REGIONAL BLOOD FLOW DURING DIGESTION IN THE CONSCIOUS DOG

By

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ABSTRACT

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Blood flows to the major organs of the resting conscious dog were measured prior to and thirty and ninety minutes after feeding using radioactive microspheres. Cannulae were chronically implanted in the left atrium (for microsphere injection) and mammary artery (for reference arterial samples). Blood flow to the heart, adrenals, adipose tissue, skeletal muscle, brain, stomach and distal jejunum was unchanged during digestion. The increase in blood flow in the small intestine spread from the duodenum and proximal jejunum at thirty minutes to the ileum ninety minutes after feeding and was confined to an increase in flow to the mucosal layer of the intestinal wall. Blood flow to the colon was unchanged except for a decrease in the distal colon at thirty minutes. Blood flow to the pancreas increased and hepatic artery flow decreased during digestion. Thus, the cardiovascular response to feeding is limited to those organs actively involved in digestion.

To my parents

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CHAPTER I

INTRODUCTION

Early studies of the postprandial cardiovascular response in conscious animals indicated that cardiac output increased significantly during digestion and resulted in an increase in blood flow to all organs of the body. As methodology improved, however, it became apparent that feeding elicits a biphasic cardiovascular response. During the presentation and ingestion of food, cardiac output, heart rate, aortic pressure and resistance in the various vascular beds are altered in a pattern which mimics an increase in sympathetic neural activity. Within five to thirty minutes following a meal, cardiac output, heart rate, aortic pressure and blood flow to the heart and kidney return to control levels while superior mesenteric artery flow starts to rise and reaches a maximum in thirty to ninety minutes. Blood flow to the limbs decreases during digestion in the resting animal while hepatic artery flow remains constant.

Due to the physical limitations of electromagnetic flowmeters, it has not been possible to measure either total or regional blood flow to a number of major organs. The development of the radioactive microsphere technique

for measuring regional blood flow has resolved this difficulty. It was the purpose of this study to utilize the radioactive microsphere technique to measure 1) blood flow to the brain, pancreas, adipose tissue, and adrenal glands and 2) regional distribution of blood flow within the brain, stomach, small intestine and large intestine in the conscious dog during digestion.

CHAPTER II

LITERATURE REVIEW

Although it had long been assumed that blood flow to the digestive organs increased during digestion, evidence in support of this hypothesis was not produced until 1910. At that time Brodie et al. (9) utilized the oncometric method (a modification of the plethysmographic method) to study blood flow through an isolated intestinal loop. They demonstrated that the luminal placement of salt solutions producing either an absorption of salt and water or an exsorption of fluid produced an increase in intestinal blood flow. In a further study that year, Brodie et al. (10) showed that the presence of Witte's peptone solution also produced a sustained increase in intestinal blood flow.

During the period 1924 to 1935, several authors studied cardiac output in humans after ingestion of a meal using a gas equilibration method based on the Fick principle (17,28,32,59). These studies reported a postprandial increase in cardiac output which varied in degree and duration with the size of the meal. An increase in pulse rate was also noted and in one report systemic arterial pressure was monitored and found to remain

unchanged (32). In his 1929 study, Grollman suggested that during digestion the splanchnic vasculature dilates and this increase in flow is compensated by the increased cardiac output without altering systemic arterial pressure (32).

The first attempts to measure regional blood flow in conscious dogs during digestion were conducted with thermostromuhr flowmeters (24,34,35). These experiments seemed to indicate that blood flow in the superior mesenteric, femoral, common carotid and left circumflex coronary arteries as well as the hepatic and exterior jugular veins increased during digestion. In 1940, however, Gregg et al. (30) demonstrated that the thermostromuhr was capable of producing qualitative as well as quantitative errors in measurement and the technique was subsequently abandoned.

In 1941, Abramson and Fierst (1) examined the peripheral circulatory response to digestion using the venous occlusion plethysmographic method on the hand, forearm and leg. The authors noted that peripheral blood flow did not change following a carbohydrate meal but that blood flow to the extremities did increase within sixty to ninety minutes of ingestion of a protein meal.

In 1950, Berman et al. (5) and Paine and Shock (53) used the balistocardiograph technique for measuring cardiac output and reported an increase in cardiac output and heart rate after a meal. Brandt et al. (7) used the bromsulphalein (BSP) clearance method for estimating splanchnic blood flow in 1955 and reported a 35 percent

increase in flow following a protein meal and an 8 percent decrease in flow following a glucose meal. In 1960, Reinenger and Nutik (55) used the BSP clearance technique to show a 25 percent increase in splanchnic blood flow in humans following a glucose meal. Arterial blood pressure remained constant throughout the experiment.

Thus most of the studies up through 1960 indicated that splanchnic blood flow increases postprandially in humans (8,14) and dogs (9,10,55) and that cardiac output increases an average of 25 to 45 percent in both species (5,17,28,32,34,53,55,59). Furthermore, the composition of the meal consumed seemed to determine the extent of the increase in splanchnic flow (8) as well as the degree and duration of the increase in cardiac output (17,32,55). Splanchnic blood flow seemed to increase more after a heavy meal than a light meal and the increase in cardiac output was greater and of longer duration after a heavy meal. Arterial pressure remained constant (14,32) and heart rate increased after the ingestion of a meal (5,17,32). Blood flow to the arms and legs was also believed to increase postprandially (1).

With the development of electromagnetic and pulsed ultrasonic flowmeters, researchers in this field began to find major discrepancies between their studies and the less direct methods of previous authors. The first of such reports came in 1961 when Rushmer et al. (57) monitored blood flow in the abdominal aorta, renal artery, superior mesenteric artery and hepatogastric artery of

conscious dogs with pulsed ultrasonic flowmeters. Following consumption of a plate of commercial dog food, they noted "a questionable reduction" of blood flow through the renal artery and abdominal aorta. During the experiment, superior mesenteric artery blood flow did not change and hepatogastric artery flow increased in only one instance.

In 1965, Jones et al. (38) studied the effects of digestion on cardiac output in humans as measured by the dye dilution technique (indocyanine green). Contrary to previous reports, they found no increase in cardiac output twenty minutes after the ingestion of a mixed meal (30 percent protein, 30 percent fat, 40 percent carbohydrate). This study was contradicted in 1966 by Dagenais et al. (19) using the same technique (dye dilution with Coomassie blue dye) to measure cardiac output in humans following a protein or carbohydrate rich meal. They found that both meals caused an increase in cardiac output, heart rate and systolic pressure which reached a peak between 180 and 270 minutes after ingestion. It should be noted that cardiac output also increased in a fasted control group but the increase in the fed group was significantly greater than that in the control group.

Burns and Schenk conducted two studies in conscious dogs between 1967 and 1969 (12,13) with electromagnetic flow transducers attached to the superior mesenteric artery and ascending aorta. They reported that a meal consisting of 15 ounces of horsemeat produced no change

in cardiac output while superior mesenteric artery blood flow increased within five minutes of feeding and reached a plateau fifty minutes later. The average increase in superior mesenteric artery blood flow was 71 percent and represented an increase in flow to that region from 7.5 to 14.6 percent of cardiac output.

