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## Influence of jejunal nutrients on transpyloric flow and pyloric resistance in pigs

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**Summary** — The effects of small intestinal infusion of nutrients on the transpyloric flow and pyloric resistance were evaluated in anaesthetized pigs. Saline versus isocaloric solutions of dextrose, triglycerides and casein were infused into a jejunal loop during saline gastric loading. Antropyloroduodenal pressures were measured with a sleeve/side-hole manometric assembly and the transpyloric flow with an electromagnetic flowmeter probe. Fundic pressure was maintained constant. Although the overall gastric emptying rate was not affected by nutrients, the stroke volume of the transpyloric flow pulses was significantly increased as a consequence of larger peak flow (dextrose) or longer duration of flow pulses (triglycerides and casein). Pyloric resistance was reduced by all nutrients owing to a change in the temporal relationship between the onset of pyloric pressure events and flow pulses so that flow pulses occurred after pyloric pressure events. In conclusion, under controlled fundic pressure, nutrient infusions decrease pyloric resistance.

**gastric emptying / nutrient / transpyloric flow / IPPW / pig**

**Résumé** — **Influence des nutriments jéjunaux sur le débit transpylorique et la résistance pylorique du porc.** Les effets de l'administration intrajéjunale de nutriments sur le débit transpylorique et la résistance pylorique ont été évalués chez le porc anesthésié. Des solutions isocaloriques de glucose, triglycérides et caséine ont été administrées, versus du sérum physiologique, dans une anse jéjunale au cours d'un repas fictif de sérum physiologique. Les pressions antropyloroduodénales ont été mesurées au moyen d'un cathéter de manométrie incluant un manchon dédié à la mesure des pressions sphinctériennes. Le débit transpylorique a été évalué par un débitmètre électromagnétique implanté au niveau du duodénum proximal. La pression fundique a été maintenue constante au moyen d'un barostat pneumatique à régulation électronique. Bien que le débit moyen d'évacuation gastrique ne soit pas modifié au cours de l'administration jéjunale de nutriments, le volume d'éjection des débits unitaires transpyloriques augmente significativement du fait d'une part d'un débit de pointe accru (glucose) et d'autre part d'une durée supérieure des débits unitaires (triglycérides et

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caséine). La résistance pylorique est réduite par tous les nutriments car la relation temporelle entre la survenue du débit unitaire et l'événement manométrique pylorique est modifiée. En conclusion, lorsque les variations de tonus du fundus sont annulées, l'administration de nutriments entraîne une diminution de la résistance pylorique.

**vidange de l'estomac / nutriment / débit transpylorique / contraction isolée du pylore / porc**

Liquid meals containing nutrients empty more slowly from the stomach than non-nutrient isotonic liquids (Hunt and Stubbs, 1975) as a result of feedback from small intestinal luminal receptors. The magnitude of this decreased emptying rate is dependent on the nutrient (Hunt, 1983), the region (Lin et al, 1992) and the length of small intestine exposed (Lin et al, 1990). The motor mechanisms by which stimulation of small intestinal receptors leads to slowing of gastric emptying are still poorly understood (Heading, 1994) but a combination of reduced propulsion and increased resistance to outflow is thought to be responsible (Miller et al, 1981; Malagelada, 1989). In both animal and human studies, small intestinal infusion of nutrients is associated with decreased fundic tone (Azpiroz and Malagelada, 1985a), reduced antral motility (White et al, 1981; Keinke and Ehrlein, 1983), stimulation of both phasic and tonic pressure waves localized to the pylorus (Heddle et al, 1988b), changes in the diameter of the pylorus (Ehrlein, 1992) and increased duodenal motility (Weisbrodt et al, 1969; Haba and Sarna, 1993). The former motility patterns observed at the pyloric region are supposed to produce an increased resistance. However, because of the methodological difficulty in assessing resistance, ie, the phenomenological description of the relationship between pressure differences and flow within the pyloric segment (Malbert et al, 1995), the pyloric resistance has never been truly quantified in situations associated with slower gastric emptying (Horowitz and Dent, 1994). We have now

measured pyloric resistance during the jejunal administration of macronutrients.

