

morphological evidence of decreased thyroid secretion when compared to tumor-free parous mice of corresponding ages. This is in agreement with the report of Larinow(8) that rabbits with tar-induced papillomata and mice with spontaneous and transplanted mammary adenocarcinoma show a depression in the height of the follicular epithelium. In these latter studies, the epithelium became increasingly lower as the tumors became larger. A lowered thyroid activity in tumor-bearing mice might well reflect metabolic changes within the host associated with the presence of tumor.

Summary. Observations of thyroid follicle epithelial heights and diameters were analyzed with respect to age and parity in C3H and C57 mice. Epithelial heights decreased and follicle diameters increased with aging and breeding. The presence of tumors in the C3H parous females was associated with de-

creased epithelial height and increased diameter of the thyroid follicles as compared to non-tumor-bearing mice of corresponding ages. These changes suggest that aging, breeding and the presence of tumor are associated with decreased thyroid function.

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Increase in Heidenhain Pouch Secretion after Portacaval Transposition in the Dog.* (23663)

JAMES S. CLARKE, JAMES C. HART AND ROBERT S. OZERAN
(Introduced by Morton I. Grossman)

*Veterans Admin. Center, Los Angeles, and Department of Surgery,
University of California Medical Center, Los Angeles*

Several studies have indicated that peptic ulcers occur with greater frequency in patients with cirrhosis of the liver than in patients without cirrhosis(1,2,3). Malnutrition, deficient amounts of biliary elements, central nervous system damage, and inflammation and congestion of the stomach mucosa have been cited as possible causes(4). Baronofsky and Wangenstein(11) showed that partial obstruction to the venous outflow of the stomach in rabbits and dogs increases the speed and incidence of ulcer formation in response to injection of histamine in beeswax. In their animals a well-developed collateral circulation developed around the liver. Excess gas-

tric secretion of acid or pepsin has not been demonstrated in patients with cirrhosis(4), although studies on this point are few. Out of 29 patients who underwent portacaval shunt at the Veterans Administration Center, Los Angeles, since 1948 two, who had no previous ulcer history, developed peptic ulcers within 9 months after shunt. Four other cases have been reported of peptic ulcers which originated or underwent exacerbation after portacaval or splenorenal shunt(5,6). These observations throw some doubt on the importance of portal hypertension *per se* in the etiology of ulcers associated with cirrhosis. The presence of a well-developed collateral circulation through which portal blood bypasses the liver is a striking feature of many patients with cirrhosis and of all with func-

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tioning portacaval shunts. It occurred to us that gastric hypersecretion on a humoral basis might take place in the presence of significant shunting of portal blood around the liver, even though basal fasting secretion was normal or low. Suppose the secretory hormone from the gastric antrum (gastrin) were inactivated in the liver, and that under normal conditions only a fraction of the gastrin originally liberated from the antrum finally passed into the systemic venous circulation via the hepatic veins. Then if portal blood were shunted around the liver, an increased amount of gastrin might gain access to the systemic venous circulation and stimulate the gastric parietal cells to secrete acid. Such a phenomenon would not be detected by the usual tests of gastric secretion, but only by tests measuring the secretory response to antral stimulation.

To test this hypothesis the effect of portacaval transposition on acid secretion from Heidenhain pouches (no vagus innervation) was determined.

Methods. Heidenhain pouches were constructed in 4 dogs weighing between 12 and 24 kg. Each pouch was drained through an inlying stainless steel cannula into a rubber football bladder, allowing quantitative 24-hour collections of the pouch secretion as described by Dragstedt, *et al.*(7). The volume of each 24-hour collection was measured, and its free acid in milliequivalents was determined by titration with 0.1 N NaOH to the color change of Toepfer's reagent. The HCl output was calculated. Each dog was fed a constant amount (2, 3, or 4 cans) of a commercial dog food (trade name Thoro Fed) during the entire experiment. Water was allowed *ad lib*. The diet was supplemented daily with 1 g of NaCl for each 100 ml of pouch secretion. After 35 to 42 daily collections each dog underwent a portacaval transposition operation as described by Child(8). In this procedure all tributaries of the portal vein are divided from the junction of the superior mesenteric and splenic veins to its bifurcation at the hilum of the liver. The portal vein and inferior vena cava are transected, transposed, and the cut ends reanastomosed end to end. As a result the portal

TABLE I. Secretion from a Heidenhain Pouch before and after Portacaval Transposition.

