The effect of meal size on the cardiovascular responses to food ingestion

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Cardiac output (CO; indirect Fick), blood pressure (BP) and heart rate (HR; oscillometry), superior mesenteric artery blood flow (SMABF; Duplex Doppler) and calf blood flow (CBF; venous occlusion plethysmography) were recorded in the fasted state and for 120 min following the ingestion of 1, 2, and 3 MJ, high-carbohydrate meals in eight healthy females. BP was unchanged following food. HR ($P < 0{\cdot}0005$) and CO ($P < 0{\cdot}005$) rose significantly following all three meals. Integrated increments in CO over the postprandial period were greater after 3 MJ compared with the 1 and 2 MJ meals ($P < 0{\cdot}05$). SMABF rose significantly following all three meals. The pattern of blood flow response was significantly different between the 1 and 3 MJ meals (interaction effect $P < 0{\cdot}02$, ANOVA), with blood flow after the 3 MJ meal being significantly greater than flow after the 1 MJ meal at 15, 60, and 90 min. Similarly, the pattern of response was significantly different after the 2 and 3 MJ meals (interaction effect $P < 0{\cdot}03$, ANOVA), with blood flow being significantly greater at 15 and 90 min after the 3 MJ meal. CBF fell significantly in the first 15 min after the 3 MJ meal and then recovered towards baseline values. No other significant changes in CBF were recorded. There are substantial peripheral and central cardiovascular changes after food in man and there appears to be a relationship between meal size and the extent of these changes.

Cardiac output: Blood flow: Meal size: High-carbohydrate meal

In the fasted, healthy subject, blood supply to the gastrointestinal tract accounts for a substantial proportion of the cardiac output (Donald, 1983). In the postprandial state blood flow to the mesenteric organs increases markedly from these fasted levels (Norryd *et al.* 1975; Moneta *et al.* 1988). Despite the mesenteric hyperaemia associated with food ingestion, cardiovascular homeostasis is maintained, with blood pressure in the young remaining unchanged (Kelbaek *et al.* 1989; Heseltine *et al.* 1990), whilst both heart rate and cardiac output increase (Gladstone, 1935; Waaler *et al.* 1990).

The pattern of the cardiovascular responses to food is partly dependent upon the composition of the meal (Qamar & Read, 1988; Sidery *et al.* 1990). There is also a relationship between the postprandial increment in cardiac output and meal size, with a larger and more prolonged cardiac response following a large meal when compared with a small meal (Waaler *et al.* 1991). It was suggested that the greater increment in cardiac output following the larger meal is a consequence of a greater demand in the mesenteric bed.

The rate of absorption of nutrients in tissues following food ingestion is a function of the blood flow to those vascular beds (Laakso *et al.* 1990). The functional advantages of a rapid nutrient delivery to the periphery following absorption from the gut are clear and an increased cardiac output would facilitate this process. The aim of the present investigation

was to study the effect of meals of differing energy content but constant fat:carbohydrate ratio on superior mesenteric artery blood flow, cardiac output and blood flow in skeletal muscle, using the calf as a muscle bed. Sampling of arterialized venous blood allows simultaneous measurements of plasma insulin and whole-blood glucose. Samples were also stored for noradrenaline analysis. Although there are limitations in the degree to which plasma noradrenaline levels reflect sympathetic nervous system activity (Esler *et al.* 1988), there is a surprisingly good correlation between such measurements and the activity of the sympathetic nervous system assessed by recording sympathetic nerve firing in the leg (Wallin *et al.* 1981).

METHODS

Eight healthy female subjects (body mass index (BMI) 21·3–25·2 kg/m^2, age range 21–26 years) were recruited for the study. None were taking any medication other than the oral contraceptive pill. All gave written informed consent to the study which was approved by the University of Nottingham Medical School Ethics Committee.

On three occasions, following an overnight fast of 10 to 15 h duration, the subjects were studied supine in a temperature-controlled room (dry bulb 26$\pm$2°). On arrival in the laboratory, subjects rested supine for 30 min, during which time the monitoring equipment was attached and a cannula for blood sampling inserted retrogradely under local anaesthetic into a vein on the dorsum of the right hand. The cannula was kept patent with a slow infusion of 154 mM-NaCl and the hand rested in a box circulated with warm air (55–60°) to obtain 'arterialized' venous blood samples. The total volume of saline infused did not exceed 350 ml on each occasion. The arterialization of venous blood for the estimation of arterial blood glucose levels has been validated previously (McGuire *et al.* 1976). Heating of the hand leads to a reduction in the transit time and thus minimizes the extraction of glucose by the hand tissue, providing a realistic alternative to arterial sampling. This method of hand heating does not affect body temperature or forearm blood flow on the other side (Gallen & Macdonald, 1990) but as yet it is not known whether this method provides accurate estimation of arterial plasma catecholamine levels.