In 1968, Fronek and Stahlgren (27) used electromagnetic flow transducers in a comprehensive study of the cardiovascular response to the presentation, ingestion and digestion of food. Cardiac output and blood flow through the brachiocephalic, external iliac and superior mesenteric arteries were measured in conscious dogs during each phase of feeding. Systemic pressure and heart rate were also monitored. When food was first presented, all measured variables increased with the exception of superior mesenteric artery blood flow, which remained unchanged. During ingestion, cardiac output, systemic pressure and heart rate continued to increase and reached a maximum within the first minute. Also during the first few minutes of ingestion, blood flow through the brachiocephalic artery continued to increase and external iliac artery flow decreased. Within one hour of feeding, cardiac output, systemic pressure and brachiocephalic and external iliac artery blood flow returned to control levels. Heart rate remained slightly elevated and superior mesenteric artery blood flow reached a plateau of 133 percent of control levels. During the third hour of digestion, cardiac output, heart rate, systemic blood pressure and

external iliac artery blood flow remained at control levels. Superior mesenteric artery blood flow remained elevated but brachiocephalic artery blood flow decreased to 80 percent of control. The authors suggested that the observed responses to presentation and ingestion of food could be attributed to a generalized sympathetic response and that the pattern of blood flow during digestion indicated a redistribution of blood flow in favor of the splanchnic region at the expense of the extremities.

In that same year, Hopkinson and Schenk (37) studied postprandial blood flow in the portal vein, hepatic artery and hepatic vein in conscious dogs with electromagnetic flowmeters. They reported a mean hepatic blood flow of 21.8 ml/min/kg of which approximately 64 percent was provided by the portal vein. During digestion, hepatic artery flow remained unchanged (7.7 ml/min/kg) while portal venous flow increased 76 percent resulting in an overall increase in hepatic blood flow of 32 percent. They also reported that cardiac output, as measured by electromagnetic flowmeter, remained unchanged during digestion.

In 1969, Vatner et al. (62) reported findings similar to those of Fronek and Stahlgren (27) using both electromagnetic and pulsed ultrasonic flowmeters. As before, they found indications of a generalized sympathetic response to anticipation and ingestion. During digestion, they noted a decrease in iliac artery blood flow of approximately 20 percent and an increase in superior

mesenteric artery blood flow of as much as 300 percent. The decrease in iliac artery blood flow, however, lasted only one hour and was eliminated or reversed if the animal changed position or walked about. Renal artery blood flow did not change. In a subsequent study in 1970, Vatner et al. (63) demonstrated that the circulatory responses to anticipation and ingestion were indeed related to sympathetic activity by attenuating the response with both alpha-adrenergic and beta-adrenergic blockade. Neither blockade was effective in eliminating the mesenteric vasodilation during digestion, however, and although cholinergic blockade could eliminate the mesenteric response, a bilateral vagotomy could not. The authors also demonstrated a cephalic phase of digestion by placing food before a muzzled dog and observing a cardiovascular response similar to that in the fed animals, although it was less pronounced and the mesenteric vasodilation lasted only fifteen minutes.

In two additional studies, in 1970 and 1974, Vatner et al. used the same techniques as in their earlier studies (62,63) to extend their work to the baboon (65) and the left circumflex artery of the dog (64). The results of these studies are much the same as their previous reports with the added observation that left circumflex coronary flow increased during the anticipation and ingestion phases of feeding but returned to control levels within fifteen to twenty minutes.

In 1975, Norryd et al. (50) studied cardiac output, pulse rate, systemic arterial pressure, superior mesenteric blood flow and portal venous pressure in the human using a dye dilution technique. All measurements were taken three to four times within one hour of feeding. The authors reported no change in cardiac output, pulse rate or systemic arterial pressure. Portal venous pressure increased 15 percent above control and superior mesenteric blood flow increased on the average by 113 percent. Administration of a barium solution with the meal followed by a fluoroscopic examination showed that some food had reached the upper part of the jejunum within 5 minutes of completion of the meal.

In 1976, Chou et al. (16) used electromagnetic flowmeters to study blood flow through the celiac and superior mesenteric arteries in anesthetized dogs in response to intragastric and intraduodenal placement of digested food. The results of these experiments suggested that blood flow increases only in those portions of the small intestine exposed to digested food. These findings were supported by previous studies by Van Heerden et al. (61) in 1968 and Yu et al. (67) in 1975 in which the authors used radioactive microspheres in anesthetized dogs to study blood flow to isolated loops of the small intestine exposed to hypertonic glucose solutions. Both studies demonstrated that blood flow increased significantly in those regions exposed to hypertonic glucose while flow in other regions did not.

In their 1976 study, Chou et al. (16) used the venous outflow and radioactive microsphere techniques to examine total and compartmental blood flow to the wall of an isolated jejunal loop exposed to digested food. The authors reported that the increase in total blood flow to the wall of the small intestine was due solely to an increase in flow to the mucosal layer while blood flow to the submucosa and muscularis remained unchanged. In 1975, Yu et al. (67) had also reported that the increase in blood flow to the intestinal wall in response to hypertonic glucose was confined to the mucosal layer while flow to the submucosa and muscularis remained constant. In 1976, however, Bond and Levitt (6) reported that blood flow to all portions of the intestinal wall increased during digestion in the conscious dog as measured with the radioactive microsphere technique.

Thus it can be seen that the current concept of the circulatory response to feeding is that, with the exception of a brief anticipatory phase, cardiac output, systemic arterial pressure and blood flow to the heart and kidneys remain unchanged. Blood flow to the small intestine rises rapidly, increasing on the average 28-132 percent following a meal, and may be compensated by a decrease in blood flow to the extremities. However, at present there are no clear data concerning the effects of digestion on blood flow to the brain, pancreas, adipose tissue, adrenal glands, stomach, small intestine or colon in the conscious dog.

CHAPTER III

METHODS

Preparation of the Experimental Animals

Adult mongrel dogs of either sex weighing between 22 and 30 kilograms were anesthetized with sodium pentobarbital (30 mg/kg) and ventilated with room air via an endotracheal tube with a positive pressure respiration pump (Harvard, Model 607, Dover, Massachusetts). The left chest was opened under aseptic conditions at the third intercostal space and an incision was made in the pericardium in the vicinity of the left atrium. The left atrium was cannulated via the left atrial appendage with biologically inert silastic tubing (Dow Corning, Midland, Michigan; i.d. = 0.078 in, o.d. = 0.125 in) for the injection of microspheres. The left mammary artery was also cannulated with the same silastic tubing for the withdrawal of a reference arterial blood sample and the monitoring of systemic arterial blood pressure and heart rate. Both tubings were filled with sodium heparin (1000 units/ml) and exteriorized at the back of the neck. The surgical incisions were closed, the lungs were reinflated and the animal was allowed to recover from surgery and anesthesia. Meperidine hydrochloride (40 mg) was administered intramuscularly immediately following surgery and

again six hours later. Procaine penicillin (400,000 units) and dihydrostreptomycin (0.5 gm) were administered intramuscularly prior to surgery and twice a day for a few days.

The animals were allowed food and water *ad libitum* after surgery and were exercised daily. They were exposed to the laboratory setting for at least one hour each day during which time the cannulas were flushed and refilled with heparin. This was done to insure the patency of the cannulas and to accustom the animal to the experimental environment in order to minimize stress.

Preparation of the Microspheres

Carbonized microspheres labeled with either scandium-46 (dia = 13.2 ± 0.7 μ), strontium-85 (dia = 13.6 ± 0.9 μ) or cerium-141 (dia = 13.9 ± 1.0 μ) were obtained from the Nuclear Product Division of the Minnesota Mining and Manufacturing Company (3M Center, St. Paul, Minnesota). The specific activity was 10 millicuries/gm and the specific gravity was 1.23 ± 0.05 gm/cc. One milligram of microspheres contained approximately 440,000 microspheres. The microspheres were delivered in a solution of 10% dextran and 0.05% Tween 80 (polyoxyethylene sorbitan mono-oleate) to prevent aggregation of the spheres. The microsphere suspensions to be used during the experiments were prepared from the stock solution a few minutes prior to use. An appropriate volume of agitated stock solution containing approximately 2.5×10^6 microspheres

(0.6 to 0.8 ml) was added to 2 ml of a 20% dextran solution in a glass centrifuge tube and the whole was treated with an ultrasonic sonifier cell disruptor (Branson Instrument Co., Long Island, New York) to achieve a uniform dispersion of the microspheres. This solution was then drawn into a 3 ml plastic disposable syringe for injection. The order of injection of the microspheres was randomized.

