sence. The literature on this subject is highly contradictory. Since Pavlov first reported osteoporosis with biliary fistulas, Looser[1] has found it to occur also with pancreatic and intestinal fistulas. Seidel[2] reports similar findings. In some reports the bone absorption was by means of osteoclasts and in others no lacunar absorption was noted although porosis was present. Modern views are distinctly against the humoral absorption of bone, the so-called halisteresis. Klinke[3] believed the bone atrophy was simply an accompaniment of general cachexia, and it is true that in most cases reported clinically this was extreme as in the recent paper of Wangensteen.[4] At any rate in a considerable series of fistulae we have not observed osteoporosis, as estimated either by X-ray or by histological demonstration of lacunar absorption. Klinke estimates that about two-thirds as much calcium is lost in the bile as in the urine. This loss hardly seems excessive. More important is the recent demonstration that calcium may be absorbed from the intestinal tract in the absence of bile. The obvious explanation seems to be that an infected bile fistula produces a marked acidosis. Our dogs, not having an acidosis, had no porosis.

Conclusion. 1. In uninfected bile fistulas no degenerative changes in the liver occur nor does osteoporosis.

7548 P

Studies on Acholic Cachexia. VI. Bile Acid Factor.*

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The classic studies of Whipple and his co-workers in this field have elucidated clearly the general problems of bile acid metabolism. Our work is in general confirmatory of these, but certain other factors enter into the situation when the cachexia becomes extreme. In no case has any ingestion of bile been permitted in our experiments and the analysis of the bile in the later cachetic stages brings out new points.

[1] Looser, *Verhandl. deutsche Path. Ges.*, 1907, **11**, 291.

[2] Seidel, *Munch. Med. Wochschr.*, 1910, **57**, 2034.

[3] Klinke, *Klin. Woch.*, 1928, **1**, 385.

[4] Wangensteen, *J. Am. Med. Assn.*, 1929, **93**, 1199.

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As has been the experience of all previous workers, the total output of bile acids varies over a wide normal range. It varies not only with the individual dog, the diet, the fluid intake and the general condition of the animal, but other unknown factors evidently cause even wider fluctuations. Careful examination of our records often fails to give any explanation of fluctuations amounting to 200-300%. In general the amounts expressed in milligrams per kilo per day were considerably less than those given by Whipple. He estimates that a normal 10 kilo dog keeps about 7-8 gm. of bile salts per kilo in circulation, and that a fistula dog puts out 80-130 mg. per kilo per day. As can be seen from our tables our dogs put out but 20-40 mg. per kilo per day in the earlier stages, and when the cachexia became extreme often excreted only a small fraction of that amount.

TABLE I.

	Average Daily Mg. B.A. for Period			
Postoperative	Dog No. 958 Wt. 19.5	Dog No. 959 Wt. 17.5	Dog No. 940 Wt. 18.8	Dog No. 960 Wt. 17.5
Days				
6	223	210	1308	375
10	327	210	1308	375
15	398	528	1308	375
19	398	432	554	991
23	184	342	554	135
27	612	212	665	135
31	604	450	914	258
36	609	466	1237	288
40	383	713	1375	853
44	418	339	1137	583
48	401	211	646	295
56	580	393	1208	441
64	460	422	1096	551
72	540	422	976	197
99	622	422	278	609
114	105	192	61	—
130	105	194	61	—
150	402	194	—	—
167	602	128	—	—

The relation of the condition of the dog to the amount of bile salts excreted is not a direct one. Two of the 4 animals here reported excreted even more freely during the terminal stages. In our experience the opposite has more often been true. It is clear, however, that, if a very high excretion may in some cases be maintained right up to death from inanition, it is logical to assume that lack of bile salts in the body is not a major causative factor in the cachexia.

Both in these and in previous experiments, it has become evident that diet is not the only factor in regulating the bile salt output in cachexia. If as Whipple says the basic endogenous bile salts from

tissue waste amount to 30-40 mg. per kilo per day and the rest is dietary, this mechanism does not necessarily work in the later cachectic stages. While in some cases the increase of meat in the diet may markedly increase the amounts of bile salts excreted, in others (dogs No. 940 and 959) the opposite occurs. It is well known that a meat diet hastens the exitus of bile fistula animals and in many cases such as this the added intoxication resulting from the meat seems to bring about a closing down of the excretory mechanism.

Conclusion. Acholic cachexia is not due to lack of bile salts in the body.

7549 P

Studies on Acholic Cachexia. VII. Effect of Viosterol.*

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The rapid loss of weight, anemia and other changes which may occur in biliary fistula have recently been attributed to lack of ability to absorb fat-soluble vitamin. Takasu[1] has postulated that lack of bile salts in the intestinal tract prevents absorption of ergosterol in the same manner that fat digestion is impaired or stopped. Murakamis[2] reports that the excretion of bile acids is quadrupled by a single cubic centimeter of irradiated ergosterol, given subcutaneously. Others have found that vitamin administration had a markedly beneficial effect on the anemia and also prevented the bone changes.

Our experiences do not substantiate any of these conclusions. As shown in a previous article, the anemia did not seem an important factor. It was not profound and occurred mostly as a terminal phenomenon. Also the bone changes have not occurred in animals who did not have an ascending hepatitis. In 2 animals in whom frequent blood counts were made there was no effect from the administration of ½ cc. viosterol (250 D per cc.). In these experiments the viosterol was given about the third month and the fall in the hemoglobin and red count was more rapid after its administration

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1 Takasu, M., *Deutsche Z. f. Chir.*, 1930, **224**, 240.

2 Murakamis, R., *J. Biol. Chem.*, 1928, **9**, 321.