Following the rest period two sets of measurements of all variables were made at 15 min intervals. Following this the subjects sat up and ate (no longer than 15 min was taken to complete the meals in all cases), in a randomized order, a standardized high-carbohydrate meal containing either 1, 2, or 3 MJ (approximately 84% energy from carbohydrate; see Table 1). Subjects immediately returned to the supine position and measurements were made at 15 and 30 min after completion of the meal and subsequently at 30 min intervals for another 90 min (a total of 120 min postprandially). Blood samples were taken at 30 min intervals. At least 1 week passed between each visit. Volume occupied by the meals did differ, with the 1 MJ meal being approximately 350 ml, the 2 MJ meal 520 ml and the 3 MJ meal 585 ml. The observers measuring blood pressure, cardiac output and limb blood flow were blinded as to the energy content of the meals.

The subjects were also studied on a fourth occasion, in which the same protocol was followed, except that 580 ml water at room temperature was ingested following the baseline period. No blood samples were taken and post-water measurements were made every 15 min for 45 min only. In addition, superior mesenteric artery blood flow was measured 5 min after water ingestion.

Cardiac output was measured using the indirect Fick principle, monitoring respiratory gases with CO_2 as an indicator. The subjects were attached to the breathing equipment using a mouthpiece and wearing a nose-clip. CO_2 concentrations were measured using an infrared CO_2 analyser (901 Mk 2; P. K. Morgan, Chatham, Kent). CO_2 production was determined from measurements of ventilation rate (with a flowmeter) and mixed expired

Table 1. *Meal composition*

Meal size	Ingredients	Percentage energy from	
		Starch	Simple sugars
1 MJ	Cornflakes and skimmed milk	54	29
2 MJ	Cornflakes, skimmed milk, bread and honey	48	36
3 MJ	Cornflakes, skimmed milk, sugar, bread and honey	43	44

air. End-tidal P_{CO_2} was used to estimate systemic arterial CO_2 tension (Pa_{CO_2}) and mixed venous (pulmonary artery) CO_2 tension ($P\bar{v}_{CO_2}$) was determined with a CO_2 rebreathing technique. The CO_2 concentration in the rebreathing mixture was approximately 10%. Rebreathing continues until there is no difference between expired and inspired CO_2 concentration (approximately 8–10 s) measured at the mouthpiece. Cardiac output was calculated from the measurements of $P\dot{v}_{CO_2}$ and the estimated Pa_{CO_2} and $P\bar{v}_{CO_2}$. This technique correlates well (r 0·96, 95% CI of the difference −0·37 to +0·47 litres/min) with cardiac output measurements made by thermodilution (Cowley *et al.* 1986). The validity of a CO_2 rebreathing method to determine cardiac output, particularly at rest, has been questioned (Reybrouck & Fagard, 1990). However, in that case the method used involved an exponential-based estimation of $P\bar{v}_{CO_2}$. The equilibrium method used in the present study to measure $P\bar{v}_{CO_2}$ appears to be more reliable, showing closer agreement than the exponential method with cardiac output measured using both the direct Fick (Muiesan *et al.* 1968) and dye dilution (Hinderliter *et al.* 1987) techniques. The reproducibility of $P\bar{v}_{CO_2}$ measurement by the equilibrium method was also shown to be excellent (Muiesan *et al.* 1968).

Time-integrated increases in cardiac output over the postprandial period were also calculated. The cardiac output increments above baseline for the first 15 min period and the subsequent 30, 60, 90 and 120 min measurements were calculated and the total extra blood volume pumped by the heart over each time period and for each subject calculated from these cardiac outputs and expressed in litres with the standard error of the mean.

Heart rate and systemic arterial blood pressure were measured by an automated oscillometric device (Accutorr 1A; Datascope, Paramus, NJ, USA) with the cuff placed around the right upper arm. Measurements were made once every 5 min and the mean of three measurements was calculated for the 15 min time windows; the mean of six was calculated for each of the 30 min time windows. The coefficient of variation of repeated measurements in fasted subjects using this technique in this laboratory is 4% for heart rate, 2% for systolic blood pressure and 2% for diastolic blood pressure.

Superior mesenteric artery (SMA) flow was measured by transcutaneous Doppler ultrasound (Diasonics Prisma; Diasonics International, Les Vlis, France) with a convex linear array probe with variable receiver characteristics. The B-mode imaging system operates with a centre frequency of 3·5 MHz. Doppler frequency of the probe is 3 MHz. The anatomical position of the SMA makes visualization of the proximal part of the vessel using ultrasound comparatively easy. Complete data on SMA flow for all three occasions were obtained in seven of the eight subjects.

The vessel of interest was visualized with a sagittal scan of the abdomen. Care was taken to ensure that the entire vessel lumen was insonated and the sample volume was placed in the proximal part of the artery, several centimetres from the bifurcation of the SMA from

the aorta. This avoids the introduction of error in flow measurements as a result of turbulent flow which may be present near the junction of the two arteries.

