

sudanophilia increased during this interval, particularly in the ACTH-treated group, in which the response surpassed that obtained in the corresponding non-scorbutic series. These observations are in accord with those of Hyman, Ragan, and Turner(8), strongly suggesting that vit. C is not essential for the secretion of adrenal hormones. The depletion of adrenal ascorbic acid seen in the non-scorbutic animals receiving Cortisone may be correlated with cortical atrophy and lessened secretory activity; this change was maximal at the end of 10 days. That adrenal concentrations of vit. C were within the normal range following ACTH therapy in the non-scorbutic guinea pigs is consistent with the observed histologic changes and with the duration of the treatment(25).

Our data give no conclusive evidence that either ACTH or Cortisone influenced the rate of growth, nutrition, or hemorrhagic tendency of the scorbutic animals in this study. Definite

effects might have been observed had the treatment been prolonged, possibly until spontaneous death. This, however, was deliberately avoided in an effort to secure optimum conditions for appraisal of wound repair.

Summary. 1. ACTH and Cortisone, in doses sufficient to alter the adrenal glands and depress the level of circulating eosinophils, failed to influence the repair of wounds in normal and in scorbutic guinea pigs. 2. It is suggested, therefore, that the connective tissue of the guinea pig may respond to adrenal hormone, if at all, less readily than that of other species studied. 3. The specificity of the "anti-scorbutic" action of Cortisone and of ACTH is questioned. 4. The adrenal response of scorbutic guinea pigs to ACTH, in the virtual absence of adrenal vit. C, suggests that ascorbic acid is not essential for the secretion of adrenal hormone. 5. The relationship of ascorbic acid to the metabolism of the adrenal cortex remains obscure.

25. Sayers, G., *Physiol. Rev.*, 1950, v30, 241.

Received March 20, 1951. P.S.E.B.M., 1951, v77.

Iodinated Organic Compounds as Contrast Media for Radiographic Diagnoses. X. Interrelationship of Gallbladder and Pancreas.* (18710)

MICHAEL RADAKOVICH, ROBERT H. GREENLAW, AND WILLIAM H. STRAIN.
(Introduced by J. J. Morton)

From the Departments of Surgery and Radiology, School of Medicine and Dentistry and Strong Memorial Hospital, University of Rochester, Rochester, N. Y.

During a study of the factors influencing the accumulation of cholecystographic media in the gallbladder of dogs, it was found that complete ligation and division of the pancreatic ducts inhibited the visualization of the viscus. This observation indicates that the pancreas plays an intimate role in gallbladder function, and, experimentally, suggests a simple method to test the completeness of ligation and division of pancreatic ducts.

The mechanisms involved in the inhibition of gallbladder visualization after pancreatic

duct ligation and division have not been determined as yet. It appears that the effect requires several days for development since dogs with pancreatic duct ligation, or with complete pancreatectomy, visualize satisfactorily if intravenous cholecystography is carried out immediately after the completion of the operative procedure. Provisionally, the inhibition of visualization seems to be due to some alteration in the concentrating mechanism of the gallbladder.

Experimental. Studies were carried out on 14 healthy, mongrel dogs ranging in weight from 13.5 to 25 kg. Preoperative control cholecystograms were made, usually by intravenous administration of the sodium salt of

* This investigation was supported (in part) by a research grant from the National Institutes of Health, and (in part) by a research grant from Eli Lilly and Company, Indianapolis, Ind.

TABLE I. Quality of Gallbladder Visualization Following Ligation and Division of Pancreatic Ducts in Dogs that Visualized Well Preoperatively.

Dog	Days post-operative	Route of administration	Medium	Gallbladder shadow	Autopsy findings
1609	8	Oral	II	0	Extensive atrophy of pancreas with fibrosis; no evidence of reestablishment of ductal system.
	12	Intrav.	II	0	
	23	"	II	Faint	
1608	7	"	II	0	All but 3 cm of pancreas atrophied and fibrosed; gallbladder dilated and contains black cryst. material.
	10	"	II	0	
	17	"	III	0	
	22	"	II	Faint	
1680	6	Intrav.	II	Faint	Pancreas atrophied to a considerable degree; pancreatic ducts dilated. Extra-hepatic biliary tract dilated — G.B. cont. thick viscous bile.
	14	Oral	II	"	
	36	Intrav.	II	Fair	
1684	6	"	II	0	Pancreas atrophied with normal tail section; gallbladder dilated.
	30	"	II	Faint	
	34	"	II	"	
	38	"	II	"	

a cholecystographic medium. The media used were: β -(4-hydroxy-3,5-diiodophenyl)- α -phenylpropionic acid (I), *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid (II), and phenol-tetraiodophthalein (III)(1). The level of dosage was constant for a given dog, and 50 mg. kg was satisfactory for most of the studies. The radiographs were made under barbiturate anesthesia eighteen hours after oral and 2 or more hours after intravenous administration. The general procedure for radiography is described in an earlier publication(1). The dogs were operated under sterile conditions. The ducts were isolated with a minimum of trauma to the gland, doubly tied with fine silk, and cut; the duodenal stump of the pancreatic duct was inverted. In later operations, to ensure that all branches of the ductal system were located, the gland was separated from the duodenum, and care taken not to interfere with the blood supply. Following a recovery period of 6-8 days, cholecystographic media were administered to the dogs at varying intervals. The same medium was used for the terminal radiographic study as for the initial control examination. Finally, the dogs were sacrificed, and the pancreas, liver, and the extra-hepatic biliary tract examined grossly and microscopically.

