GASTROENTEROLOGY 1988;95:1294–301

Duplex Ultrasound Measurement of Postprandial Intestinal Blood Flow: Effect of Meal Composition

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Duplex ultrasound was used to evaluate the effects of 350-cal, 300-ml protein, fat, carbohydrate, and mixed (Ensure-Plus) liquid meals on celiac, superior mesenteric, and femoral artery blood flow in 7 healthy volunteers. Ingestion of separate water and mannitol solutions served as controls for volume and osmolarity. Duplex parameters of peak systolic velocity, end-diastolic velocity, mean velocity, and volume flow were determined before, and serially for 90 min after, ingestion of each test meal. Maximal changes were compared with baseline values. There were no significant changes in any of the blood flow parameters derived from the celiac or femoral arteries after any test meal ingested. In contrast, maximal changes in all superior mesenteric artery parameters were increased significantly over baseline ($p < 0.05$) after each of the test meals except water, with end-diastolic velocity showing proportionally the greatest increase. The study demonstrates that duplex ultrasound can provide a noninvasive means of studying the reactivity of the splanchnic arterial circulation to different stimuli and documents differing blood flow responses to variation of nutrients.

Although it is well documented that intestinal blood flow increases markedly in response to a meal, in humans the mechanisms controlling this postprandial hyperemic response are not well understood (1–4). A major impediment to the study of this aspect of human physiology has been the lack of a noninvasive technique capable of measuring intestinal blood flow in unanesthetized subjects. Attempts to understand human postprandial splanchnic blood flow have therefore been confined to extrapolations from animal data or from limited experiments using angiographic techniques or laparotomy with direct application of electromagnetic flowmeters (5,6). The invasive nature of these techniques clearly makes them unsuitable for serial examinations and most forms of clinical investigation.

Since its development in the late 1970s, duplex ultrasound has become a reliable noninvasive method of assessing both arterial and venous blood flow (7–9). Recent advances in engineering have made possible the development of 2.5–3-MHz scanheads. These low-megahertz devices permit deeper Doppler ultrasound penetration from the skin surface, therefore making it possible to study visceral vessel blood flow noninvasively. The technique is actively being used in investigations of portal vein flow (10) and has recently been used to document an increase in superior mesenteric artery (SMA) blood flow after consumption of a mixed meal (11,12). The purpose of the present study was to confirm the use of duplex ultrasound in detecting the effects of a mixed meal on celiac and superior mesenteric artery blood flow. In addition, we sought to evaluate the effect of individual nutrient types on human visceral arterial flow using both previously reported duplex parameters and the theoretically more accurate parameter of end-diastolic velocity.

Materials and Methods

Subjects and Meals

Seven healthy volunteers (5 men and 2 women with an age range of 28–38 yr) served as subjects for the study. No subject was taking any form of medication. All were nonsmoking, nondiabetics without known gastrointestinal or peripheral vascular disease, and all were of normal weight for their age, height, and sex.

Subjects ingested six separate liquid meals, consisting of mixed contents (Ensure-Plus; Ross Laboratories, Colum-

Abbreviation used in this paper: SMA, superior mesenteric artery.

0016-5085/88/$3.50

Table 1. Composition of Study Meals

Meal	Volume (ml)	Calories (kcal)	Osmolarity (mosmol/L)
Mixed[a]	300	355	550
Carbohydrate[b]	300	350	550
Fat[c]	300	347	<100
Protein[d]	300	350	<100
Mannitol[e]	300	0	550
Water	300	0	0

[a] Ensure-Plus (Ross Laboratories, Columbus, Ohio): 240 ml (protein 13.0 g, fat 12.6 g, carbohydrate 47.3 g) + 60 ml of H_2O. [b] Polycose (Ross Laboratories, Columbus, Ohio), 175 ml (2 cal/ml) + 125 ml of H_2O. [c] Microlipid (Chesebrough-Pons Inc., Greenwich, Conn): 93 ml (3.75 cal/ml) + 207 ml of H_2O. [d] Bacto-Peptone (Difco Laboratories, Detroit, Mich.). [e] City Chemical, New York, N.Y.

bus, Ohio), carbohydrate, fat, protein, mannitol, and water on separate days after an overnight fast. Meals were randomly administered to each subject with the time between each experiment varying from 1 day to 1 wk. All meals were standardized for caloric content, osmolarity, and volume (Table 1). The study was approved in January 1987 by the Human Subjects Review Committee of the University of Washington, Seattle, Washington.