The angle of insonation was recorded and used to convert the Doppler Shift values (kHz) into blood flow velocity (cm/s). Care was taken to ensure that wherever possible the same angle of insonation was used in each individual (mean angle of insonation was 39°, SD 3·5°). Error brought into the flow calculation due to an angle of insonation of 39° would be in the range of 7% (Gill, 1985). Recordings were made with the subjects' breath held in mid inspiration and mean values of time-averaged velocity (TAV) were taken from at least eight Doppler waveform complexes. Using manually operated on-screen callipers systolic vessel diameter was measured during the baseline period of each study session. It was assumed that vessel diameter remained unchanged during the experimental protocol and the mean of the vessel diameter measurements for each subject was used with the TAV in the volume flow calculations. Blood flow was calculated from the equation:

$$\text{blood flow} = 3{\cdot}142 \times D^2 \times \text{TAV} \times 60/4 \text{ ml/min},$$

where D is the vessel diameter.

A comparison of SMA flow measurement by Duplex ultrasound (calculated from the time-averaged flow velocities) and electromagnetic flowmetry has been made in which a strong correlation between the two techniques was found (Nakamura *et al.* 1989). The same paper reported a coefficient of variation in the measurement of volume flow very similar to our own.

Calf blood flow was measured by venous occlusion plethysmography (Greenfield *et al.* 1963) with mercury-in-silastic strain gauges (Whitney, 1953). An occlusion cuff placed around the thigh was inflated to 40 mmHg to prevent venous return from the limb. Inflation took place in a cyclical manner, with the change in calf circumference being measured using the strain gauge. Flow both in and out of the foot was prevented during measurements using an occlusion cuff placed around the ankle and inflated to 200 mmHg. During each measurement period, a minimum of six measurements of flow were made and the mean value used in the subsequent statistical analysis. The coefficient of variation for measurement of calf blood flow by venous occlusion plethysmography on different days is 11·5% (Roberts *et al.* 1986). In our laboratory under resting conditions a 10% alteration in blood flow is the minimum change that can be detected using this technique.

Vascular resistances for the calf and the SMA were calculated from blood flow values and mean arterial blood pressure (obtained using the Accutorr 1A). For these calculations it was assumed that brachial artery pressure was a reliable index of calf and mesenteric perfusion pressures, although disparity between central and peripheral blood pressure measurements have been noted (Rowell *et al.* 1968). Any differences are likely to be minimized in healthy volunteers, and be similar on the three occasions.

Arterialized blood samples were used to measure blood glucose (YSI 23 AM; Yellow Springs Industries, Yellow Springs, OH, USA) immediately. The remainder of the arterialized blood samples were centrifuged and the plasma separated. Plasma (3 ml) was mixed with 75 μl EGTA-glutathione (antioxidant) and stored at −80° for later determination of noradrenaline and adrenaline concentrations using HPLC with electrochemical detection (Macdonald & Lake, 1985). All samples for any one subject were run on the same day. The intra-assay coefficient of variation was 6% for noradrenaline and 8% for adrenaline, the inter-assay values being 8% and 10% at the levels of catecholamine present in these samples. Plasma was also stored at −20° for subsequent determination of insulin concentration by radioimmunoassay using a double-antibody technique developed in-house. The intra-assay coefficient of variation is 8% and the inter-assay value is 12% over a range of plasma insulin from 5 to 50 mU/l.

Statistical analysis

Statistical analysis of the results was performed by two-way analysis of variance with repeated measures (ANOVA) using the package BMDP (BMDP Statistical Software; Los Angeles, CA, USA). Where the ANOVA indicated a significant treatment–time interaction the exact level of significance at each time point was calculated using a paired *t* test, using the variance term for the interaction from the ANOVA table, with a Bonferroni correction applied for multiple testing.

For clarity, data are presented in the Figures as changes from baseline, each point being the mean with its standard error. The data reported in the text on the responses to the meals are the maximum changes from baseline values, and the 95% confidence intervals (CI) of the changes unless stated otherwise.

RESULTS

Control study

There were no significant changes in any of the measured variables following the ingestion of water.

Systolic and diastolic blood pressure

There was no difference in blood pressure in the fasted state on the three occasions. Neither systolic nor diastolic blood pressure changed significantly following any of the meals in these young subjects.

Heart rate

Heart rate rose significantly following all three meals ($P = 0{\cdot}00001$), with a maximum rise of 5·9 beats/min after the 1 MJ meal (95% CI of the increase 2·4 to 9·4 beats/min), 10·5 beats/min after the 2 MJ meal (95% CI of the increase 6·5 to 14·5 beats/min) and 13·3 beats/min after the 3 MJ meal (95% CI of the increase 8·8 to 17·8 beats/min). There was a significant difference in the pattern of response in heart rate following the 1 and 3 MJ meals (interaction effect $P = 0{\cdot}0005$, ANOVA; Fig. 1). Heart rate was significantly higher 15 min after the 3 MJ compared with the 1 MJ meal (*t* test with Bonferroni correction). There was no difference between the pattern of response after the 2 and 3 MJ and the 1 and 2 MJ meals. There was a significant difference in individual maximum increases in heart rates between the 1 and 2 MJ meals only (*t* test $P < 0{\cdot}05$; Fig. 2).