Dog		No. of 24 hr col- lections	Mean acid out- put, meq/24 hr	% increase
73	Before	39	23.6 $\pm$ 9.1*	299
	After	42	94.1 $\pm$ 26.5	
74	Before	35	25.8 $\pm$ 14.1	295
	After	24	101.9 $\pm$ 58.6	
95	Before	42	2.6 $\pm$ 1.4	630
	After	30	19.1 $\pm$ 8.0	
96	Before	40	1.4 $\pm$ 1.2	849
	After	35	13.3 $\pm$ 2.8	

* Stand. dev.

t for 4 sets = 15.40. P < .001.

vein drains into the upper cut end of the inferior vena cava, completely by-passing the liver, and the lower inferior vena cava drains into the upper cut end of the portal vein, maintaining a large flow of systemic venous blood to the liver. As soon as the dog was eating the same amount as before operation collections were again made and continued for 24 to 42 days.

The *results* are set out in Table I. Each dog showed a profound increase in mean acid output after portacaval transposition. There was generally an increase in both the volume and acidity of the juice secreted by the pouch. All the dogs lost weight slowly during the experiment.

Dog # 74, who was the smallest of the 4, became dehydrated and anorexic 5 days after transposition due to loss of large amounts of fluid and chloride in the pouch secretion. 1000 ml of 0.9% NaCl were given subcutaneously on each of 3 successive days and his appetite returned. On the 23d day after transposition dehydration and anorexia again occurred, parenteral fluids were not given, and he died the next day. Autopsy revealed no cause of death other than extreme dehydration. The mean acid output for Dog # 74 was calculated using all post-transposition collections including those low values occurring when the dog was eating poorly.

Dogs # 73 and # 95 died of perforating ulcers in their pouches 112 and 55 days after transposition, respectively. Dog # 96 is alive and well 42 days after transposition. The dogs that died had grossly normal livers, open portacaval anastomoses, and no ulcerations

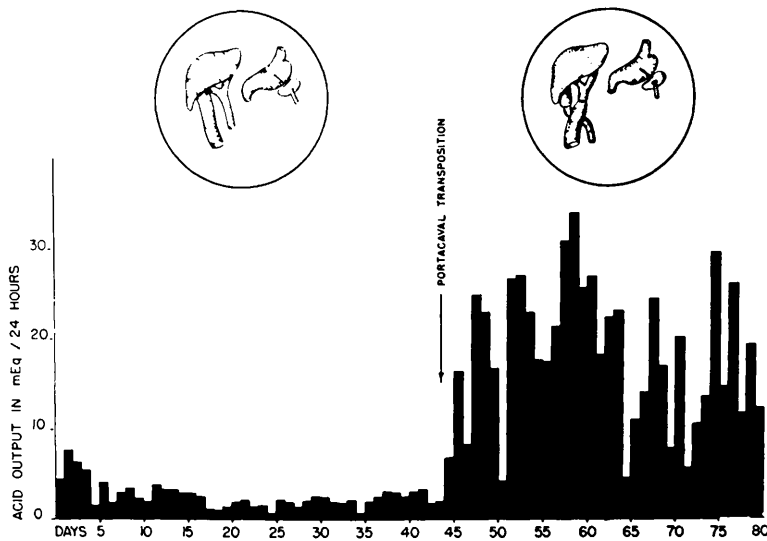


FIG. 1. Effect of portacaval transposition on secretion of Heidenhain pouch. Dog #95.

of the stomach or duodenum.

Discussion. Portacaval transposition was selected in this study because a method was desired which would provide a complete shunting of portal blood around the liver and still cause minimal impairment of hepatic function. Child and co-workers(8) found that hepatic regeneration was absent in dogs with Eck fistulae, and was good, though not entirely normal, in dogs with portacaval transpositions. Silen, *et al.*(9) concluded after careful studies that both laboratory and histologic findings in dogs with transpositions were very similar to those of normal animals. Tolerance to oral ammonium lactate was diminished both in dogs with Eck fistulae and in others with portacaval transpositions, but this was much more marked in the former. Thus, the observed increase in pouch secretion after transposition probably is not due to impairment of parenchymal liver function.