Procedure

A duplex scanner combines B-mode and pulsed Doppler ultrasound in a single instrument in association with a microcomputer. Blood flow measurements are performed by first imaging the vessel of interest with the B-mode ultrasound component of the scanner. The ability to visualize the vessel under study is fundamental in duplex scanning, as it enables the pulsed Doppler sample volume cursor to be positioned within the vessel at a known angle of insonation (Figure 1). This angle, referred to as the Doppler angle, is the basis for the computer-derived calculation of duplex blood flow parameters based on Doppler frequency shift. The Doppler angle is automatically calculated and displayed by the software of the duplex machine and therefore can be maintained constant within each examination. This eliminates angle-induced errors in frequency shift as a source of variability in the calculation of duplex velocity parameters.

The resolution of the instrument depends on the frequency of the Doppler probe employed. Low-frequency scanheads (2.5–3 MHz) provide deeper penetration of the ultrasound beam but at the cost of a poorer B-mode image. However, when the vessel of interest is <2–3 cm from the skin surface, a 10-MHz scanhead can be used to provide excellent visualization of very small vessels. Our laboratory routinely uses duplex ultrasound to evaluate tibial

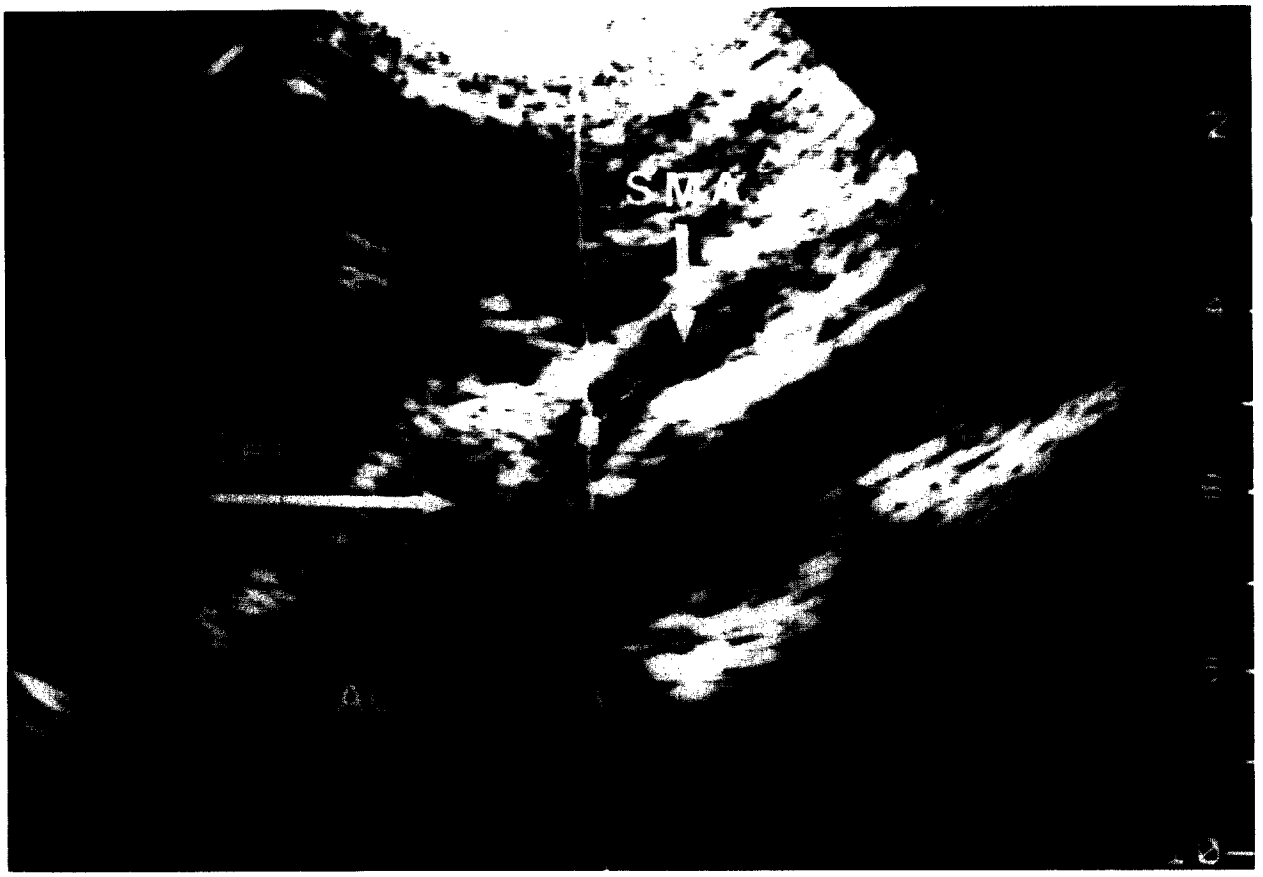

Figure 1. Longitudinal B-mode ultrasound view of the celiac (*Cel*) and superior mesenteric artery (*SMA*) originating from the anterior surface of the aorta (*Ao*). The pulsed Doppler sample volume is placed within the lumen of the SMA.

artery blood flow in adults and renal artery blood flow in premature infants.

Each subject was positioned supine on an examination table with the head of the table elevated 30°. Using a duplex scanner (Ultramark 8; Advanced Technology Laboratories), four duplex blood flow parameters—peak systolic velocity, mean velocity, end-diastolic velocity, and calculated volume flow—were obtained during a 30-min rest period and then serially at 10, 20, 30, 40, 60, and 90 min after a 1–3-min period required for ingestion of the test meal. The cross-sectional diameter of each artery was also measured at the beginning of each examination using the software available in the duplex scanner. Manual placement of the two-dimensional measurement cursor is, however, necessary before the computer calculation of the distance between cursors.