Cardiac output

Cardiac output rose significantly after all the meals ($P = 0{\cdot}0001$). The maximum rise in cardiac output following the 1 MJ meal was 2·19 l/min (95% CI of the increase 0·96 to 3·42 l/min), 1·78 l/min after the 2 MJ meal (95% CI of the increase 0·76 to 2·79 l/min) and 3·15 l/min after the 3 MJ meal (95% CI of the increase 1·58 to 4·72 l/min; Fig. 1). There was a significant difference between individual maximum increases in cardiac output between the 2 and 3 MJ meals (*t* test $P = 0{\cdot}03$). The mean time-integrated postprandial increments in cardiac output after the three meals were 80·1 (SE 24·5), 104·1 (SE 42·2) and 244·0 (SE 49·7) l respectively, with the time-integrated cardiac output after the 3 MJ meal being significantly greater than after the 2 MJ meal (*t* test $P = 0{\cdot}04$; Fig. 2).

Total peripheral resistance (TPR)

TPR fell significantly following all three meals (95% CI of the change −3·5 to −10·7, −3·3 to −17·3, and −3·1 to −20·1 respectively). However, the pattern of responses was different, with TPR remaining low throughout the experimental period after the largest

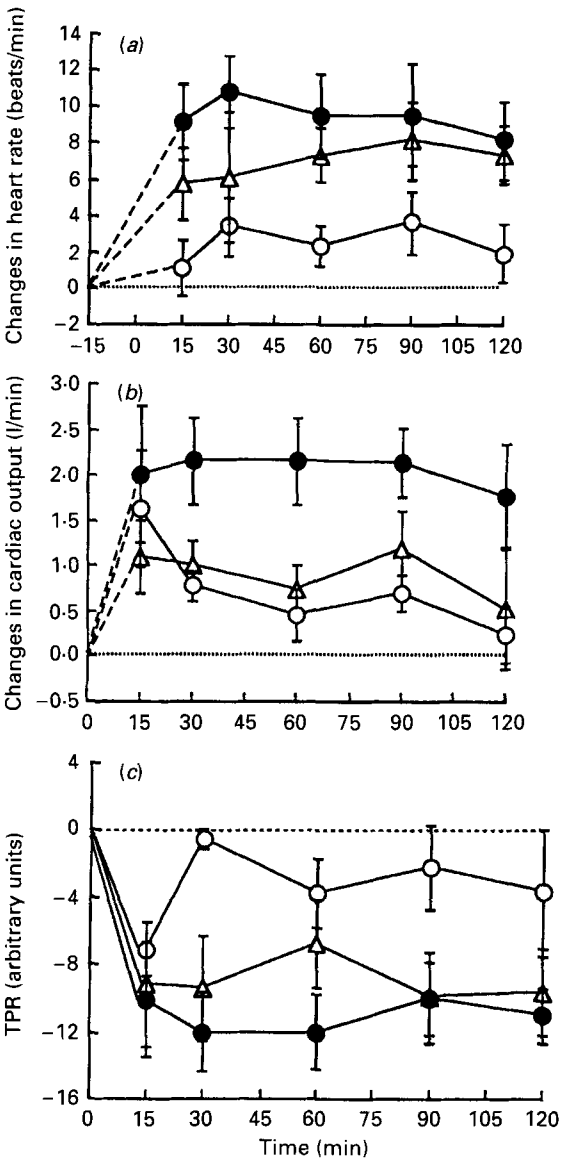

Fig. 1. Heart rate (beats/min; *a*), cardiac output (l/min; *b*) and total peripheral resistance (TPR; *c*) changes from baseline values (shown as a dotted line) following the ingestion of 1 (○), 2 (△) and 3 MJ (●) meals. Values are means with their standard errors represented by vertical lines. There was a significant rise in both heart rate and cardiac output following all the meals. TPR fell initially after all meals. The pattern of response was different between the largest and smallest meals for all three variables.

meal and recovering to values not significantly different from baseline values 30 min after the small meal (interaction effect $P = 0{\cdot}02$, ANOVA; Fig. 1).