Gastric emptying is an integrated process (Malbert and Mathis, 1994) and is dependent on the relationship between motor events in different regions of the stomach and proximal small intestine. Furthermore, the stomach is capable of considerable compensation before the overall rate of gastric emptying is compromised (Malbert and Mathis, 1994). Since nutrients infused at the jejunal level decrease fundic tone (Azpiroz and Malagelada, 1985a), it is impossible to evaluate the effect of small intestinal nutrient infusion on pyloric resistance unless the influences of compensatory mechanisms located proximal to the pylorus (fundic tone) are minimized or nullified. In our experimental design, we incorporated a barostat bag positioned in the fundus to nullify fundic pressure changes associated with modifications of the fundic tone (Azpiroz and Malagelada, 1986). Hence, using this experimental procedure, changes in transpyloric flow are only representative of antro-duodenal motility and pyloric resistance.

The aim of this study was to measure the pyloric resistance during chemical stimulation of the small intestine to evaluate the variations in pyloric resistance and to test the hypothesis that an increased pyloric resistance is partially responsible for the delayed emptying induced by intestinal nutrient stimulation. Isocaloric loads of dextrose, lipid and amino-acid were used as inhibitory substances.

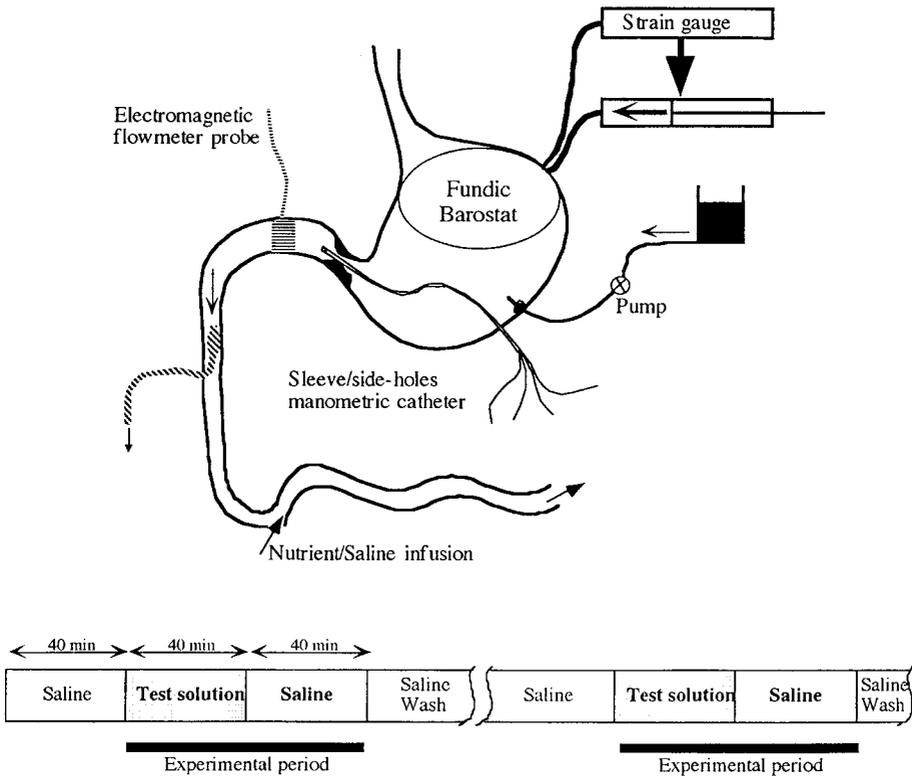
**MATERIALS AND METHODS**

**Experimental protocol**

Eight Meishan female pigs (mean weight,  $36.5 \pm 3.4$  kg) aged 4 months were used. The animals were fasted for 24 h before each experiment. Recordings were made with the animals in a dorsal recumbent position. Recordings started at a minimum of 160 min after completion of the surgical procedure. This delay was necessary to observe at least one regular activity phase of the migrating motor complex. At completion of this

phase, saline was infused into the stomach and data recorded demonstrated that the duodenal outflow rate was permanently higher than 4 mL per minute. This minimum outflow rate was selected because it was within the range found in conscious pigs after gastric instillation of 1 000 mL saline (Treacy et al, 1990) and it enabled a steady pyloric resistance for prolonged periods (Malbert and Mathis, 1994; Malbert et al, 1995).