Peak systolic velocity represents maximum flow velocity recorded during each cardiac cycle. Mean velocity is a computer-derived value determined by integrating the area under each individual velocity waveform. End-diastolic velocity was recorded immediately before the next systolic upstroke and is known to correlate with end organ resistance to blood flow (Figure 2A) (13).

Volume flow was calculated from the mean velocity and the B-mode-determined fasting cross-sectional area of the vessel according to the following formula:

$$\text{Volume flow} = 3.14 \times \tfrac{1}{4}(\text{diameter}^2) \times \text{mean velocity}.$$

Only the fasting diameter of the vessel was used in volume flow calculations. The diameter of muscular arteries changes very little (<10%) over the normal physiologic range of blood pressures (14). Given this limited artery compliance, the small size of the celiac and SMA arteries (<0.8 cm), the fact that dimension cursors must be placed manually, and the somewhat limited resolution of deep abdominal vessels by B-mode imaging, we believe that the ability of duplex scanning to actually detect minimal changes in vessel diameter is questionable. We therefore refer to our volume flow measurements only as "calculated volume flow."

All values were expressed as a percentage of the corresponding fasting values determined before the ingestion of each test meal. Right brachial pulse rate and blood pressure were also monitored throughout each examination.

Statistical Analysis

All data were coded and entered into a computer. Statistical analysis was performed using the Statistical Package for the Social Sciences (15). Changes in blood flow parameters were compared at times of maximal change from baseline for each meal using Student's *t*-test for unpaired data.

Results

Artery Size

Mean femoral artery diameter was 0.78 cm (range, 0.93–0.49 cm). Corresponding values for the celiac and superior mesenteric artery were 0.66 cm (range, 0.40–0.80 cm) and 0.59 cm (range, 0.44–0.68 cm), respectively.

Femoral Artery Flow

Mean duplex blood flow parameters from the common femoral artery in the fasting state are shown