SMA blood flow

SMA flow rose significantly following all three meals, with a peak flow of 836 ml/min being reached at 15 min after the 1 MJ meal (95% CI of the change 66 to 474 ml/min), and a peak flow of 825 ml/min being reached at 60 min after the 2 MJ meal (95% CI of the

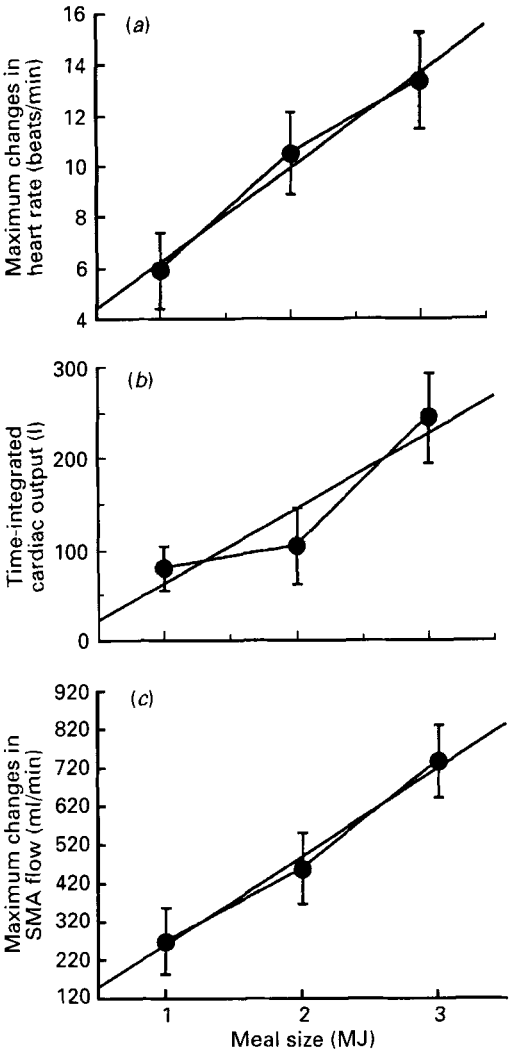

Fig. 2. Graphs showing the relationship between meal size (MJ) and (*a*) the maximum increase in heart rate (beats/min), (*b*) the time-integrated increase in cardiac output above baseline (l) and (*c*) the total blood flow above baseline through the superior mesenteric artery (SMA; ml/min). The maximum increase in heart rate after the 2 and 3 MJ meals was significantly greater than after the 1 MJ meal. The time-integrated increase in cardiac output was significantly greater after the 3 compared with the 1 and 2 MJ meals. The total blood flow above baseline through the SMA was significantly greater after the 3 compared with the 1 MJ meal only.

change 240 to 673 ml/min). A peak flow of 1189 ml/min was reached 15 min after the 3 MJ meal (95% CI of the change 514 to 956 ml/min). The pattern of blood flow response was significantly different between the 1 and 3 MJ meals (interaction effect $P = 0{\cdot}01$, ANOVA), with blood flow after the 3 MJ meal being significantly greater than flow after the 1 MJ meal at 15, 60, and 90 min (*t* test with Bonferroni correction at each time point). Similarly, the pattern of response was significantly different after the 2 and 3 MJ meals (interaction effect $P = 0{\cdot}02$, ANOVA), with blood flow being significantly greater at 15 and 90 min after the 3 MJ meal (*t* test with Bonferroni correction; Fig. 3).

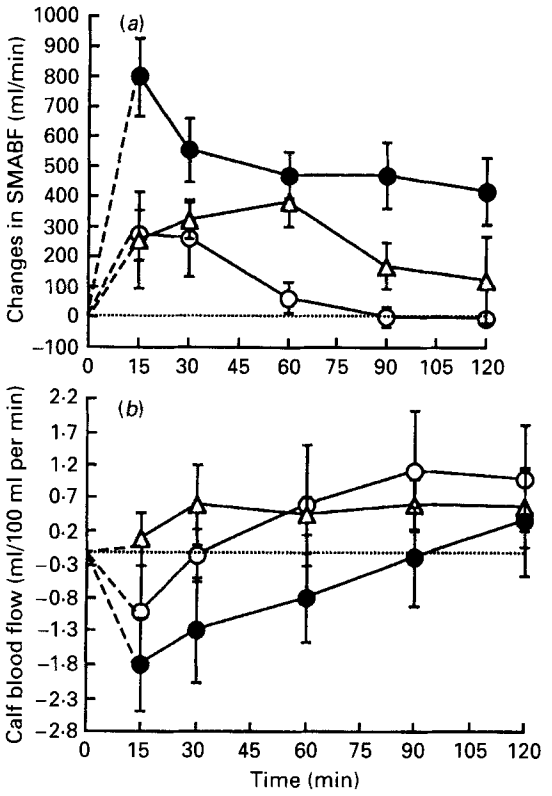

Fig. 3. Superior mesenteric artery blood flow (SMABF; ml/min; *a*) and calf blood flow (ml/100 ml per min; *b*) changes from baseline values (shown as a dotted line) following the ingestion of 1 (○), 2 (△) and 3 MJ (●) meals. Values are means with their standard errors represented by vertical lines. SMABF increased following all three meals. The pattern of response was different between the largest and smallest meals. Calf blood flow fell significantly following the 3 MJ meal only. The rise in flow from the 15 min value to the value at 90 min after the 1 MJ meal and 120 min after the 3 MJ meal was significant.