Experimental Protocol

Series 1

All animals were fasted for 24 hours prior to the experiment. On the day of the experiment, the animals were exercised and allowed to defecate and urinate approximately 30 minutes prior to the start of the experiment. They were then brought to the experimental area and made to lie down, whereupon the cannulas were flushed and filled with normal saline. The arterial pressure catheter was attached to a Statham Pressure Transducer (Model No. P 23 Gb) and systemic arterial pressure was recored on a Sanborn Model 964 recorder. After a steady arterial pressure recording had been obtained for fifteen minutes, the first microsphere injection was prepared.

The microspheres were injected into the left atrium while a reference arterial blood sample was withdrawn from the mammary artery with an infusion/withdrawal pump (Harvard, Model 901, Dover, Massachusetts) at a rate of 7.75 ml/min for two minutes. Systemic blood pressure and

heart rate were monitored prior to and after microsphere injection. Upon completion of the injection, both cannulas were capped and the dog was free to move about. The dog was not allowed to see or smell food until the first microsphere injection (control) had been completed. The dog was then given a meal of a commercial dog food containing 12% protein and 7% fat (Alpo Beef Chunks, Allen Products Co., Allentown, Pennsylvania) and water and was allowed to eat undisturbed.

The second and third microsphere injections were made thirty and ninety minutes after completion of the meal. The procedure for each injection was the same as the first and the animal was allowed to move about between injections. Upon completion of the third injection, the animal was sacrificed with sodium pentobarbital and an intracardiac injection of a saturated potassium chloride solution.

Series 2

In this series, the surgical preparation and experimental procedure were identical to Series 1 except that the animals were not fed during the experiment. The second and third injections were made at times corresponding to the 30 and 90 minute injections in the test series.

Tissue Sampling

After the animal was sacrificed, duplicate samples of tissue were taken from the organs to be studied in order to determine their radioactivity. Each sample was placed in a pre-weighed disposable counting tube and

weighed. Sample weight was determined by subtracting the weight of the tube from the weight of the tube and sample. The samples weighed approximately one gram and filled the tube to a height of 1 to 2 cm. The organs studied and the method of sampling are as follows:

Reference Arterial Sample: The blood collected during the injection period was heparinized and placed in disposable plastic counting tubes. The withdrawal rate was divided by the total radioactivity of the sample to provide a constant for the conversion of radioactivity (counts/min) to blood flow (ml/min).

Skeletal Muscle: Eight to ten random samples of muscle were taken from both the forelimb and hindlimb of the animal. The average of the blood flows determined from these samples is reported.

Heart: Four random samples were taken from the left ventricle and two random samples were taken from the right ventricle. The average flow for each ventricle is reported.

Adipose Tissue: At least two random samples of fat were taken from the abdominal cavity with an additional two to four samples taken from other regions of the body when available. The average of the available samples is reported.

Liver: Duplicate samples were taken from each lobe of the liver and the average of all the samples is reported as hepatic artery blood flow. There is some error in this method due to hepatic trapping of microspheres

passing through the arterio-venous shunts of the intestinal tract; however, it is small (2-3%) (21,29).

Pancreas: Duplicate samples were taken from both the head and tail region and the average blood flow in each region is reported separately.

Adrenal Glands: Either the left or right adrenal gland was removed and the whole was counted. The blood flow reported is calculated from the total radioactivity of the organ.

Brain: The entire brain was removed and divided into seven regions based on the standard anatomical landmarks (Medulla, Pons, Thalamus-Midbrain, Hypothalamus, Pituitary, Cerebellum and Cerebrum). Each region was then divided into the standard one gram samples and the radioactivity of all samples from each region was counted and added to give the total radioactivity from which the total blood flow to each region was calculated. Total brain blood flow was calculated using the weighted average of the regional blood flows. Additionally, blood flow to the grey and white matter of the brain was determined from random samples of the caudate nucleus and corpus callosum, respectively.

Gastrointestinal Samples: All samples of the stomach and intestinal wall were divided into duplicate samples of the mucosal, submucosal and muscularis layers by blunt scraping. An average blood flow was calculated for each portion of the wall and total wall flow was calculated as

the weighted average of the three layers. The weight distribution of the three layers is taken from the work of Yu (67). The following samples were taken:

a) Stomach Body
b) Stomach Antrum
c) Duodenum, within 15 cm of the pylorus
d) Proximal Jejunum, within 5 cm of the ligament of Treitz
e) Distal Jejunum, taken approximately 100-150 cm from the ligament of Treitz
f) Ileum, within 15 cm of the ileocecal juncture
g) Proximal Colon, within 35 cm of the ileocecal juncture
h) Distal Colon, within 35 cm of the rectum

Calculation of Blood Flow

The radioactivity of all samples was measured using the Searle 1185 series gamma counter. The energy windows used were ^{46}Sc, 700-1150 keV; ^{85}Sr, 464-564 keV; ^{141}Ce, 95-195 keV. Separation of the isotope peaks was accomplished using a preprogrammed Wang 800 series computer. Radioactivity was expressed as counts per minute and blood flow was calculated from the following formula:

$$BF = \frac{C_s \times 100 \times RBF}{C_r}$$

where BF = blood flow to the tissue or organ in ml/min/100 gm; C_s = counts/gm of sample; RBF = reference blood

flow (rate of withdrawal from the reference artery); and C_r = total counts in the reference blood sample.

Expression of Data and Statistical Methods

The calculated blood flow for each organ at control, 30 and 90 minutes in both series is expressed as the mean ± the standard error of the mean (Mean ± S.E.M.). The blood flow in a tissue or an organ at thirty minutes was compared to control and blood flow at ninety minutes was compared to control levels using Student's t-test for paired comparisons (49). The level of significance was taken at $P<0.05$.

CHAPTER IV

RESULTS

The animals in this study exhibited no outward signs of distress during the injection of microspheres. Between injections, the animals either remained in a resting position or moved to another area of the laboratory and lay down. During both series of experiments, arterial blood pressure and heart rate remained constant. The average control arterial blood pressure in the test series was 96 ± 3.1 mm Hg and the heart rate was 133 ± 8.7 beats/min. In the fasted series, the average control arterial blood pressure was 96 ± 8 mm Hg and the heart rate was 130 ± 15 beats/min.

As seen in Table 1, blood flows to the various regions of the brain in the test series were not significantly altered 30 and 90 minutes after feeding with one exception. Blood flow to the cerebral hemispheres significantly decreased by 8.28 ml/min/100 gm (-14 percent) 30 minutes after completion of the meal. This resulted in a corresponding significant decrease in total brain blood flow of 7.27 ± 2.18 ml/min/100 gm (-12 percent). However, as indicated in Table 2, the pattern of total and regional brain blood flow in the test series is identical to that of the

Table 1. Mean ± S.E.M. total and regional blood flow (ml/min/100 gm) to the brain in the conscious dog before and after feeding

Region	Time (min) after feeding		
	-10(Control)	30	90
Medulla	37.93± 2.78	35.09± 2.92	37.28± 3.47
Pons	49.38± 4.69	44.80± 5.88	48.63± 6.14
Thalamus-Midbrain	59.32± 3.72	54.91± 4.78	53.18± 5.10
Hypothalamus	61.40± 7.41	55.05± 9.27	55.15± 5.85
Pituitary	104.50±15.38	125.40±22.35	129.04±34.01
Cerebellum	64.22± 2.97	55.84± 5.05	60.88± 5.87
Cerebral Hemispheres	61.06± 3.34	52.80± 4.43*	54.15± 4.09
Grey Matter	98.90± 8.72	96.09± 7.34	91.39± 8.33
White Matter	21.91± 1.66	18.99± 3.41	18.93± 2.31
Total	59.60± 3.26	52.33± 4.39*	53.51± 4.16

*Values are statistically significant relative to control at $P<0.05$, $N = 8$.

