in the blood and was given four injections of neoarsphenamine. In 1937 she received four injections of a bismuth preparation.

Marital history: Husband living and well. Seven children all living and well. No abortions.

Examination was essentially negative except for the presence of a burn-like scar in the left upper chest anteriorly which we believe had been caused by a gumma. Gastric analysis (with histamine) showed free hydrochloric acid present in normal quantities.

X-ray studies of the stomach and duodenum: The stomach was found to be hypotonic with sluggish peristalsis and choreic movements. A filling defect was seen in the second portion of the duodenum. Six hours post-cibam the stomach still contained about 20 per cent of the opaque meal.

We would like to have explored the abdomen, but the patient refused consent. She was, therefore, given an ambulatory Sippy diet, tincture of belladonna, and intensive antiluetic treatment.

On May 5, 1938, about forty days after she was first seen, she had received four injections of neoarsphenamine and four of bismuth. In September, 1938, her gastro-intestinal symptoms had lessened greatly. She had received twelve injections of neoarsphenamine and twenty-two of bismuth, together with some potassium iodide. The blood Kahn was 4+. On November 8, 1938, to-and-fro peristalsis was still visible near the navel. On November 14, 1938, however, the old filling defect in the duodenum had disappeared and there was no gastric retention. On January 25, 1939, examination of the spinal fluid was negative and the blood Kahn was negative. Antisyphilitic treatment was continued. On April 19, 1939, the duodenal bulb appeared to be pulled posteriorly, perhaps by adhesions. There was no gastric stasis. The patient was well until November 22, 1939, when she had an acute intestinal upset, and again the Kahn was positive. On December 22, 1939, X-ray examination showed no disease in stomach or duodenum, and after that the patient felt well. She gained weight and looked like a different woman.

SUMMARY AND COMMENT

We recognize that the diagnosis of duodenal syphilis in this case is only presumptive, but the disappearance of the lesion under antisyphilitic treatment makes this diagnosis the most acceptable one. As Eusterman has said, "in all cases of syphilis in which a demonstrable gastric lesion is present, the condition should be regarded as syphilitic until it is proved otherwise."

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The Effect of Small Intestinal Distention Upon Bile and Urine Flow--Its Possible Relationship to the Hepatorenal Syndrome*

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CLINICAL acceptance of the hepatorenal syndrome as an entity is more general today because of the accumulation of experimental and clinical evidence (1). The hepatorenal syndrome has been recognized in a wide variety of conditions such as intestinal obstruction, liver trauma, burns and generalized peritonitis (2). There still is, however, considerable disagreement as to the factors and mechanisms involved in its production in the different clinical conditions. Helwig and his associates (3, 4) have expressed the belief that damaged liver tissue elaborates some potent toxin which acts more or less specifically on the kidneys. Boyce and McFetridge (5) doubt that there is any specific action of the toxic substance upon the kidneys and suggest that kidney failure results from the action of foreign proteins excreted by the convoluted tubules. Infection has been suggested by Touroff (6) as a cause of the kidney damage in cases dying from "liver shock." A number of other possibilities exist which might account for the frequent combined failure of the liver and kidney function in the hepatorenal syndrome of intestinal obstruction. It is possible that the intestinal distention might affect the liver and kidney function through an alteration of the blood flow and oxygen supply and through nervous reflex inhibition of their secretory activity. This paper presents the results of our experiments upon dogs in which we have tried to evaluate some of these factors as possible contributory causes of the hepatorenal syndrome in intestinal obstruction.

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METHODS

The experiments were performed upon 10 dogs fasted for 18 hours and anesthetized with sodium pentobarbital (30 mgm. per kilogram of body weight intravenously). The blood pressure was recorded from the cannulated left carotid artery. The respiration was recorded from a bellows around the chest of the dog. Bile flow was studied in 7 dogs by cannulating the common bile duct close to the duodenum after ligation of the cystic duct near the common duct. The drops of bile were recorded by an electrical recorder. A ligature was placed around the duodenum and a large cannula was tied into the terminal ileum which was also ligated distal to the cannula. The cannula was attached to a mercury manometer and an inflation bulb by means of a Y tube. The abdominal wall was then closed with heavy silk suture. A control basal flow of bile was then obtained after about 30 minutes. Intestinal distention was maintained at pressures of 20, 40 and 70 mm. of mercury for a period of ½ hour each. Oxygen was administered by nasal catheter (8 liters per minute) to determine what effect it had upon the bile flow with the intestine distended to pressures of 40 and 70 mm. of mercury.

The excretion of urine was studied in a similar manner upon 3 dogs. Each ureter was cannulated and the flow of urine was recorded on a revolving kymograph drum by electrical recorders. A uniform, mild diuresis was maintained by continuous intravenous drip administration of 1000 cc. of physiologic sodium chloride solution over a period of 4 hours.

