. of fat per day. From the 12th to the 15th her diet was diminished to 50 gm. of fat per day. This decrease was likewise not reflected in the biliary excretion of cholesterol.

During the course of the experiment, cholesterol in doses of 1 gm. and bile acids in doses of 0.5 gm. were administered on various occasions, both separately and together. In each case they were given at 8:00 A. M. and the subsequent 4 hour specimens analyzed for 24 hours. During the entire period her stools were free from bile.

The data may be summarized as follows: The fact that the patient was a diabetic did not bring about an increase in the amount

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of cholesterol either in the concentration or daily output. Variations in the dietary fats and proteins had no effect on the biliary cholesterol excretion. The feeding of cholesterol, either alone or in combination with bile acids, had no effect whatsoever. No relation existed between the cholesterol content and the volume of bile excreted. In these studies no changes in the bile salt-cholesterol ratio of sufficient magnitude to approach the critical level for precipitation have been found. The responsibility for gall stone formation seems to lie in the gall bladder rather than in the liver.

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Is Cholesterol Excreted by the Gall Bladder Mucosa?

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This problem constantly recurs in gall stone studies and the following data may throw some light on it.

Pus cells contain a very high percentage of cholesterol and for that reason exudation into the gall bladder will of course increase the cholesterol content. Rous¹ and more recently Andrews² have called attention to the great tendency of the gall bladder of the dog under experimental manipulation to become infected.

The blood of the dog contains up to 300 mg. per 100 cc. of cholesterol and the bile 10-20 mg. In fistula dogs this may even be lower. It is obvious therefore that the leakage of a single drop of blood or serum into any experimental preparation (such as a needle hole) would completely vitiate the results of most experiments.

Numerous experiments made in our laboratory, mostly for other purposes, have been reviewed and the following data secured: In 36 dogs whose common duct had been tied for 24 hours or less the cholesterol content of the bladder bile was 57 mg. per 100 cc. In 42 dogs who had had common duct ligature for 3 to 80 days there was a cholesterol content of the bladder bile of 51 mg. per 100 cc.

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¹ Rous, P., and McMaster, P. D., *J. Exp. Med.*, 1923, **37**, 11.

² Andrews, E., and Hrdina, L. *Arch. Surg.*, 1931, **23**, 201.