The total volumes of blood flow above baseline in the postprandial period after the three meals were 12·1 (SE 5·9), 32·9 (SE 8·9) and 47·7 (SE 6·6) l. Total flow volume after the 3 MJ meal was significantly greater than that after the 1 MJ meal only (*t* test $P = 0{\cdot}02$; Fig. 2).

Peak flow velocity

Peak flow velocity increased significantly following all three meals ($P < 0{\cdot}001$). The maximum changes in peak flow velocity after the three meals were 42 cm/s (95% CI of the increase 15 to 69 cm/s), 50 cm/s (95% CI of the increase 29 to 71 cm/s) and 81 cm/s (95% CI of the increase 63 to 99 cm/s) respectively. There was no significant difference in the pattern of flow velocity changes after the three meals.

Calf blood flow

Although calf blood flow tended to fall initially following all three meals, there was a significant fall in the first 15 min only after the 3 MJ meal (95% CI of the change $-0{\cdot}36$ to $-3{\cdot}22$ ml/100 ml per min). The trend was then for calf blood flow to rise, although flow did not rise above baseline after any of the meals during the experimental period. The rise from the 15 min calf blood flow value to the 120 min value following the 3 MJ meal was

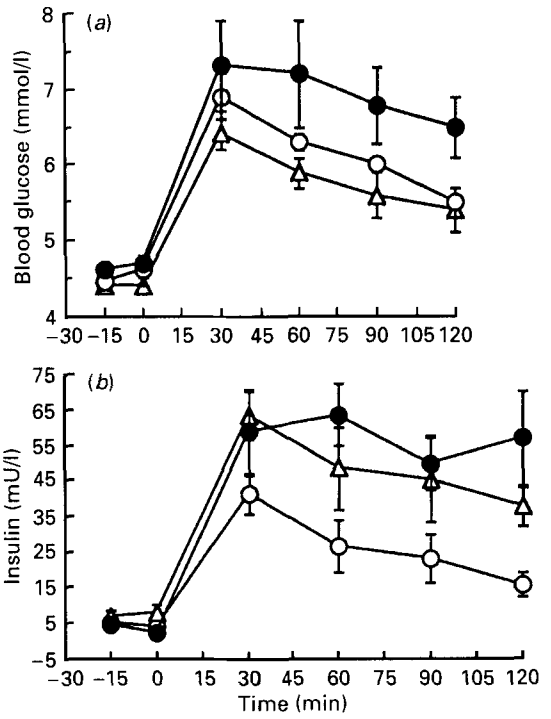

Fig. 4. Blood glucose (*a*) and plasma insulin (*b*) before (*t* 0) and after the ingestion of 1 (○), 2 (△) and 3 MJ (●) meals. Values are means with their standard errors represented by vertical lines. There was a significant rise after all three meals. The pattern of response in blood glucose was significantly different between the 3 MJ meal and the two smaller meals. The plasma insulin response was different between the 3 and 2 MJ meals and the smallest meal. The area under the glucose curve was greater after the 3 MJ meal compared with the 2 MJ meal only.

significant (95% CI of the increase 0·27 to 3·97 ml/100 ml per min). The rise from the 15 min value to the value at 90 min following the 1 MJ meal was also significant (95% CI of the increase 0·5 to 3·78 ml/100 ml per min; Fig. 3).

Blood glucose

Blood glucose rose significantly after all the meals ($P = 0{\cdot}0001$, ANOVA). There was no significant difference between the peak blood glucose concentrations following any of the three meals. The areas under the glucose curves following the 2 MJ and the 3 MJ meals were significantly different (*t* test, $P = 0{\cdot}001$). There was no difference between the 1 and 3 MJ meals (Fig. 4).

Plasma insulin

Plasma insulin concentrations rose significantly following the three meals ($P = 0{\cdot}0001$, ANOVA). Again, there was no difference in the peak insulin response following any of the three meals. There was a difference in the pattern of response following the 1 and 3 MJ meals (interaction effect $P = 0{\cdot}002$, ANOVA; Fig. 4).