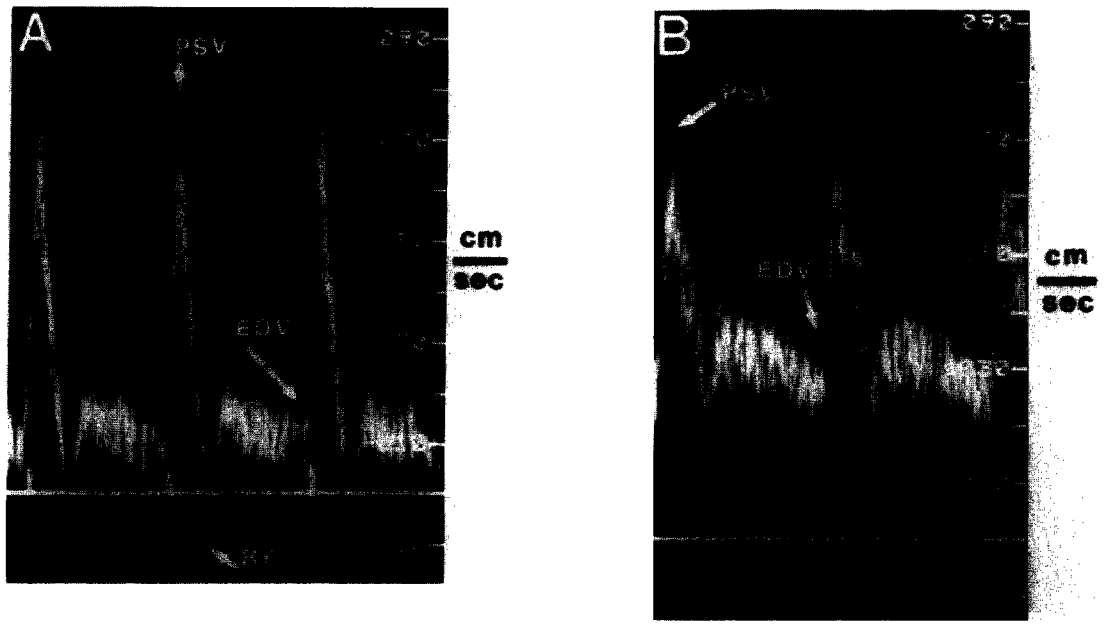

Figure 2. *A.* Fasting SMA Doppler waveform. Peak systolic velocity (*PSV*) and end-diastolic velocity (*EDV*) are measured directly; the area under the waveform is integrated by a microcomputer to compute mean velocity. Note the early diastolic reverse flow (*RF*) characteristic of the fasting SMA waveform. *B.* Fasting celiac artery Doppler waveform. There is continuous flow throughout diastole and absence of reverse flow.

Table 2. Fasting Duplex Blood Flow Parameters[a]

	Peak systolic velocity (cm/s)	End-diastolic velocity (cm/s)	Mean velocity (cm/s)	Volume flow (ml/min)
Celiac artery	101 ± 3.5	33 ± 1.4	52 ± 1.7	1083 ± 75
SMA	113 ± 3.9	15 ± 1.1	31 ± 1.4	538 ± 37
Femoral artery	83 ± 2.5	0 ± 0.2	10 ± 0.6	269 ± 22

SMA, superior mesenteric artery. [a] Mean ± SEM.

in Table 2. There were no significant changes in peak systolic velocity, mean velocity, end-diastolic velocity, or volume flow recorded from the common femoral artery after any of the test meals.

Celiac Artery Flow

The duplex-derived velocity waveform obtained in the fasting state from the celiac artery had a characteristic configuration with forward flow throughout diastole. End-diastolic velocity was typically about one-third peak systolic velocity (Figure 2*B*). Mean duplex blood flow parameters from the fasting celiac artery are shown in Table 2.

Table 3 shows the maximal postprandial changes in celiac artery velocities and flows in response to the various test meals. There were no statistically significant increases in the measured celiac artery flow parameters in response to any of the test meals.

Table 3. Maximal Percentage Increase Over Fasting Values in Duplex Flow Parameters: Celiac Artery[a]

Meal	Peak systolic velocity (cm/s)	Mean velocity (cm/s)	Volume flow (ml/min)	End-diastolic velocity (cm/s)
Mixed	20 ± 6	18 ± 4	18 ± 4	24 ± 9
Carbohydrate	14 ± 6	1 ± 4	1 ± 4	38 ± 9
Fat	−2 ± 4	10 ± 8	10 ± 8	4 ± 7
Protein	4 ± 2	21 ± 6	21 ± 6	14 ± 6
Mannitol	12 ± 10	29 ± 17	37 ± 19	11 ± 6
Water	1 ± 5	14 ± 5	14 ± 5	6 ± 10

[a] Mean ± SEM.

Superior Mesenteric Artery Flow

The characteristic configuration of the velocity waveform obtained from the SMA in the fasting state differed from that of the celiac artery. The SMA demonstrated early diastolic flow reversal followed by forward diastolic flow. In addition, SMA end-diastolic velocity was low, approaching zero in most cases (Figure 2*A*).