Table 2. Mean ± S.E.M. total and regional blood flow (ml/min/100 gm) to the brain in the conscious fasted dog

Region	Time (min) of measurement*		
	-10(Control)	30	90
Medulla	39.98± 3.51	38.53± 3.61	43.21± 9.72
Pons	54.96± 9.57	51.79± 8.43	56.95±13.44
Thalamus-Midbrain	62.12± 5.91	57.26± 9.01	60.83±10.26
Hypothalamus	69.79±11.19	68.87±11.72	79.09±25.13
Pituitary	122.75±64.58	153.34±43.41	170.69±75.81
Cerebellum	62.59± 3.83	59.08± 7.78	68.68±10.14
Cerebral Hemispheres	59.09± 8.16	51.67± 8.16**	56.60±13.42
Grey Matter	97.57±10.20	91.14±16.22	97.85±24.49
White Matter	19.80± 1.23	20.74± 1.65	26.98± 3.81
Total	58.83± 7.39	52.44± 7.61**	57.76±12.62

*Measurements were taken at times corresponding to those in the test series.

**Values are statistically significant relative to control at $P<0.05$, $N = 4$.

fasted series. At the time corresponding to the first postprandial measurement of blood flow in the test series, the average blood flow to cerebral hemispheres and total brain in the fasted series decreased by 8.32 ± 0.90 (-12 percent) and 7.75 ± 1.60 ml/min/100 gm (-11 percent), respectively. These changes are not statistically different from those in the test series ($P>0.05$, Student's t-test, unpaired comparison).

Tables 3 and 4 show the average blood flows to various organs and tissues. Blood flow to the skeletal muscle, right and left ventricles of the heart, the adipose tissue and the adrenal gland showed no significant change 30 or 90 minutes after feeding (Table 3). Hepatic artery blood flow, however, decreased significantly from 61.03 ± 13.30 to 37.57 ± 8.24 ml/min/100 gm thirty minutes after feeding and remained below control levels at 42.00 ± 6.75 ml/min/100 gm ninety minutes after feeding. Blood flow to the pancreatic head and tail increased markedly at thirty and ninety minutes after feeding. The blood flow in the head region of the pancreas nearly doubled at thirty minutes from the control level of 170.58 ± 30.01 ml/min/100 gm to 301.78 ± 37.88 ml/min/100 gm and reached 343.63 ± 93.95 ml/min/100 gm within ninety minutes of feeding. In the tail region, blood flow rose markedly from a control level of 149.37 ± 28.39 ml/min/100 gm to 300.92 ± 32.75 ml/min/100 gm within thirty minutes and peaked at 324.35 ± 98.31 ml/min/100 gm ninety minutes after feeding. In the

Table 3. Mean ± S.E.M. blood flow (ml/min/100 gm) to various organs of the conscious dog before and after feeding

Organ	Time (min) after feeding		
	-10(Control)	30	90
Skeletal Muscle	5.17± 0.91	3.84± 0.80	3.88± 1.14
Right Cardiac Ventricle	54.84± 7.80	51.52± 6.67	51.17± 8.55
Left Cardiac Ventricle	95.74±15.73	78.71±10.23	81.66±14.52
Adipose Tissue	12.02± 2.57	18.76± 4.09	8.45± 3.34
Adrenal Gland	288.23±39.45	306.36±58.20	285.02±47.04
Liver (Hepatic Artery)	61.03±13.30	37.57± 8.24*	42.00± 6.75*
Pancreas Head	170.58±30.01	301.78±37.88*	343.63±93.95*
Pancreas Tail	149.37±28.39	300.92±32.75*	324.35±98.31*

*Values are statistically significant relative to control at $P<0.05$, $N = 8$.

fasted series (Table 4), blood flow to the skeletal muscle, right and left ventricles of the heart, the adrenal gland, the liver and both the pancreatic head and tail was unchanged. Blood flow to the adipose tissue in the fasted series, however, did decrease from the control value of 12.54 ± 3.35 ml/min/100 gm to 6.79 ± 3.36 ml/min/100 gm at the time corresponding to ninety minutes after completion of the meal in the test series.

The average total and regional blood flows to the wall of the gastric body in both the fasted and test series can be seen in Table 5, while that of the gastric antrum can be seen in Table 6. In both cases, there were no significant changes in blood flow to the three layers of the stomach wall or in total wall flow in either series. In order to prove that the radioactive microsphere technique is capable of detecting an increase in gastric blood flow in our experimental setting, 1.0 mg of histamine phosphate was administered subcutaneously to a conscious dog. As shown in Figure 1, blood flow to the whole wall and mucosa of the gastric body and antrum was markedly increased despite a decrease in systemic arterial blood pressure of 15 mm Hg.

The effects of feeding on the total and regional blood flow of the duodenum are demonstrated in Table 7. Blood flow to the mucosal layer of the duodenum rose from a control level of 113.30 ± 21.03 ml/min/100 gm to 219.99 ± 68.85 ml/min/100 gm at thirty minutes after feeding and then to 228.97 ± 40.03 ml/min/100 gm ninety minutes after

Table 4. Mean ± S.E.M. blood flow (ml/min/100 gm) to various organs of the fasted conscious dog

Organ	Time (min) of measurement*		
	-10(Control)	30	90
Skeletal Muscle	2.39± 0.73	2.93± 0.20	2.88± 0.44
Right Cardiac Ventricle	45.62± 2.90	45.64± 3.09	51.67± 4.34
Left Cardiac Ventricle	81.92± 2.16	75.76± 8.62	93.40± 5.09
Adipose Tissue	12.54± 3.35	5.88± 1.67	6.79± 3.36**
Adrenal Gland	323.17±40.63	382.15±54.63	368.00±48.78
Liver (Hepatic Artery)	35.68± 0.78	37.62± 4.02	30.02± 7.22
Pancreas Head	197.16±59.31	123.75±28.48	127.85±26.45
Pancreas Tail	190.68±68.20	116.15±22.05	118.62±28.44

*Measurements were taken at times corresponding to those in the test series.

**Values are statistically significant relative to control at $P<0.05$, $N = 4$.

Table 5. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the gastric body in the conscious dog

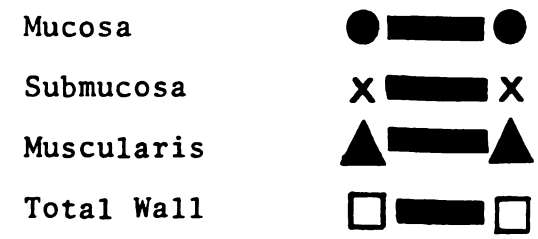
	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	81.24±18.67	64.29±13.55	75.11±20.00
Submucosa	8.42± 3.81	3.46± 1.54	6.88± 3.51
Muscularis	5.27± 0.98	4.06± 0.74	6.09± 1.40
Total Wall	43.82± 9.32	33.99± 6.81	40.67±10.42
Fasted N = 4			
Mucosa	109.47±12.67	88.25±16.94	83.92±15.60
Submucosa	3.20± 1.34	6.67± 3.17	3.64± 1.30
Muscularis	11.04± 6.16	13.60± 5.05	30.80±18.15
Total Wall	59.73± 8.11	49.45± 8.91	53.32±11.12

