A fifth group of 88 adults with diseases other than typhoid fever were tested with the typhoid filtrate; 42 of these skin reactions were negative; 27 weakly positive and 19 strongly positive. A sixth group of 47 children, ranging in age from 3 to 15 years, received the intradermal tests with *B. typhosus* filtrate. Thirty-six of the children were in a cardiac camp and were not ill at the time the tests were made. The other 11 children were in a children's hospital ward and were convalescing from a variety of diseases. So far as could be determined, none had had typhoid fever or antityphoid vaccination. Nine positive reactions occurred in this group, but only two persisted 48 hours. One occurred in a boy 13 years old convalescing from an acute poliomyelitis, and the other in a boy of 13 who had a history of repeated attacks of acute rheumatic fever.

The skin reactions with the filtrate of *B. typhosus* suggest that the reaction is allergic in nature. A positive reaction apparently indicates immunity to typhoid fever, since those immunized against typhoid fever, those with a history of typhoid fever, and those in the course of typhoid fever tend to react positively in most instances, while only 40% of other adults and 4% of children react positively. The results indicate that preliminary skin tests might determine whether or not artificial immunization against typhoid fever was necessary in a given individual.

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Contraction and Evacuation of Gall-Bladder Caused by Highly Purified "Secretin" Preparation.

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The numerous reports in the literature showing the marked efficacy of fats, egg yolk and protein in emptying the gall-bladder convinced us that the effect of "secretin" on the evacuation and motor activity of the gall-bladder should be studied, since it is well known that these substances stimulate the pancreas, and that "secretin" (very impure solutions) promotes the formation of bile.

For some time we (Kloster, Ivy and Lueth) have been working on the purification of "secretin". Starting with the "new secretin" of Weaver, Luckhardt, and Koch,[1] we prepared solutions of such

purity that from 1 to 3 mg. of dried material excites pancreatic secretion in 10 to 20 kilo dogs. These purified solutions of "secretin" have been used in this study. They are vaso-dilatin free, and have no objective deliterious effects when injected intravenously in anesthetized or unanesthetized animals.

One series of experiments were performed as follows: A cat was barbitalized, the pancreatic duct was cannulated, and a cannula was placed into the gall-bladder through a small opening in the fundus. On the injection of the purified "secretin" (2 mg.) the intra-gall-bladder pressure rises after a very brief latent period, sometimes before the needle is withdrawn and always before the pancreatic juice and bile begins to flow. Normal saline controls proved negative. The pressure begins to decline in from ½ to 1 hour after the injection.

To avoid the possibility that the increase in gall-bladder pressure was not due to an inflow of bile, we tied the cystic duct or cannulated the bile duct. In the experiments in which the cystic duct was tied, the gall-bladder pressure was increased, but not to the extent of the first series of experiments. This difference, we believe, was due to some interference with the blood supply of the gall-bladder, which is very difficult to avoid in the cat on ligating or clamping the cystic duct. In the experiments in which the bile duct was cannulated before it entered the duodenal wall, the gall-bladder pressure was raised as much as in the first series of experiments.

When cats are prepared as above, the injection of 1 mg. of atropine sulphate does not have any effect on the action of the "secretin" preparation on motor activity of the gall-bladder.

In another series of experiments we filled the gall-bladder of the dog with lipiodol (iodized oil), using anesthesia and aseptic technic. From 12 to 24 hours later, the dog trained to lie quietly on the table, one dose of "secretin" was injected intravenously every 10 minutes for 1 hour, and roentgenograms were made two minutes after each injection. These injections practically emptied the gall-bladder in the course of an hour in some dogs; in others from one-third to one-half of the iodized oil was evacuated. In some of these dogs changes in the contour of the gall-bladder could be seen fluoroscopically. The above phenomena were observed when the dose of "secretin" amounted to as little as 4 mg. of solid material.

In one dog, the gall-bladder was visualized by using the tetra-iodophenolphthalein technique. An intravenous injection of "secretin" every 10 minutes for 1 hour caused the gall-bladder shadow to decrease approximately ¼ in size. In 2 dogs the hepatic ducts were tied and the common bile duct ligated, the cannula being con-

nected to the outside by means of a rubber tube which was clamped. Twenty-four hours after the operation, the animal lying quietly, the rubber tube was connected to a glass tube serving as a manometer, and a recording tambour. One dog's dose of "secretin" was injected every 4 or 5 minutes for 20 minutes. A steplike rise in the intra-gall-bladder pressure resulted; the pressure was raised in one instance from 180 mm. of bile pressure to 240 mm. in about 30 minutes, and maintained for a little more than ½ an hour, after which it started to decline. In barbitalized dogs, or dogs under light anesthesia, with the cystic duct clamped and the fundus of the gall-bladder cannulated, an injection of a "secretin" preparation causes a rise in intra-gall-bladder pressure.

These observations establish that a highly purified dilatin-free extract of intestinal mucosa on intravenous injection causes the gall-bladder to contract, *i. e.*, to increase its postural tone, and to evacuate. The active principle is either "secretin", or some substance closely associated with it. We have evidence to support the contention, that the duodenum plays some rôle in controlling the passage of bile into its lumen.

[1] Weaver, M. M., Luckhardt, A. B., and Koch, F. C., *J. Am. Med. Assn.*, 1926, lxxxvii, 640.