In contrast to the celiac artery, SMA blood flow measurements showed statistically significant maximal increases in all blood flow parameters after all of the test meals except the water meal (Table 4 and Figure 3). In addition, there were differences in response to the various test meals. After the carbohydrate meal, mean velocity, volume flow, and end-

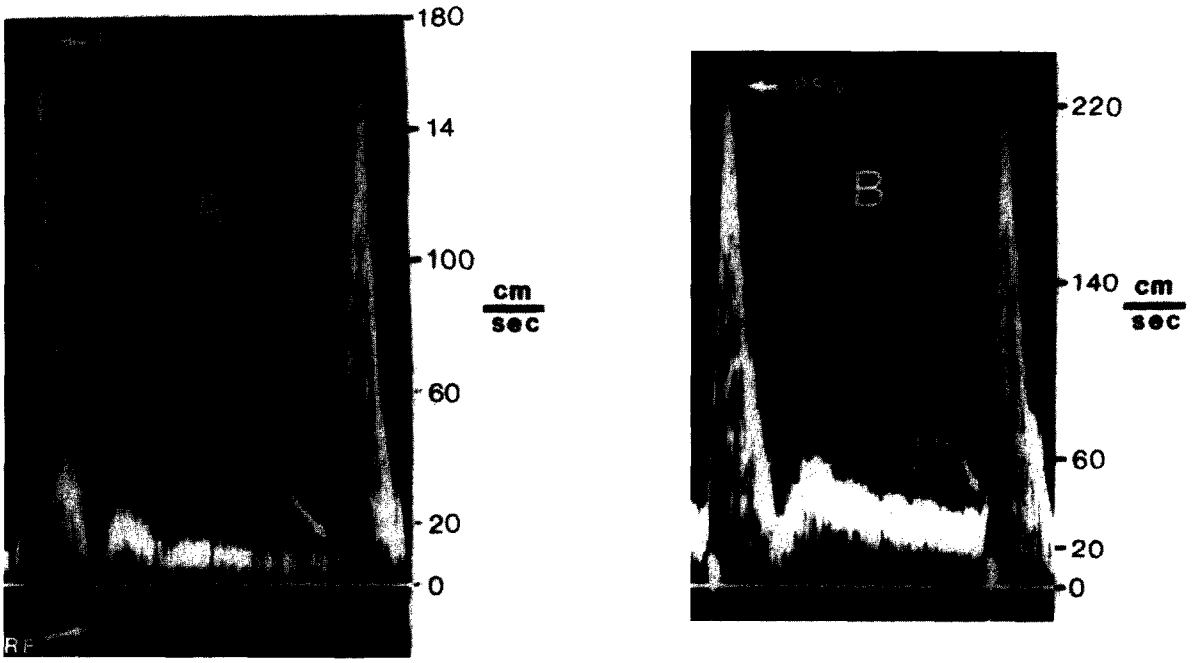

Figure 3. Superior mesenteric artery waveform before (*A*) and 30 min after (*B*) ingestion of the mixed meal. Note loss of reverse flow (*RF*) and increases in peak systolic velocity (*PSV*) and end-diastolic velocity (*EDV*) after feeding.

Table 4. Maximal Percentage Increase Over Fasting Values in Duplex Flow Parameters: Superior Mesenteric Artery[a]

Meal	Peak systolic velocity (cm/s)	Mean velocity (cm/s)	Volume flow (ml/min)	End-diastolic velocity (cm/s)
Mixed	42 ± 4	164 ± 30	164 ± 30	321 ± 100
Carbohydrate	30 ± 8	118 ± 23	118 ± 23	113 ± 20
Fat	42 ± 15	116 ± 25	117 ± 25	140 ± 47
Protein	22 ± 10	78 ± 15	78 ± 15	114 ± 21
Mannitol	33 ± 7	43 ± 10	48 ± 11	102 ± 45
Water	5 ± 7	24 ± 8	24 ± 8	34 ± 17

[a] Mean ± SEM.

diastolic velocity peaked 20 min after ingestion. Peaks in these same variables occurred slightly later, at 30 min, after ingestion of the other test meals (Figures 5–7). Maximal increases in duplex parameters, however, tended to be greater after ingestion of the fat and mixed meals (Figures 4–7). Finally, even though increases in duplex parameters in response to protein were less than those of the carbohydrate, fat, and mixed meals, they appeared to be better sustained (Figures 4–7).