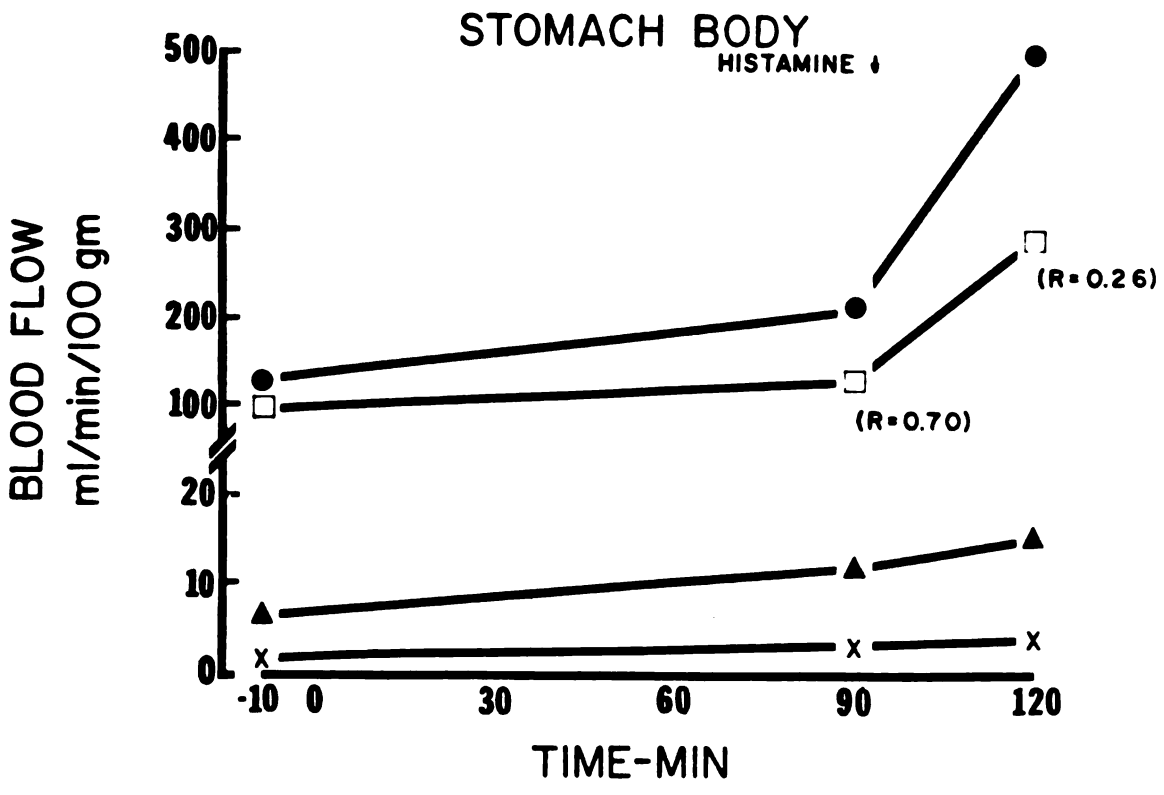
Table 6. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the gastric antrum in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	93.06±18.22	137.01±34.06	143.44±41.10
Submucosa	17.10± 9.60	15.85± 8.61	13.96± 5.31
Muscularis	11.15± 2.55	7.80± 1.71	9.79± 1.17
Total Wall	53.23±10.44	73.84±17.42	77.32±20.86
Fasted N = 4			
Mucosa	59.39±15.61	75.25±27.47	47.28± 1.96
Submucosa	7.76± 3.59	15.87± 7.82	13.28± 4.30
Muscularis	9.89± 3.50	16.88± 4.97	16.89± 5.84
Total Wall	34.16± 7.47	45.80±16.37	31.32± 0.09

Figure 1. The effects of histamine on the total and regional blood flow (ml/min/100 gm) to the wall of the gastric body and antrum.

At -10 minutes, a control measurement of blood flow was made. At 0 minutes, the dog ate only a small portion of the meal. At 90 minutes, a second measurement of blood flow was made and immediately thereafter 1.0 mg of histamine phosphate was injected subcutaneously. At 120 minutes, a third flow measurement was made. N = 1




STOMACH BODY
HISTAMINE
BLOOD FLOW
ml/min/100 gm
500
400
300
200
100
20
10
0
(R=0.26)
(R=0.70)
-10
0
30
60
90
120
TIME-MIN

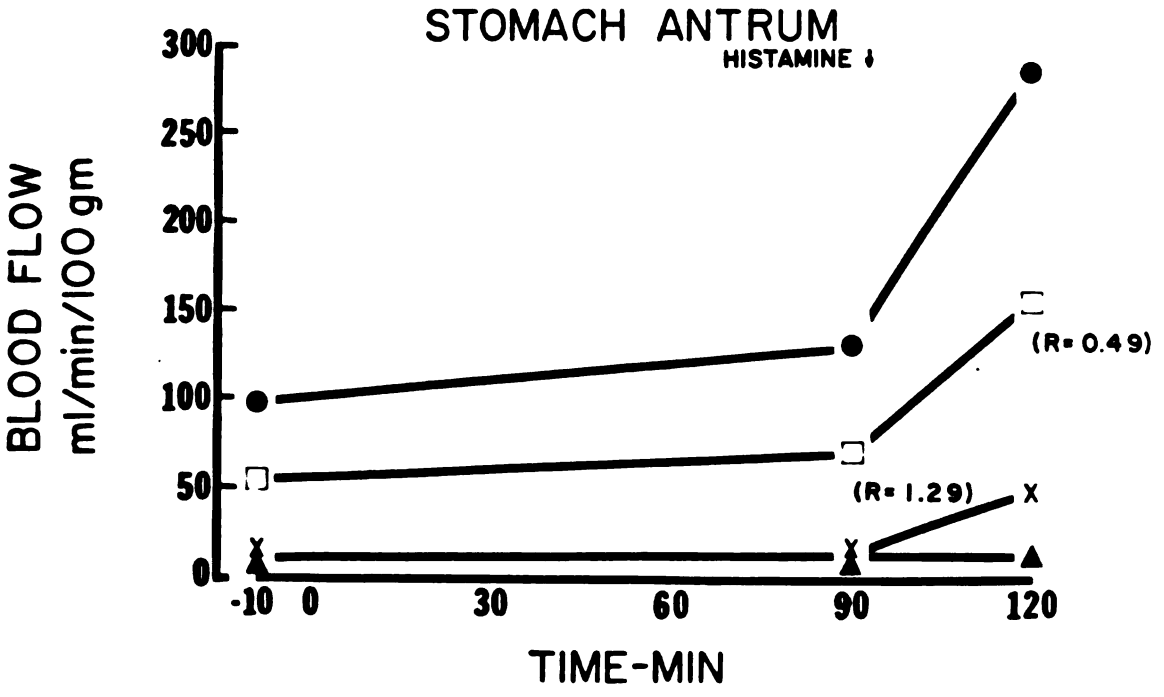

STOMACH ANTRUM
HISTAMINE
BLOOD FLOW
ml/min/100 gm
300
250
200
150
100
50
0
(R=0.49)
(R=1.29)
-10
0
30
60
90
120
TIME-MIN

Figure 1

Table 7. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the duodenum in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	113.30±21.30	219.99±68.85*	228.97±40.03*
Submucoa	4.66± 1.43	18.84±17.28	15.97±13.89
Muscularis	10.99± 2.23	14.00± 2.21	13.55± 3.19
Total Wall	78.44±14.33	151.72±45.70*	157.28±26.46*
Fasted N = 4			
Mucosa	129.33±10.12	171.62±14.12*	118.48±53.48
Submucosa	11.37± 6.38	7.57± 2.42	2.98± 1.36
Muscularis	14.29± 3.60	14.37± 3.48	13.50± 4.32
Total Wall	90.70± 8.67	117.72± 9.43	104.61±12.72

*Values are statistically significant relative to control at $P<0.05$.

feeding. Blood flow to the submucosa and muscularis remained constant throughout the experiment. As a result, blood flow to the total duodenal wall increased from 78.44 ± 14.43 ml/min/100 gm to 151.72 ± 45.70 ml/min/100 gm within thirty minutes of feeding. Ninety minutes after feeding, it reached 157.28 ± 26.46 ml/min/100 gm. In the fasted series, blood flow to the mucosal layer of the duodenum was also significantly above control levels at the time of the second microsphere injection. However, total blood flow to the wall of the duodenum was not significantly altered in the fasted series (Table 7).