A jejunal loop, 70 cm in length, formed by the first jejunal segment distal to the ligament of Treitz, was infused at  $5 \text{ mL} \cdot \text{min}^{-1}$  for 40 min with a test solution consisting of either saline



**Fig 1.** Surgical preparation (top panel) and study plan to evaluate the effects of small intestinal nutrients on pyloric resistance. Test solutions (saline or nutrients) were infused in a small intestinal loop for 40 min. Saline was infused in the loop during 40 min before and after the test solution. Between each experimental period, a saline wash was performed until the flow patterns were not significantly different from those recorded before the initial infusion in the loop.

(hereafter called test saline) or one of the three nutrient containing solutions in a randomized order: 300g.L<sup>-1</sup> dextrose, 10% triglycerides emulsion (Intralipid, KabiVitrum Ltd), 226g.L<sup>-1</sup> casein hydrolysate (enzymatic hydrolysate, Bayer). All nutrient containing solutions delivered 4.6 kJ.mL<sup>-1</sup>. The pH of the solutions was adjusted to 6.8 and their osmolarities were 1 322, 337 and 2 389 mosm.L<sup>-1</sup>, respectively. After the 40 min nutrient infusion, an additional 40 min infusion of saline was performed. This infusion was included in the experimental period since within this period, nutrient remained partially present in the loop (fig 1). About 30 min of saline infusion were required to clear the loop after infusion of the triglycerides emulsion, as indicated by the colour of the effluent.

For 40 min before each test infusion, saline was infused at a rate of 5 mL.min<sup>-1</sup>. After each experimental period, saline was also infused in the loop for a minimum of 40 min (40–100 min range) to enable a recovery from the previous test infusion. Infusion of a different test solution was initiated only when the stroke volume of the flow pulses was greater than 0.5 mL and the interval between antral pressure events was less than 40 s (Malbert and Mathis, 1994). These threshold values were also found, in all animals, before the initial test infusion (Malbert et al, 1995).

### Anaesthesia

Pigs were preanaesthetized with Ketamine (5 mg.kg<sup>-1</sup> intramuscularly, gift of Rhône Merieux). Suppression of the pharyngo-tracheal reflex was obtained by administration of halothane (5% v/v) via a face mask immediately before intubation. A venous cannula was inserted into the marginal vein of the ear to infuse a mixture of  $\alpha$ -chloralose (60 mg.kg<sup>-1</sup>, Sigma) and urethane (500 mg.kg<sup>-1</sup>, Sigma) that was used alone for the remainder of the study. The pigs were mechanically ventilated by a Siemens SAL 9000 ventilator with a tidal volume of 15 mL.kg<sup>-1</sup> at a respiratory rate of 18 breaths.min<sup>-1</sup>. Ventilation was adjusted to obtain normocapnia (end-tidal carbon dioxide pressure at 35–45 mmHg). Normocapnia at baseline was measured using an infrared capnograph (Engström Eliza) with air sampling at the Y piece of the ventilator. The fractional inspired concentration of oxygen was set at 0.6 and pulse oxymetry (SpO<sub>2</sub>) was continuously monitored using a sensor (Ohmeda, pulse oxymeter) attached to the pig's tail. During

the surgical procedure, a catheter was inserted in the carotid artery and connected to a pressure transducer to measure continuously the heart rate, systolic, diastolic and differential pressures. A surgical level of anaesthesia (no eye lid reflex, no change in blood pressure or heart rate in response to distress) was maintained by supplemental injection of chloralose–urethane mixture without additional use of halothane (Malbert and Mathis, 1994). When the heart rate increased by more than 20% or when the systolic plus the differential pressures increased by more than 20%, chloralose–urethane mixture was administered at 200 mL.h<sup>-1</sup> to avoid alteration in hemodynamic function. Internal temperature of the pigs was maintained constant ( $\pm 0.5$  °C) by a heating element included in the surgical table and proportionally regulated by the animal rectal temperature. Volemia was also maintained constant via constant IV infusion of Ringer–Lactate at 70 mL.h<sup>-1</sup>.