Discussion

It is clear from the large amount of work involving duplex ultrasound being done at our laboratory and other institutions that it is a sensitive method of detecting changes in arterial blood flow parameters. The method noninvasively produces measurements of blood flow that are observer-independent and reproducible over time (16,17). It is now well established in the quantitative assessment of carotid and extremity arterial flow (18,19) and has recently been applied to investigations of the visceral circulation. Preliminary evidence suggests duplex scanning can be used to diagnose celiac and superior mesenteric artery stenosis (20). It also appears to provide a noninvasive means of following aortomesenteric bypass grafts in the postoperative period (21) and has begun to be used in the assessment of visceral blood flow after feeding (10,22).

It is important, however, to be aware of potential sources of error. This is especially true with regard to determination of calculated values such as volume flow or mean velocity. Technical factors that may affect these calculations include both errors in determination of the angle of insonation (thereby affecting the determination of Doppler frequency shift) and errors in the B-mode measurement of vessel diameter. Perhaps more important, the assumptions of parallel blood flow velocity vectors and a uniform velocity profile across the vessel lumen that are involved in the calculation of volume flow and mean velocity are probably not completely correct (23,24). In an effort to minimize potential errors inherent in the calculation of derived values we also chose to measure end-diastolic velocity as a measure of the peripheral resistance in the mesenteric circulation. It has been previously shown in animal models that Doppler-measured end-diastolic velocity correlates inversely with end organ resistance (13,25). As this is a directly measured parameter, it provides a measure of mesenteric resistance independent of many of the theoretic and technical factors that may adversely affect the accuracy of calculated values. Although our data show that changes in mesenteric resistance are paralleled by changes in mean velocity and volume flow, the direct measurement of end-diastolic velocity probably provides the most accu-

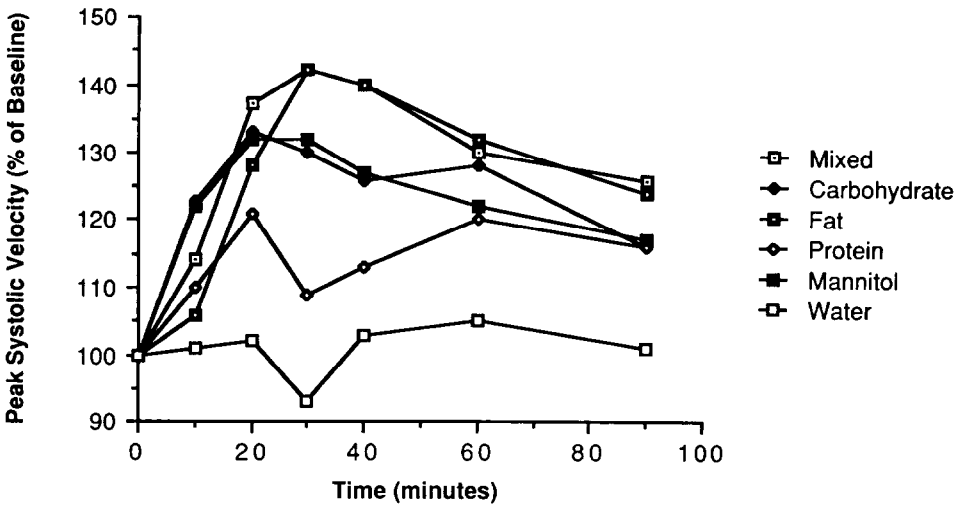

Figure 4. Peak systolic velocity in the SMA in response to various test meals. There was a significant increase in PSV ($p < 0.05$) with all meals except water. Peak systolic velocity is expressed as percentage of the fasting value.