The average total and regional blood flows to the proximal jejunum are shown in Table 8. As can be seen, there were no changes in total or regional blood flow in this portion of the jejunum in the fasted series. In the test series, however, the pattern of response was identical to that of the duodenum. Mucosal blood flow more than doubled from 114.25 ± 25.70 ml/min/100 gm to 270.72 ± 84.01 ml/min/100 gm within thirty minutes of feeding and then rose to 295.06 ± 70.11 ml/min/100 gm ninety minutes after completion of the meal. Again, submucosal and muscularis blood flow remained unchanged resulting in an increase in blood flow to the jejunal wall from 74.76 ± 16.36 ml/min/100 gm to 180.63 ± 51.33 ml/min/100 gm and then to 193.07 ± 42.97 ml/min/100 gm. As seen in Table 9, however, neither total nor compartmental blood flow changed in the wall of the distal jejunum in either the test or fasted series.

Table 8. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the proximal jejunum in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	114.25±25.70	270.72±84.01*	295.06±70.11*
Submucosa	9.91± 4.84	22.37±18.26	38.99±35.77
Muscularis	5.95± 1.84	28.23±13.13	9.01± 1.54
Total Wall	74.76±16.36	180.63±51.33*	193.07±42.97*
Fasted N = 4			
Mucosa	143.34±23.14	173.09±32.69	193.93±36.57
Submucosa	12.63± 5.80	15.97± 8.44	9.53± 3.86
Muscularis	12.48± 5.63	11.02± 2.44	11.50± 3.41
Total Wall	95.48±15.46	114.17±19.55	134.94±16.23

*Values are statistically significant relative to control at $P<0.05$.

Table 9. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the distal jejunum in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	156.32±34.82	207.89±59.38	255.45±59.45
Submucosa	10.19± 4.82	10.82± 6.28	6.18± 2.43
Muscularis	11.67± 1.63	12.72± 3.07	7.53± 2.36
Total Wall	89.68±25.14	136.13±37.27	164.14±37.81
Fasted N = 4			
Mucosa	126.29±17.21	157.84±40.19	116.92±18.93
Submucosa	3.64± 0.58	6.45± 2.28	2.53± 1.79
Muscularis	6.21± 1.49	12.81± 4.12	5.91± 1.21
Total Wall	81.68±11.09	103.57±26.09	75.57±12.08

In the ileum, there were no changes in either total or compartmental blood flow in the fasted animal, nor were there any changes thirty minutes after feeding in the test series (Table 10). Ninety minutes after completion of the meal, however, mucosal flow in the ileum of the fed dog increased from a control level of 127.71 ± 30.40 ml/min/100 gm to 238.77 ± 70.42 ml/min/100 gm. As before, there were no changes in submucosal or muscularis blood flow and consequently total blood flow to the ileal wall rose from 74.06 ± 17.08 ml/min/100 gm prior to feeding to 136.17 ± 38.50 ml/min/100 gm ninety minutes after completion of the meal.

In Table 11, it is evident that total and compartmental blood flows were not altered in the proximal colon in either series of experiments at thirty or ninety minutes. This is also true for the distal colon in the fasted series. As can be seen in Table 12, however, mucosal blood flow in the distal colon of the test series did show a marked decrease from 149.65 ± 21.70 ml/min/100 gm to 97.77 ml/min/100 gm thirty minutes after feeding. Neither submucosal nor muscularis blood flow was altered and total blood flow to the wall of the distal colon fell from 64.13 ± 7.96 ml/min/100 gm to 39.44 ± 7.19 ml/min/100 gm. All blood flows returned to control levels ninety minutes after completion of the meal.

Table 10. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the ileum in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	127.71±30.40	93.12±17.73	238.77±70.42*
Submucosa	2.60± 0.64	4.20± 2.28	7.34± 5.22
Muscularis	9.12± 1.49	13.38± 4.81	9.19± 1.84
Total Wall	74.06±17.08	56.34± 9.63	136.17±38.50*
Fasted N = 4			
Mucosa	150.73±53.58	150.70±55.14	135.47±52.65
Submucosa	7.77± 3.41	7.44± 2.26	3.31± 1.25
Muscularis	14.12± 7.05	8.03± 2.02	6.86± 1.26
Total Wall	89.17±28.87	86.64±29.77	77.55±29.73

*Values are statistically significant relative to control at $P<0.05$.

Table 11. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the proximal colon in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	153.47±33.73	139.65±40.15	157.90±42.65
Submucosa	19.05±10.62	5.61± 2.72	10.95± 4.37
Muscularis	8.37± 2.42	8.00± 3.74	10.69± 7.21
Total Wall	62.74±11.55	53.15±14.11	63.88±15.94
Fasted N = 4			
Mucosa	257.95±12.83	316.49±35.01	250.00±35.40
Submucosa	8.11± 2.37	11.64± 4.86	7.44± 3.68
Muscularis	6.13± 1.26	9.83± 3.77	5.26± 1.38
Total Wall	97.40± 3.69	120.87±14.22	94.02±12.82

Table 12. Mean ± S.E.M. total and compartmental blood flow (ml/min/100 gm) to the wall of the distal colon in the conscious dog

	Time (min) after feeding		
Compartment	-10(Control)	30	90
Fed N = 8			
Mucosa	149.65±21.70	97.77±20.95*	139.02±40.24
Submucosa	25.51±11.71	12.31± 9.10	14.72± 9.28
Muscularis	11.84± 4.32	4.11± 1.31	10.93± 5.52
Total Wall	64.13± 7.96	39.44± 7.19*	58.05±16.95
Fasted N = 4			
Mucosa	174.69±44.59	230.17±70.72	172.98±43.02
Submucosa	11.15± 5.33	13.14± 5.05	7.84± 2.43
Muscularis	6.26± 1.02	10.57± 6.10	4.94± 1.62
Total Wall	67.97±15.53	90.32±25.78	66.14±15.11

*Values are statistically significant relative to control at $P<0.05$.

CHAPTER V

DISCUSSION

It has been well established that splanchnic blood flow increases after a meal in man (14,46,50), primates (65) and dogs (6,12,13,27,37,63,64). Furthermore, the most recent evidence indicates that cardiac output (6,12, 13,27,37,50,63-65), renal blood flow (64,65) and coronary blood flow (64,65) are transiently altered during ingestion but return to control levels fifteen to thirty minutes after completion of the meal. There is some evidence indicating a postprandial decrease in blood flow to the extremities in the conscious dog (27,64,65) and one study reports that hepatic artery blood flow remains at control levels during digestion while portal venous blood flow and consequently total hepatic blood flow increases (37). Although the postprandial distribution of blood flow among the layers of the wall of the gastrointestinal tract has been studied, the results are contradictory. Studies in anesthetized dogs have shown that blood flow increases only in those portions of the small intestine actually exposed to chyme (16,61) and that this is due solely to an increase in blood flow to the mucosal layer of the intestinal wall while flow to the submucosa and muscularis remains constant (16,67). A recent study in

conscious dogs, however, suggests that blood flow increases in all compartments of the intestinal wall during digestion (6). Although a feeling of drowsiness is often experienced after a heavy meal, the possibility that this may be associated with a change in either regional or total brain blood flow has not been examined. In addition, the effects of digestion on blood flow to the pancreas, adrenal glands and adipose tissue in the conscious dog are unknown. The purpose of this study, therefore, was to use the radioactive microsphere technique to examine the effects of digestion on blood flow to the brain, pancreas, adrenal glands and adipose tissue and to further examine the postprandial distribution of blood flow within the brain and the wall of the gastrointestinal tract in the conscious dog.