In forming a Heidenhain pouch the vagus nerves to the pouch are cut. The secretion from such a pouch is largely in response to humoral agents as evidenced by its low levels in fasting and after antrum resection(10). The increase in secretion found in these experiments therefore is of humoral origin. Among humoral substances which immediately come to mind are gastrin and ammonia. Gastrin is a potent hormone stimulating Hei-

denhain pouch secretion and it is conceivable that gastrin is inactivated in the liver. Ammonia is a substance which enters the portal blood from the digestive tract and is normally cleared from this blood by the liver. Since the dog food (Thoro Fed) eaten by these animals contains at least 10% crude protein, there was an adequate source for ammonia formation in the gut. However, the exact agent at work here to increase secretion after transposition and its anatomical site of origin remain to be determined.

Summary. 1) Heidenhain pouch secretion in dogs is markedly increased following portacaval transposition. 2) This may be due to increased effect, after shunting of portal blood around the liver, of a humoral secretagogue which originates in the abdominal viscera and is normally inactivated or excreted by the liver. 3) This finding offers a new approach to the cause of the ulcer diathesis exhibited by patients with cirrhosis of the liver.

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Physiological Aspects of Aging. I. Efficiency of Absorption and Phosphorylation of Radiothiamine.* (23664)

H. H. DRAPER (Introduced by B. C. Johnson)

Division of Animal Nutrition, University of Illinois, Urbana

Mills and associates(1,2) have reported that the thiamine requirement, in terms of dietary concentration, is approximately twice as great for old rats as for growing rats. Thiamine was found to be unique among the B vitamins in this respect. Friedemann *et al.* (3) observed that oral doses of more than 5 mg were poorly absorbed by humans, whereas many times this quantity of other water-soluble vitamins is efficiently absorbed, and Kirk and Chieffi(4) estimated that 50% to 75% of a dose of 5 mg of thiamine hydrochloride apparently was unabsorbed by either young or old subjects. In the present study the absorption of radioactive thiamine by rats 1 month to 2 years old, and by young rats in deficient, normal and supernormal states of thiamine nutriture was studied. As an index of the influence of aging on the conversion of thiamine to its phosphoric acid esters, and on the efficiency of the general phosphorylation mechanism, the radioactive compounds in the liver were partitioned into phosphorylated and unesterified forms which were estimated separately.

Methods. Albino rats of the Sprague-Dawley strain were maintained on a stock diet with a supplement of 2500 I.U. Vit. A per month. Individuals of various ages were

fasted for 24 hours and placed in a urino-fecal separator(5). An oral dose of 120 μ g of radiothiamine (thiazole-2-C¹⁴) with a specific activity of 6 μ C/mg was administered by stomach tube under light ether anesthesia. Urine and feces were collected for a 48-hour period; the animals then were sacrificed and the livers were removed and stored at -18°C. The feces were dried for 12 hours at 105°C, ground finely, and a 1 g sample was digested for 16 hours under toluene at 37°C, using 20 mg papain and 20 mg clarase in 25 ml 0.5% acetate buffer at pH 4.5. The hydrolysates were filtered through No. 1 Whatman paper and washed several times with distilled water. Duplicate 200 λ aliquots were plated for counting in a Tracerlab Q-gas windowless gas flow counter connected to a Nuclear scaler. The efficiency of the extraction procedure was determined by plating a fine suspension of the undigested residue and of the original ground samples, prepared by agitating vigorously for 5 minutes in a Waring blender. For a series of samples a recovery of at least 95% of the total fecal radioactivity was obtained in the filtrate. Hydrolysates of feces from 2 treated animals were chromatographed on filter paper as described below and radioautographs were prepared. Only one spot, at R_f .66, corresponding to that of thiamine, was detected, indicating that this was the sole radioactive compound present in significant amounts after hydrolysis. Separation of thiamine and its phosphoric acid esters in liver was achieved

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