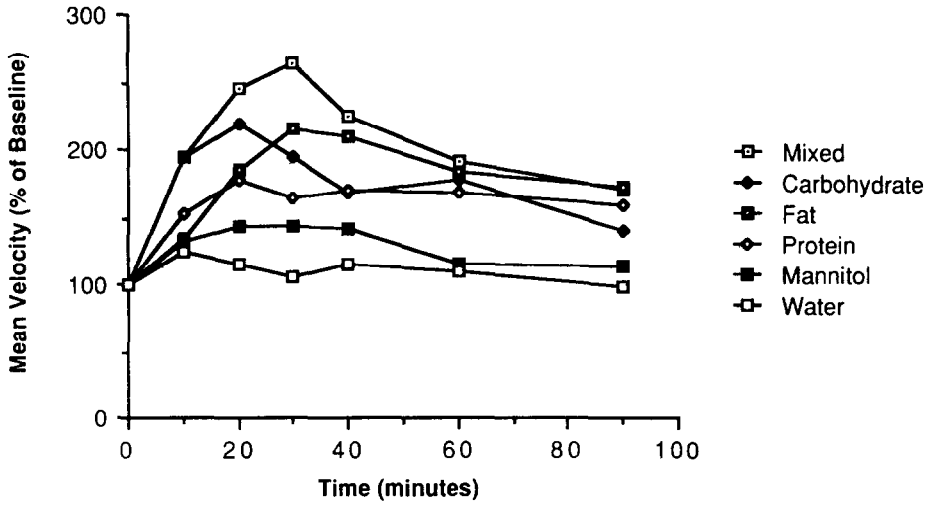

Figure 5. Mean velocity in the SMA in response to various test meals. There was a significant increase in mean velocity ($p < 0.05$) with all meals except water. Mean velocity is expressed as a percentage of the fasting velocity.

rate and certainly, to this point, the most theoretically sound duplex ultrasound measure of postprandial mesenteric hyperemia.

Clearly the regulation of human splanchnic arterial blood flow is of major scientific and clinical interest. Extrapolation from animal data is useful but not completely satisfactory. Not only may there be differences between species but also among animals of the same species depending on whether the animal is conscious or anesthetized. For example, Granger et al. (2), in a dog model, reported an absence of mesenteric hyperemia in response to protein ingestion. The same author, however, later reported an increase in intestinal hyperemia with protein ingestion in a rat model (26). This latter study also reported an increase in intestinal blood flow in conscious but not anesthetized rats after a mixed meal (26). Other earlier investigators have also implied a greater intestinal hyperemic response in conscious dogs versus anesthetized dogs (27,28).

This investigation confirms previous studies in establishing the ability of duplex ultrasound to detect the intestinal blood flow response to feeding in conscious humans (6,11,22). In addition, this study has sought to detail the effects of various individual nutrients on a number of duplex parameters. Increased SMA velocities and calculated volume flows were evident within 10 min of ingestion of all test meals except water. Blood flow response was maximal at 20 and 30 min and persisted for at least 90 min after the test meal. These findings are in general agreement with investigations in animal models us-

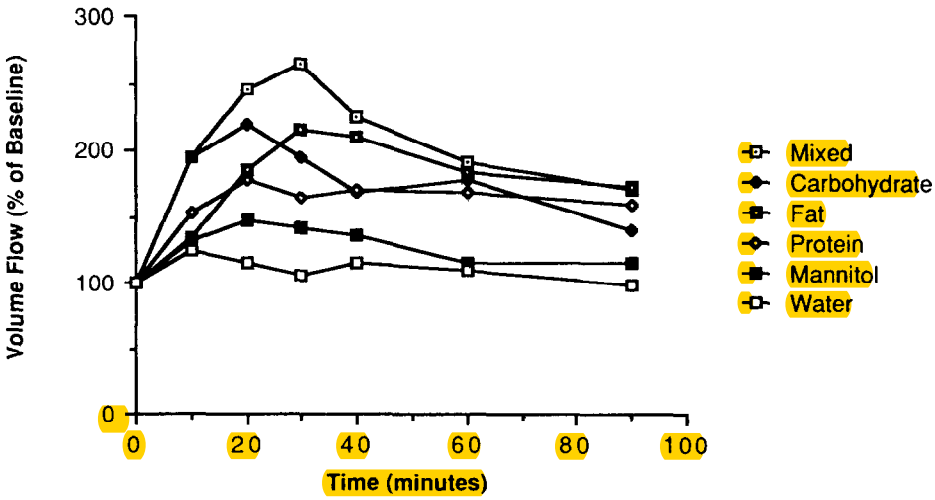

Figure 6. Doppler-calculated volume flow in the SMA in response to various test meals. There was a significant increase in volume flow ($p < 0.05$) with all meal types except water. Volume flow is expressed as a percentage of the fasting value.