The validity of the microsphere method for determining both total and regional organ blood flow has been well established (2,3,15,21,22,29,36,39,47,66,67). The blood flows reported in this study fall within the range of flows reported in the literature for the brain (50-70 ml/min/100 gm) (26,47), adipose tissue (7-12 ml/min/100 gm) (4), muscle (2-5 ml/min/100 gm) (26), heart (60-80 ml/min/100 gm) (26), adrenal glands (300-400 ml/min/100 gm) (60), stomach (40-60 ml/min/100 gm) (22), small intestine (70-90 ml/min/100 gm) (15,29) and large intestine (60-80 ml/min/100 gm) (15). Blood flow to the pancreas was considerably higher than reported in previous papers, but this may be due to a depression of pancreatic blood flow as a result

of the extensive surgical preparation and anesthesia required in earlier studies. Hepatic artery blood flow at the control injection in the fed series was higher than has been reported in other studies (37,41). The submucosal and muscularis blood flows reported here are less than those reported by other authors (2,22,29) but are consistent with other studies within this laboratory.

As seen in Table 1, total brain blood flow decreases slightly thirty minutes and then returns to control ninety minutes after a meal. This decrease in total brain blood flow thirty minutes after feeding is due to a corresponding decrease in flow to the cerebral hemispheres while blood flow to the other regions of the brain remains unchanged. However, as shown in Table 2, both total and regional brain blood flow in the fasted series follow the same pattern and, in the case of total and cerebral hemisphere blood flow, the degree of change is the same ($P>0.05$, Student's t-test, unpaired comparison). The treatment of the animals and the method of injection were identical in all experiments and no behavioral differences were noted between the animals of either series. Since the results are identical in both the experimental and control series, the decrease in brain blood flow must have been caused by some common factor which is unrelated to the digestive state of the animal. Therefore, it must be concluded that digestion has no effect on either regional or total brain blood flow.

Skeletal muscle blood flow was not significantly changed in either the test or control series, as shown in Tables 3 and 4. This study agrees with that of Fronek and Stahlgren (27), who found that digestion had no effect on blood flow through either the brachiocephalic or iliac arteries during the first 90 minutes of digestion. Although Vatner et al. (64,65) reported a slight increase in iliac artery resistance during the first hour after feeding, they stated that this was abolished or reversed if the animal arose or changed position during this period and in no case did it last beyond one hour.

As seen in Tables 3 and 4, blood flow to the right and left cardiac ventricles remained constant in both series of experiments. This finding supports the results of a study by Vatner et al. (64) of the effects of digestion on coronary blood flow in conscious dogs. In their study, Vatner et al. measured the blood flow through the left circumflex coronary artery with electromagnetic flowmeters and reported that, with the exception of a transient increase during ingestion, coronary artery blood flow remained at control levels throughout the postprandial period.

Blood flow to the adrenal glands remained constant in both series of experiments, as seen in Tables 3 and 4, as did blood flow to the adipose tissue in the test series (Table 3). Blood flow to the adipose tissue in the control series was significantly decreased at the time corresponding to ninety minutes after feeding in the test series

(Table 4). This result, however, is difficult to interpret given the sensitivity of this vascular bed to even low levels of sympathetic neural activity or circulating catecholamines. It has been shown that stimulation of the sympathetic nerves to canine adipose tissue causes vasoconstriction (51) and, although the response is more variable, circulating catecholamines can have the same effect (4). Therefore, it is possible that sympathetic activity increased during the experiment in the control series due to the stress of a prolonged fast and resulted in a decrease in blood flow to the adipose tissue at the time of the last injection. It is also possible that this change in blood flow may be due to technical error.

Table 5 shows that blood flow to the gastric body was not significantly different from control at thirty and ninety minutes after completion of the meal. It was expected that flow to the gastric body and/or antrum should increase following a meal or at least thirty minutes after a meal as gastric juice and gastrin secretion are increased during this period. Thus, in order to verify the ability of the microsphere technique to detect changes in gastric blood flow in this experimental setting, histamine phosphate (1 mg) was administered subcutaneously in one dog and blood flow was measured thirty minutes later. Histamine administered at this dose (40 μg/kg) subcutaneously has been shown to stimulate hydrogen ion secretion within thirty minutes (48) and produce an increase in blood flow to the wall of the stomach (2). As seen in

Figure 1, blood flow to the wall of the gastric body and antrum doubled within thirty minutes of the administration of histamine. Therefore, the pattern of gastric blood flow during digestion as seen in this experiment, Tables 5 and 6, is a real phenomenon and is not due to technical error.

In the small intestine, blood flow increased significantly in the duodenum and proximal jejunum thirty minutes after feeding while flow to the distal jejunum and terminal ileum remained at control levels (Tables 7, 8, 9 and 10). Ninety minutes after feeding, blood flow to the duodenum and proximal jejunum remained elevated while flow to the distal jejunum was unchanged and flow to the terminal ileum increased significantly. Thus, in the small intestine the postprandial hyperemia appears to be confined to the proximal regions during the early stages of digestion and subsequently spreads to the more distal regions. An angiographic study in man has also shown that blood flow to the duodenum and upper jejunum increases within twenty minutes after a meal of ice cream (46). Furthermore, Chou et al. (16) have found that in anesthetized dogs blood flow in the small intestine increases only in those areas exposed to digested food. Thus, the pattern of blood flow changes in the small intestine observed in this study appears to follow the aboral flow of chyme in the small intestine.

A fluoroscopic study has shown that a portion of a meal containing barium can reach the upper jejunum as early as

five minutes after a meal (50), while examination of the gastrointestinal tract at autopsy in this study clearly demonstrated that chyme was present in all regions of the small intestine at the time of the last measurement. Thus, at 30 and 90 minutes after a meal, chyme containing the digested products of food is present in the duodenum and proximal jejunum resulting in an increase in blood flow to those regions. Although chyme may not have reached the distal jejunum 30 minutes after feeding, it is known to have been present ninety minutes after the meal and yet the blood flow to this region was not significantly different from control at either time. This may be due to the fact that even if the chyme were present in this region, it may not have contained a sufficient amount of the digested products of food to produce a hyperemia. Borgstrom et al. (7) have shown that in humans 90 to 100 percent of all fat, carbohydrate and protein present in chyme is absorbed within the first 100 cm of the jejunum. Studies in this laboratory have shown that the constituents of chyme responsible for the postprandial hyperemia in the jejunum are the digested products of food (45,58) and that the hyperemic effect depends on the concentration of the nutrients (43). Thus a solution containing 20% or more of digested food made from the same dog food as used in this study can produce a significant increase in jejunal flow but a 10% solution of that same digested food cannot (43). Neither undigested food nor bile in the jejunal lumen can produce an increase

in jejunal blood flow. Therefore, the absence of a hyperemia in the distal jejunum during this experiment is probably due to the fact that chyme containing the amount of nutrients necessary to produce a hyperemia does not reach this region within the first ninety minutes after feeding. Although bile in the jejunum does not alter jejunal blood flow, bile in the ileal lumen does produce a marked increase in blood flow to the ileum (44). Thus, blood flow to the ileum is not altered thirty minutes after feeding (Table 10), probably because chyme has not yet reached this region but at ninety minutes it has reached the ileum and the bile in the chyme produces a significant increase in ileal blood flow (Table 10).