Plasma noradrenaline and adrenaline

Baseline plasma noradrenaline levels were 1·17 (SE 0·09), 1·30 (SE 0·22) and 0·90 (SE 0·13) nmol/l before the 1, 2 and 3 MJ meals respectively. Plasma noradrenaline rose only after the 3 MJ meal ($P = 0{\cdot}0001$, ANOVA), from a baseline value of 0·83

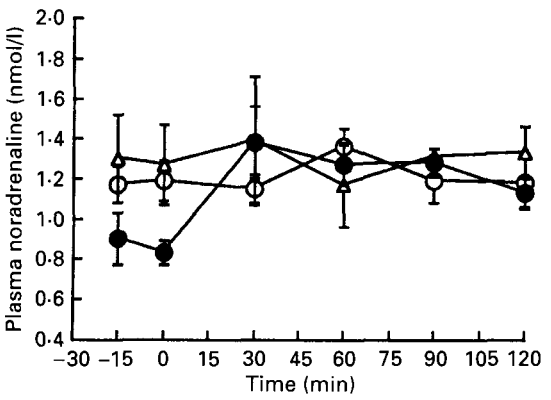

Fig. 5. Plasma noradrenaline changes from baseline values following the ingestion of 1 (○), 2 (△) and 3 MJ (●) meals. Values are means with their standard errors represented by vertical lines. Plasma noradrenaline rose only after the 3 MJ meal ($P < 0{\cdot}009$, ANOVA). This was the only time point at which plasma noradrenaline was significantly above baseline.

(SE 0·06) nmol/l to 1·38 (SE 0·18) nmol/l 15 min after the meal (95% CI of the increase 0·07 to 1·03 nmol/l). This was the only time point at which plasma noradrenaline was significantly above baseline (Fig. 5).

Baseline plasma adrenaline levels were 0·20 (SE 0·03), 0·25 (SE 0·09) and 0·18 (SE 0·03) nmol/l before the 1, 2 and 3 MJ meals respectively. Plasma adrenaline did not change after ingestion of any of the meals.

DISCUSSION

Cardiac output rose significantly following ingestion of all three high-carbohydrate meals. The increase was most rapid following the 1 MJ meal, peaking at 15 min. Cardiac output peaked between 30 and 60 min after the 2 and 3 MJ meals. There is some variance as to the time at which the peak cardiac response is achieved following food ingestion (Fagan *et al.* 1986; Waaler *et al.* 1990, 1991), although meal composition appears to be important in the time course of these changes (Dagenais *et al.* 1966). The cardiac response after both the 1 and 2 MJ meals is reflected in the mesenteric response, with both peaking at 15 min after the 1 MJ and 60 min after the 2 MJ meal. The time courses of the initial changes in cardiac output do not reflect the initial blood flow changes in the mesenteric bed following the 3 MJ meal, when maximum hyperaemia in the mesentery was attained within the first 15 min and the cardiac output peak at about 60 min. However, both cardiac output and mesenteric blood flow were maintained at elevated levels throughout the postprandial period after the 3 MJ meal. Postprandial increases in stroke volume have been demonstrated previously (Kelbaek *et al.* 1987, 1989; Waaler *et al.* 1991) although not consistently (Fagan *et al.* 1986). Stroke volume and heart rate have been shown to contribute equally to the postprandial rise in cardiac output (Waaler *et al.* 1991). In the present study calculated stroke volume did increase significantly after all three meals. A fall in TPR may account for a fraction of the postprandial rise in stroke volume (by reducing afterload), but increases in stroke volume of 41% (Kelbaek *et al.* 1989) suggest a rise in pre-load and possibly in contractility of the heart. Thus, the exact mechanism of the increase in stroke volume is not clear either from the literature or from this study.

A 'dose–response' relationship exists between meal size and the total volume of blood pumped by the heart above baseline over a 2 h period (Waaler *et al.* 1991). The present study confirms and extends this relationship and also demonstrates that the same

relationship exists between the meal size and both the maximum change in SMA flow and the total volume of blood flowing through the artery over a 120 min postprandial period.

Maximal hyperaemia was reached within 15 min after ingestion of two of the three meals. This rapid response following meals high in carbohydrate has been observed after both solid (Sidery *et al.* 1990) and liquid (Moneta *et al.* 1988; Qamar & Read, 1988) carbohydrate meals. In the present study maximal flow following the intermediate meal was not reached until 60 min after food, but blood glucose levels peaked 30 min after food. A delayed hyperaemia has been observed after a high-fat meal which does not coincide with the peak blood glucose levels (Sidery *et al.* 1990). This observation, that peak blood glucose levels and peak mesenteric blood flow do not always coincide, is confirmation that the mechanisms mediating mesenteric blood flow are complex and not fully understood.

In the present study TPR fell following all three meals, with no difference in the extent of the fall. This is despite an increasingly greater initial hyperaemia with an increase in meal size. There was an initial fall in calf blood flow following the 3 MJ meal only. Assuming that blood pressure measured at the upper arm reflects peripheral blood pressure, the recorded fall in blood flow in the calf is the result of increased vascular resistance: could this increase in resistance in the calf be responsible for the fact that values of TPR are no different after the meals, despite the significantly greater initial mesenteric response following the 3 MJ meal? A postprandial increase in vascular resistance in vascular beds other than those associated with digestion and absorption has been demonstrated previously (Sidery *et al.* 1990). Skeletal muscle blood flow increased significantly following the initial fall after ingestion of the largest of the meals.