TABLE I

Effect of acute intestinal distention upon the flow of bile, respiration and blood pressure in the nembutalized dog

Dog		Intraenteric Pressure in MM. of Mercury					
		Control	20	40	70	70 Plus Oxygen	Control After Release of Pressure
1.	Blood pressure mm. of mercury	180	180	180	180		180
	Respiration	17	23	25	25		20
	Bile flow cc. per hour*	10.8	9.0	11.4	11.4		9.0
	Per cent change		— 16%	+ 5%	+ 5%		— 16%
2.	Blood pressure	170	170	165	165		—
	Respiration	10	16	16	20		20
	Bile flow	9.0	7.2	8.4	6.6		4.8
	Per cent change		— 20%	— 6%	— 26%		— 36%
3.	Blood pressure	170	170	170	170		—
	Respiration	6	8	6	11		7
	Bile flow	7.8	6.6	6.6	5.4		5.4
	Per cent change		— 15%	— 15%	— 30%		— 30%
4.	Blood pressure	110	110	110	110	100**	
	Respiration	40	52	58	58	40	
	Bile flow	10.8	9.0	8.4	9.0	10.2	
	Per cent change		— 16%	— 22%	— 16%	— 5%	
5.	Blood pressure	110	100	100	100	98**	
	Respiration	36	32	40	44	44	
	Bile flow	12.6	9.0	7.2	7.8	9.6	
	Per cent change		— 28%	— 42%	— 38%	— 23%	
6.	Blood pressure	138	100	100	100	100	
	Respiration	48	60	64	60	48	
	Bile flow	7.8	7.8	7.8	6.6	7.8	
	Per cent change		0%	0%	— 15%	0%	
7.	Blood pressure	115	118	110	120	120	120
	Respiration	40	52	44	60	52	60
	Bile flow	8.4	7.8	7.2	4.8	7.8	8.4
	Per cent change		— 7%	— 14%	— 42%	— 7%	0%

*Calculated on the basis of a 10 minute control period preceding distension and a 10 minute period during distension.
**Intraenteric pressure of 40 mm. of mercury plus oxygen therapy.

In all experiments care was taken to avoid kinking of the cannulae when the intestine was distended.

RESULTS

No significant alteration of the blood pressure was observed in any of the 10 dogs upon distention of the entire small intestine. In some instances there was a temporary elevation of 5 to 10 mm. of mercury, in other instances a fall of 5 mm. and in some no change occurred. The respiratory rate increased in all of the 10 dogs and the depth of the respirations decreased upon distention of the intestine. Administration of oxygen by nasal catheter decreased the respiratory rate in 3 of the 4 dogs treated.

Table I shows that acute distention of the entire small intestine with intraenteric pressures ranging from 20 to 70 mm. of mercury caused a decrease in the flow of bile in 6 of the 7 dogs. The decrease varied from 6 to 42 per cent of the control flow. With an intraenteric pressure of 20 mm. of mercury the decrease in bile flow was 16, 20, 15, 16, 28, 0 and 7 per cent. When the pressure was increased to the diastolic blood pressure (70 mm. of mercury) a further decrease in bile flow was observed ranging from 16 to 42 per cent. Nasal oxygen increased this flow in dogs 4, 5, 6 and 7.

The effect of various intraenteric pressures upon urine secretion is presented in Table II. Pressures of 20 mm. of mercury caused an increased flow of urine of 11, 120 and 57 per cent in the 3 dogs. Higher pressures of 40, 60 and 90 mm. of mercury resulted in an increase of urine flow of 50 to 360 per cent above the control level. Release of the pressure was followed by a 12 and 14 per cent reduction below normal in the urine flow in dogs 4 and 6.

DISCUSSION

The nerve fibers of the vagi have been found to exert an excitatory or inhibitory secretory effect upon the liver in the dog and monkey by Tanturi and Ivy (7) in 1938. Ivy believes that the splanchnic nerves contain inhibitory secretory fibers. However, it is difficult to prove the presence of such fibers in the hepatic nerves since they exert such a marked effect upon hepatic circulation. Goldman and Ivy (8) have found an inhibition of the bile flow from 18 to 80 per cent below the control level by distention of the entire colon in dogs and rhesus monkeys. This inhibition did not occur upon the redistention of the colon after section of the hepatic nerves. This evidence indicates that distention of the colon inhibits the flow of bile from the liver by a nerve reflex through the hepatic nerves. They never distended the colon beyond the limit of compressibility but they did not measure the intracolonic pressure. They did not study the effects of distention of the small intestine.

Distention of the small intestine in our dogs to an intraenteric pressure of 20 mm. of mercury (28 centimeters of water) is comparable to intraenteric pressures reported by Wangensteen (9) in clinical and experimental cases of small bowel obstruction where he found pressures ranging from 4 to 30 centimeters of water. In 5 cases of obstruction of the colon intraenteric pressures varying from 12 to 52 centimeters of water were found (37 mm. of mercury). Our results show that these intraenteric pressures caused a 7 to 42 per cent decrease in the bile flow in 6 of our 7 dogs. Since higher pressures may occur in some clinical cases of intestinal obstruction and in order to determine the effect of altered blood flow, intraenteric pressures varying from 40 to 90 mm. of mercury were also used in our experiments. Blalock and Mason (10) found that 80 per cent of the blood supply and 38 to 78 per cent of the oxygen supply to the liver in dogs is carried by the portal circulation. McMichael (11) found that in the cat the liver obtains about two-thirds of its oxygen