### Animal preparation

A midline abdominal incision was made to insert sensors designed to measure motor activity and transpyloric flow as follows.

A manometric assembly incorporating a sleeve sensor was located astride the pylorus. The assembly had three side holes and a sleeve sensor (length = 4 cm) adapted specifically for the measurement of pyloric pressure (Dent, 1976). The 3.5 mm diameter manometric probe was inserted into the antrum through a small incision in the ventral corpus and positioned so that one side hole was located in the terminal antrum –2 cm from the oral end of the sleeve and one within the pyloric canal at 2 cm from the oral end of the sleeve. The third sidehole was positioned in the duodenal bulb about 4 mm from the distal end of the sleeve. The manometric assembly was sutured to the duodenal wall and anchored by a purse suture to the antrum to maintain the correct position of the sideholes (Malbert et al, 1992).

A flowmeter probe (Malbert and Latour, 1987) was inserted in the duodenal lumen with its proximal edge less than 5 mm from the distal end of the pylorus as described previously (Malbert et al, 1992). The duodenal effluent was drained through a silicon tube (8 mm ID) with its tip positioned 12 cm from the distal end of the flowmeter. A pressure of 490 Pa (above atmo-

spheric pressure) was maintained between both ends of the catheter (fig 1).

A silicon tube (10 mm OD, 8 mm ID) inserted 15 cm orad to the pylorus delivered normal saline into the stomach at a constant rate of  $5 \text{ mL}\cdot\text{min}^{-1}$ . A polyurethane bag with a maximal capacity of 700 mL connected to a double lumen tube (10 mm OD, 8 mm ID) was also positioned in the fundus and sutured to the fundic wall at the point of entry. The bag was attached to a computer-controlled pneumatic barostat (Malbert and Ruckebusch, 1989b) that maintained the intrabag pressure at 980 Pa (above atmospheric pressure), a pressure that did not modify the gastrointestinal motility pattern (Azpiroz and Malagelada, 1985b) or the gastric emptying rate of liquid meal (Ropert et al, 1993), (fig 1). The combination of the barostat and the constant intragastric infusion of saline maintained a constant distension of the stomach and minimized any influence of changes in fundic tone on gastric emptying (Ropert et al, 1993).

Jejunal infusion and nutrient drainage were performed by isolating the lumen of the first jejunal arcade aboral to the ligament of Treitz from the remaining gut and inserting two catheters (10 mm OD, 8 mm ID), one at the proximal and one at the distal side of the loop inside the lumen. Neuromuscular continuity with the distal duodenum at one end and with the proximal jejunum at the other end was maintained by two bridges (7 mm in width, 10 mm in length) incorporating the *tunica muscularis* (Quigley et al, 1987).

## Measurements

### Motor events

The side-holes in the manometric assembly were perfused with degassed distilled water using a low-compliance pneumohydraulic pump (IP 8000, Gould, France), at a reservoir pressure of 760 mmHg, giving a constant flow rate of  $0.3 \text{ mL}\cdot\text{min}^{-1}$  (Arndorfer et al, 1977). The sleeve channel was perfused at  $0.5 \text{ mL}\cdot\text{min}^{-1}$  by a shorter capillary tube. Pressures were recorded with Gould P23XL pressure transducers and plotted on a multichannel recorder (ES 2000, Gould, France). Sudden occlusion of each catheter side-hole resulted in pressure rise over  $400 \text{ mmHg}\cdot\text{s}^{-1}$ . Pressures were digitized on line at a frequency of 10 Hz using a microcomputer (Macintosh II, Apple Computer) with an A/D card (NB MIO 16, National Instruments, Austin; MAD, Synectics, Stockholm and LabView 3.1, National

Instruments, Austin). The data were stored continuously on a hard disk for further analysis.