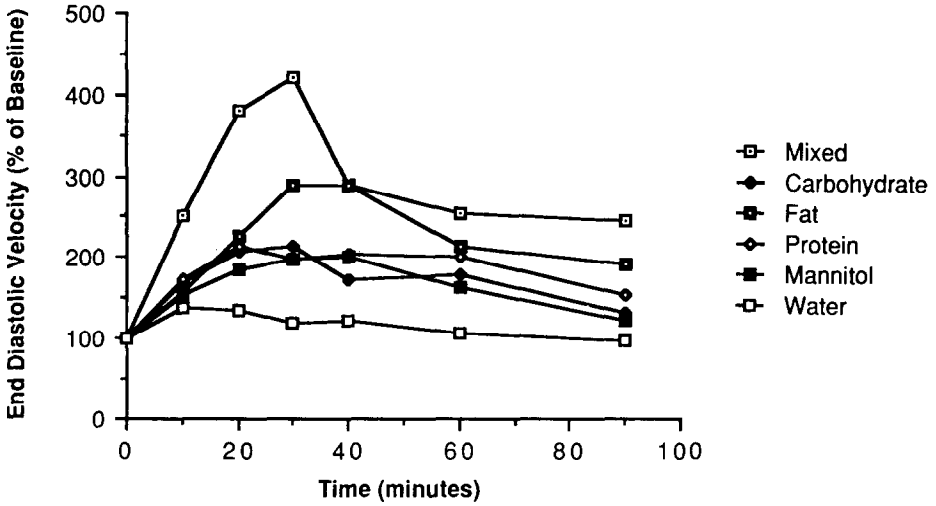

Figure 7. End-diastolic velocity in the SMA in response to various test meals. There was a significant increase in end-diastolic velocity ($p < 0.05$) with all meals except water. End-diastolic velocity is expressed as a percentage of the fasting value.

ing flowmeters or implantable pulse Doppler devices (29,30).

In this study no significant increase in celiac artery flow or velocity was observed with any test meal. This may reflect the preponderance of celiac artery flow to the stomach, liver, and spleen, organs whose arterial flow in animal studies does not appear to increase significantly with feeding (1,26,28).

We found that increases in SMA blood flow parameters varied according to meal type. Maximal response occurred earliest with the carbohydrate meal. This may be due to more rapid emptying of the stomach with carbohydrate or to a more rapid release of intestinal factors affecting blood flow in response to carbohydrate. The maximal blood flow response, however, to a *single* nutrient occurred after the fat meal. This suggests that fat provides the greatest individual stimulus to human intestinal blood flow. Earlier animal studies have also suggested that fats, particularly long-chain fatty acids, are especially important in inducing intestinal hyperemia (1). The fact that blood flow increased maximally with the mixed meal may imply a synergistic effect of the various nutrients on splanchnic arterial blood flow. Although still statistically significant, the flow changes after a protein meal were less than those observed after ingestion of other nutrients. The smaller effect of protein may explain the varying ability to detect a change with protein in the animal models noted above.

We also found that a nonabsorbable osmotic agent, mannitol, caused mild mesenteric hyperemia, indicating that osmolarity is at least one of the factors involved in this response. This observation in humans is in contrast to data reported by Kvietys et al. (31), who could not demonstrate an increase in mesenteric flow in response to a nonabsorbable osmotic agent in dogs.

The data in this study strongly support the idea that duplex ultrasound can provide a noninvasive method to serially examine splanchnic arterial blood flow. Given differences among species and the potential effects of anesthesia, it should prove helpful in the investigation of the physiologic control of the human mesenteric circulation. Although we have used duplex ultrasound to examine the postprandial hyperemic response of the celiac and superior mesenteric arteries in relation to various meal types, it may also be useful to further define the normal mesenteric circulatory response to other stimuli. The method should be easily adaptable to serial investigation of various gastrointestinal disease states. This could include patients at risk of mesenteric ischemia because of low cardiac output or mesenteric vascular disease. Patients with postoperative dumping syndromes after gastrointestinal surgery and patients on potentially vasoconstricting or vasodilating drugs may also prove to have interesting findings when examined with splanchnic arterial duplex scanning.

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Received February 1, 1988. Accepted June 20, 1988.

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This work was supported in part by National Institutes of Health grant No. 62-1821, 20898.