In all cases where blood flow to the wall of the small intestine increased during digestion, it was due solely to an increase in blood flow to the mucosal layer of the intestinal wall while blood flow to the submucosa and muscularis remained at control levels. This finding is in agreement with that of Chou et al. (16,67) in the anesthetized dog but contradicts that of Bond and Levitt (6) in the conscious dog. The study by Bond and Levitt, however, is subject to some criticism. Several investigators (2,29,31) have suggested that while the microsphere method can clearly distinguish muscularis flow from that of the mucosa-submucosa, it may not be able to separate the mucosal and submucosal flows when the size of the spheres is not uniform. Microspheres are found to be preferentially trapped in the submucosa as sphere diameter

increases, although the sum of mucosal and submucosal radioactivity remains the same regardless of sphere size, i.e., they behave as if they were in a single compartment. Thus when Bond and Levitt divided their samples into villi, crypts and submucosa-muscularis, they may have been attributing increases in mucosal blood flow which were distributed to the submucosa to increases in muscularis flow. This error could be especially significant if the microspheres used were of relatively large diameter (the size of the spheres was not reported in the abstract).

In contrast to the small intestine, blood flow to the large intestine for the most part remains unchanged during digestion. As seen in Table 11, blood flow to the wall of the proximal colon remains at control levels throughout the experiment. In Table 12, it is evident that blood flow to the wall of the distal colon is significantly decreased thirty minutes but returns to control levels ninety minutes after feeding. Shortly after a meal, the feces in the middle colon is rapidly moved towards the rectum (20) as a result of the gastro-colic and duodeno-colic reflexes which produce mass movement in the colon. Chou et al. (15) have demonstrated that tonic contraction in the colon results in a decrease in total wall blood flow due to a decrease in flow to the mucosal layer. The decrease in blood flow to the wall of the distal colon thirty minutes after the meal is also due to a decrease in blood flow to the mucosal layer and

may possibly be the result of this phenomenon of mass movement.

Thus it can be seen that in the intestine, the presence of chyme in the duodenum and upper jejunum thirty minutes after feeding produces a significant increase in blood flow in those regions while flow to the distal jejunum and terminal ileum remains at control levels. Simultaneously, there may be a mass movement of feces from the middle colon to the rectum resulting in an overall decrease in blood flow to the distal portion of the colon. Within ninety minutes of feeding, some chyme has reached the terminal ileum producing an increase in blood flow to that region, while the increase in blood flow to the duodenum and proximal jejunum is sustained. Blood flow to the distal jejunum is not significantly different from control at either thirty or ninety minutes after feeding. Blood flow to the large intestine is not significantly different from control ninety minutes after completion of the meal. In all cases where blood flow to the intestinal wall increased, it was due solely to an increase in flow to the mucosal layer.

In conjunction with the marked postprandial intestinal hyperemia, blood flow to the pancreatic head and tail nearly doubled thirty and ninety minutes after feeding (Table 3). Several authors have demonstrated a direct correlation between pancreatic secretory activity and blood flow in response to various stimuli including intestinal hormones (23) and the placement of food in the

upper jejunum (42). It is probable, therefore, that the presence of chyme in the upper region of the small intestine thirty and ninety minutes after feeding stimulates pancreatic secretion which is accompanied by an increase in pancreatic blood flow as seen in this experiment.

As seen in Table 3, hepatic artery blood flow falls significantly below control levels thirty minutes and remains below control levels ninety minutes after feeding. This finding contradicts that of Hopkinson and Schenk (37) in which the authors used an electromagnetic flowmeter to measure hepatic artery, portal venous and hepatic venous blood flow following a meal. They reported that hepatic artery blood flow remained constant while portal venous and consequently total hepatic blood flow increased significantly. However, Norryd et al. (50) have shown that a mean increase in superior mesenteric artery blood flow of 121 percent in humans can result in a mean increase in portal venous pressure of 15 percent. Furthermore, Hanson and Johnson (33) have shown that in dogs there exists a reciprocity of flow between the portal vein and hepatic artery, such that an increase in portal venous pressure will cause an increase in hepatic artery resistance. Therefore, it is not unreasonable to expect that a postprandial increase in portal venous blood flow due to a sustained intestinal hyperemia may cause a decrease in hepatic artery blood flow as seen in this study.

In general, the present study shows that blood flow to the brain, heart, adrenal glands, skeletal muscle and

adipose tissue is not altered during digestion while blood flow to the small intestine and pancreas is markedly increased. Furthermore, all increases in blood flow in the small intestine are limited to those regions where chyme is present and are due solely to an increase in blood flow to the mucosal layer of the intestinal wall. Blood flow to the body and antrum of the stomach is not significantly altered thirty or ninety minutes after feeding. Hepatic artery blood flow decreases during digestion while blood flow to the large intestine remains at control levels except for a slight decrease in blood flow to the distal colon thirty minutes after feeding. Thus the results of this study indicate that the cardiovascular response to digestion is limited to those organs actively involved in the process.

CHAPTER VI

SUMMARY AND CONCLUSIONS

It has been demonstrated that heart rate, cardiac output, systemic arterial blood pressure and blood flow through the left circumflex coronary artery, renal artery and hepatic artery are not altered during digestion while blood flow through the superior mesenteric artery rises rapidly within the first thirty minutes of feeding and remains elevated for several hours. However, there are no clear data on the effects of digestion on blood flow to the pancreas, adrenal glands, adipose tissue and skeletal muscle as well as total and regional blood flow to the brain and the wall of the gastrointestinal tract. Therefore, in this study the radioactive microsphere technique was used to measure blood flow to the major organs of the conscious dog prior to and thirty and ninety minutes after feeding. The results indicate that:

1) Blood flow to the heart, adrenal glands, adipose tissue, skeletal muscle, gastric body and gastric antrum was not significantly altered during digestion.
2) The digestive state of the animal has no effect on either total or regional blood flow to the brain

3) Thirty minutes after feeding, blood flow to the
   a) duodenum increases
   b) proximal jejunum increases
   c) distal jejunum is unchanged
   d) ileum is unchanged
   e) proximal colon is unchanged
   f) distal colon decreases
4) Ninety minutes after feeding, blood flow to the
   a) duodenum remains elevated
   b) proximal jejunum remains elevated
   c) distal jejunum is unchanged
   d) ileum increases
   e) proximal colon is unchanged
   f) distal colon returns to control levels
5) In all cases where intestinal blood flow was altered during digestion, it was due solely to a change in blood flow to the mucosal layer while flow to the submucosa and muscularis remained unchanged.
6) Blood flow to the pancreas increased during digestion.
7) Hepatic artery blood flow decreased during digestion.

These results indicate that the cardiovascular response to digestion is limited to those organs actively involved in the digestive processes, that is, the small and large intestine, the pancreas and the liver. Furthermore, within the small intestine, the pattern of changes in blood flow

appears to follow the aboral movement of chyme down its length and supports the concept that blood flow increases only in those regions where chyme is present and absorption of nutrients or bile is taking place. In addition, whenever blood flow in the small intestine increases during digestion, it is due solely to a change in blood flow to the mucosal layer of the intestinal wall, the layer in which all postprandial absorption and secretion occurs. Blood flow to the large intestine is unchanged during digestion except for a transient decrease in blood flow to the distal colon thirty minutes after feeding. This may be associated with the mass movement of chyme from the middle colon towards the rectum due to a gastro-colic or duodeno-colic reflex. Blood flow to the pancreas increases markedly during digestion and is probably related to an increase in pancreatic secretory activity. Hepatic artery blood flow, on the other hand, decreases during digestion, possibly due to the increase in portal venous blood flow as a result of the postprandial intestinal hyperemia. This response may be mediated by an autoregulatory mechanism known as the "reciprocity of flow" between the hepatic artery and portal vein.

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