Blood glucose rose significantly following all three meals. There was a slight anomaly between the blood glucose response following the 1 MJ and the intermediate size meal. Different glycaemic responses to meals of identical sugar, starch and energy contents but varying insoluble and soluble dietary fibre contents have been demonstrated (Torsdottir *et al.* 1989). The results of the present study may be a consequence of a difference in the nature of the carbohydrate in the 2 and 1 MJ meals. Peak mesenteric blood flow was not reached until 60 min after the intermediate meal, in contrast to the other meals. This different pattern of response might also be related to carbohydrate type, and clearly warrants further study.

Plasma noradrenaline rose significantly following the largest of the three meals only. Increases in plasma noradrenaline have been observed in man following glucose ingestion (Rowe *et al.* 1979, 1981). Similarly, increases in sympathetic activity, detected using microelectrode recordings, have been shown following ingestion of glucose and xylose in man (Berne *et al.* 1989). A link between the increased plasma noradrenaline levels and the cardiovascular changes associated with food ingestion is not clear. There is a differential effect of meals of different composition on plasma catecholamines, with 120% (0·98 to 2·22 nmol/l) increases in plasma noradrenaline levels following a 2·4 MJ high-carbohydrate meal and no changes after a high-fat meal of the same energy content (Heseltine *et al.* 1990).

To summarize, a 'dose–response' relationship between the cardiac and mesenteric response and the energy content of meals has been demonstrated. A similar relationship between cardiac output and meal size has been observed for meals ranging from approximately 2 to 5 MJ (Waaler *et al.* 1991). There was a decrease in vascular resistance in the mesenteric bed after food and substantial increases in superior mesenteric blood flow were observed. The mechanism responsible for the substantial postprandial increments in cardiac output is not clear. TPR falls after food ingestion (Fagan *et al.* 1986; Kelbaek *et al.* 1989) and blood pressure remains either unaltered (Heseltine *et al.* 1990) or there is a slight widening of pulse pressure (de Mey *et al.* 1987) in young, healthy subjects. The

cardiac changes seen in the postprandial state may in part be mediated by the autonomic nervous system. Unloading of peripheral baroreceptors would lead to increased activity of sympathetic cardiac fibres. Reduced atrial filling and distension would lead to increased vasomotor tone.

Deleterious effects of food ingestion are well documented in angina patients, with a significant reduction in exercise capacity and the time until depression of the ST segment of the electrocardiogram in the postprandial state compared with the fasted state (Fagan *et al.* 1982; Cowley *et al.* 1991). Similarly, there is a reduction in exercise tolerance in chronic heart failure patients after food ingestion (Muller *et al.* 1992). The mechanisms of these effects are unclear, but the evidence suggests that abnormal central and peripheral cardiovascular responses may be responsible. In angina the degree of myocardial ischaemia is the same during exercise in the pre- and postprandial states (Colles *et al.* 1993), lending credence to the hypothesis that increased postprandial myocardial oxygen consumption and not reduced coronary blood flow results in the earlier onset of ischaemic pain. Reduced exercise tolerance in heart failure is almost certainly due to abnormal peripheral blood flow responses. In view of this, food ingestion may act to exacerbate the already abnormal state in skeletal muscle during exercise.

Postprandial hypotension has been observed in both institutionalized elderly (Lipsitz *et al.* 1983) and also in healthy elderly subjects (Lipsitz & Fullerton, 1986; Heseltine & Potter, 1990). High-carbohydrate meals result in significantly greater falls in blood pressure compared with meals of any other composition (Potter *et al.* 1989). The mechanism for this is not clear. These subjects do not demonstrate significant cardiac responses to food ingestion, despite similar vascular changes in the mesenteric bed to those seen in the young (Sidery *et al.* 1993). Food ingestion represents a substantial cardiovascular challenge, with the magnitude of the cardiovascular responses being directly related to the energy content of the meal ingested. The implications of such findings for those patients with compromised cardiovascular and autonomic function and the elderly are clear. A smaller meal elicits a smaller central and mesenteric response. The impact of such meals in individuals with pathology of the autonomic or cardiovascular systems will be less, hopefully with cardiovascular homeostasis being maintained through more subtle vascular changes which are more likely to be within the capabilities of these patients. Advice to patients with regard to meal composition is more complex. High-carbohydrate meals elicit rapid central and mesenteric responses, and, as mentioned, tend to lower blood pressure in the healthy elderly more than any other meal type. However, high-fat meals, whilst delaying peak cardiovascular responses, result in more prolonged mesenteric hyperaemia than other meals (Moneta *et al.* 1988; Sidery *et al.* 1994). Small, mixed meals containing less-readily available, complex carbohydrate are likely to be the least challenging of all meal types to the individuals discussed.

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