TABLE II

Effect of acute intestinal distention upon the secretion of urine, respiration and blood pressure in the nembutalized dog

Dog		Intraenteric Pressure in MM. of Mercury					
		Control	20	40	60	90	Control After Release of Pressure
1.	Blood pressure mm. of mercury	120	110	116	120	120	120
	Respiration	26	40	40	29	37	37
	Urine flow cc. per hour*	31.6	35.2	40	47.6	57.2	26.8
	Per cent change		+ 11%	+ 26%	+ 50%	+ 81%	— 12%
2.	Blood pressure	80	80	82	90	85	80
	Respiration	24	36	40	34	22	40
	Urine flow	20	44	40	92	36	36
	Per cent change		+ 120%	+ 100%	+ 360%	+ 80%	+ 80%
3.	Blood pressure	120	116	112	112	—	116
	Respiration	14	20	15	21	—	26
	Urine flow	19.6	30.8	16.0	22.0	—	16.8
	Per cent change		+ 57%	— 18%	+ 12%	—	— 14%

Mild diuresis by 1000 cc. of physiological sodium chloride solution intravenously over a period of 4 hours throughout the course of the experiment.
*Calculated on the basis of a 10 minute period before and during distension.

from the portal vein. In addition to the possible reflex nervous inhibition of the flow of bile it was thought that the decrease in portal blood flow produced by intestinal distention might be an additional factor in decreasing the bile flow from the liver. When the intraenteric pressure in our dogs was raised above the diastolic blood pressure (70 mm. of mercury) a further decrease in bile flow was observed in 4 of our 7 dogs. The administration of oxygen by nasal catheter after a distention of 40 and 70 mm. caused the bile flow to speed up in all of the treated dogs (4, 5, 6 and 7). Two possible factors may be responsible for this further decrease in bile flow. The first is an anoxemia following a decrease in the depth of the respirations because of the limited excursion of the diaphragm with severe intestinal distention. The second factor is a possible decrease in the portal circulation with distention of the intestine above the diastolic blood pressure. This inhibition is lessened by increasing the oxygen content of the blood by oxygen therapy as observed in our dogs.

Instead of decreasing the urine flow from the kidneys, intestinal distention resulted in an increased flow in all of our dogs. This may be explained on the basis of an increased blood flow through the kidneys due to a decrease in the mesenteric circulation brought about by distention of the intestine. Secretory inhibition on a nerve reflex basis was not evident. The absence of a secretory nerve reflex correlated with the failure of one of us (J. G. S.) to demonstrate secretory nerve fibers to the kidney while in Dr. Ivy's laboratory (12).

The blood pressure remained fairly constant throughout the course of the experiments. Small fluctuations of 5 and 10 mm. of mercury upon distention of the intestine were transient and subsided in several minutes.

Intestinal distention caused an increase in the rate and a decrease in the depth of respiration. Oxygen therapy slowed the hyperpnea. The decreased depth of respiration is due to decreased excursion of the diaphragm. Arterial blood oxygen analysis upon patients with abdominal distention showed a moderate anoxemia to be present. These observations will be reported elsewhere.

This work shows that mild intestinal distention (20 and 40 mm. of mercury) causes a nerve reflex inhibition in the flow of bile from the liver of 15 to 42 per cent below the control level. Distention severe enough (70 mm. mercury) to decrease the portal blood flow and oxygen supply to the liver may cause an inhibition of 26 to 42 per cent. This inhibition of liver function may make the liver more susceptible to injurious substances. Reflex nervous inhibition of kidney activity did not occur. An increase in the flow of urine was observed instead. This evidence would seem to indicate that impairment of liver function precedes renal impairment in the hepatorenal syndrome of cases of intestinal obstruction.

CONCLUSIONS

1. Experimental acute intestinal distention in nembutalized dogs caused a reflex inhibition of the bile flow. Intraenteric pressures of 20 and 40 mm. of mercury resulted in a decrease in the bile flow of 7 to 42 per cent below the control level.

2. A decrease in the portal blood flow and oxygen supply to the liver produced by distention of the entire intestine to pressures of 70 mm. of mercury caused a further decrease in bile flow in 4 of our dogs. Oxygen therapy lessened this inhibition in all of the dogs treated.

3. Nervous reflex inhibition of the flow of urine did not occur upon distention of the small intestine to pressures of 20, 40, 60 and 90 mm. of mercury. An increase in urine flow from 11 to 81 per cent occurred. This was attributed to an increased blood flow through the kidneys.

4. The blood pressure was not significantly altered by distention of the small intestine.

5. The depth of respiration was decreased and the rate was increased by distention. Oxygen therapy decreased the respiratory rate and lessened the depression of bile flow produced by distention of the small intestine.

6. Inhibitory nervous reflexes, decreased blood flow and anoxemia probably are factors involved in decreasing liver function and thereby make the liver more susceptible to damage in cases of intestinal distention.

7. Inhibition of liver function probably precedes inhibition of kidney function in the hepatorenal syndrome of intestinal obstruction.

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