Results. In 7 of the 14 operated dogs, gallbladder visualization was inhibited after the operative procedure. The faint shadows that were obtained revealed that the viscus was greatly dilated in 6 of the 7 animals. At autopsy the dogs showed atrophy of the acinar tissue, varying degrees of fibrosis, greatly dilated pancreatic ducts, and dilated gallbladders. Stones were found in one dog, and a black sludge in the bile of 2 other animals. Representative data from the experiments are collected in Table I.

In 5 operated dogs the gallbladder visualized satisfactorily. At terminal laparotomy or autopsy, incomplete ligation or regeneration of ducts was evidenced by the presence of normal appearing pancreatic tissue with patent ducts communicating with the duodenum. In 2 animals the patency of the ducts was demonstrated by the free flow of pancreatic juice following secretin stimulation.

That the effect is not one that develops immediately is shown by the results obtained with 2 dogs that were used for acute experiments. Intravenous cholecystography with medium II was carried out immediately after the pancreatic ducts had been tied and cut in one animal, and shortly after complete pancreatectomy in the other dog. The gallbladders of both dogs visualized well after a 2 hour interval.

Discussion. The experimental results dem-

1. Jones, G. E., Grohowski, A. L., Robertson, H. D., Ramsey, G. H., Schilling, J. A., and Strain, W. H., *Radiology*, 1948, v51, 225.

onstrate the close relationship of the gallbladder and the pancreas in a novel way, and suggest that the pancreas controls the tone of the gallbladder. The operative procedure deprives the duodenum of the external secretion of the pancreas and at the same time leads to atrophy of the organ. It is conceivable that lack of sodium bicarbonate and of the pancreatic enzymes in the duodenum may bring about an alteration in the hormonal control of the gallbladder. On the other hand, atrophy of the pancreas may lead to the deficiency of some principle from the pancreas that is essential to good gallbladder function.

After ligation and division, the pancreatic ducts have a marked tendency to recanalize or to establish collateral ducts. Since this occurred in 5 of the dogs, these processes evidently take place fairly readily. This group of unsuccessful operations provides evidence, however, that surgical manipulation of itself is not responsible for the failure of gallbladder visualization in the successfully operated animals. Presumably, the surgical trauma and degree of innervation to the gallbladder region is the same in both groups of animals.

As this work shows, there is always some uncertainty as to the operative result when the pancreatic ducts are tied and cut. Use of intravenous cholecystography, particularly with *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid, appears to furnish a convenient way of establishing the status of the pancreas and the pancreatic ducts in operated dogs. Additional work will be required to determine the limitations of the method and whether it is

valid in dogs after an extended period of time.

In some ways the experimental results parallel certain clinical observations. Elman(2) pointed out that the gallbladder may not visualize if intravenous cholecystography is carried out during episodes of acute pancreatitis. Since then this observation has been confirmed by Silvani and McCorkle(3). Comfort and associates(4) have added further clinical reports on the failure of the gallbladder to visualize during acute and chronic pancreatitis. It is evident from the several reports, however, that the clinical picture is not too well defined.

Additional work is in progress to clarify both the experimental and clinical aspects of the interrelationship of the pancreas and the gallbladder.

Summary. Studies on dogs show that successful ligation and division of the pancreatic ducts inhibits the visualization of the gallbladder by cholecystographic media whether administered orally or intravenously. Failure of visualization appears to be due to the development of physiological stasis of the viscus. The experiments demonstrate a close relationship of the two organs and suggest that the pancreas may control the tone of the gallbladder

2. Elman, R., *Am. J. Digest. Dis.*, 1939, v4, 732.

3. Silvani, H. L., and McCorkle, H. J., *Ann. Surg.*, 1948, v127, 1207.

4. *inter al.*, Comfort, M. W., Gambill, E. E., and Bagenstoss, A. H., *Gastroenterology*, 1946, v6, 239.

Received April 20, 1951. P.S.E.B.M., 1951, v77.

Depression of Fecal Urobilinogen by Aureomycin and by Terramycin.* (18711)

WILLIAM C. ROBBINS.[†] (Introduced by David P. Barr.)
(With the technical assistance of Carol Adams)

From the Department of Medicine, New York Hospital-Cornell Medical Center.

Modification of the intestinal flora by drugs

and the resultant effects on the nutrition and

* This study was aided in part by grants from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health

Service; Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.; and Charles Pfizer and Co., Brooklyn, N. Y.