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Studies on Acholic Cachexia. V. Pathological Changes.*

ALEXANDER BRUNSCHWIG, ARTHUR D. BISSELL AND EDMUND ANDREWS.

From the Department of Surgery, The University of Chicago.

Many observers have reported extensive pathological changes in the organs of animals suffering from cachexia cholipriva. These have in general consisted of 3 processes; (1) degenerative changes in the liver, pancreas, heart and skeletal muscles, (2) osteoporosis, and (3) hepatitis, due to ascending infection from the cannula. Whether the first 2 types of changes are due to lack of bile in the system or due to ascending infection of the liver has not been clearly understood.

Our experience with bile fistulas made by various methods has been that ascending cholangitis was nearly always present, in some cases being of a severe type. The bile canaliculi were surrounded by rosettes of infiltrating cells and degeneration of the lobules of the liver was marked. However, with fistula made by the Dragstedt cannula, this has not occurred. The liver showed no signs of infection. The bile ducts were clear, no bile thrombi were found and even when the fistula had persisted for 5 months there were absolutely no infiltrations of leucocytes about the bile ducts, and no fibrosis. In these cases there was a corresponding absence of other signs of liver damage. Central necrosis, ordinarily seen over large areas did not occur. The cells stained clearly and contained no vacuoles or fat droplets. Iron stains showed that a small amount of pigments was hemosiderin and not bile pigment. This was also seen in the spleen but was not of a high degree. Normally, the dog has considerable pigment deposits of this type in the spleen and liver. Similarly, in spite of the extreme emaciation of the animals the other viscera were normal. The myocardium showed no waxy degeneration nor did the skeletal muscle. The intestinal and gastric mucosa was normal. Konjetzky gastritis was not present as has been reported previously, there being no eosinophiles in the submucous layers. The adrenals were normal, except for the total absence of any fat droplets, or lipoid.

Not only in the series here reported, but in an extensive former series of bile fistulas, has osteoporosis been conspicuous by its ab-

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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.

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

ARTHUR D. BISSELL AND EDMUND ANDREWS.

From the Department of Surgery, The University of Chicago.

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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