### Flow rate

The flow probe was connected to an electromagnetic flowmeter as described previously (Malbert and Latour, 1987; Malbert and Mathis, 1994; Malbert et al, 1995). The electromagnetic flowmeter was based on a Gould flowmeter (SP 2002) and was connected to a micro-controller (SAB 80515, Siemens, Munchen, Germany), which continuously adjusted the baseline. Retrograde flow was detected as a deflection of the flow path below the baseline. As in previous studies (Malbert and Ruckebusch, 1991; Malbert and Mathis, 1994), the whole recording setup was calibrated in vitro using a custom made pulsatile pump that propelled saline at different flow rates and flow pulse durations. The duodenal effluent was continuously weighed by a load cell (QB 742, Phi mesure, France) for subsequent determination of non-pulsatile flow, ie, flow episodes lasting more than 8 s.

### Data analysis

Analyses were performed using the analysis software of MAD (Synectics, Stockholm) and Labview 3.1 (National Instruments, Austin).

### Gastroduodenal pressures

All pressures were referenced to a virtual plane 10 cm above the surgery table to suppress any hydrostatic pressure between the output of the side-holes and the external pressure transducers. Pressure events were defined as phasic increases in pressure greater than 10 mmHg that lasted more than 1 s. Basal antral, pyloric and duodenal pressures were calculated as the mean of all data points between pressure events. Pressure and flow events were considered to be temporally related when the time interval between the onset of a pressure event in the terminal antrum or pylorus and the onset of a flow pulse was less than 10 s ( $-10 \text{ s}$ ,  $+10 \text{ s}$ ). Pyloric pressure events not temporally associated ( $\pm 2 \text{ s}$ ) with terminal antral or proximal duodenal pressure events (Hedde et al, 1988a) were considered as isolated pyloric pressure events (IPPWs).

### Flow rate

For each flow pulse: peak flow rate (in millilitre per second), stroke volume (in millilitres) and

pulse duration (in seconds) were automatically derived from the curve  $V' = f(t)$  according to the previously described methods (Malbert and Ruckebusch, 1989a; Malbert et al, 1992). A flow pulse was defined as a flow increase above the baseline greater than  $0.5 \text{ mL}\cdot\text{s}^{-1}$ , that lasted more than 1 s and less than 8 s. Multiple criteria, which included the beginning and end slopes, decline time, shoulder slope, were used to define the onset of flow pulse (Malbert et al, 1995). Separation of merged flow pulses from those with multiple peaks was performed using interpeak duration and height parameters. Non-pulsatile flow was quantified by subtracting the volume of pulsatile flow from the total volume of duodenal effluent.

### *Pyloric resistance*

Values for pyloric resistance were calculated from the pressure and flow data by an analysis of the relationship between the pressure and flow rate (Malbert and Ruckebusch, 1991). Pyloric resistance depends on the flow rate and the pressure gradient across the pylorus, and hence, pyloric resistance changes during each flow pulse. The mean resistance for each flow pulse was calculated as the mean flow divided by the mean pressure during the flow pulse. Mean resistance values corresponded to the mean of 50 flow pulses.

### Statistical analysis

Data are presented as mean values  $\pm$  SEM. Pressure and flow events were quantified for 10 min intervals starting at the beginning of test infusions and continuing for 80 min. During this period, differences between nutrient containing solutions and saline test solution were assessed using Fisher PLSD tests. Statistical significance was tested by repeated measure one-way or two-way analysis of variance where  $P < 0.05$  was considered to be significant.

## RESULTS

### Motor Activity

#### *Test saline infusion*

The basal pressure recorded by the sleeve sensor during saline infusion (0–80 min) was  $23.8 \pm 1.94 \text{ mmHg}$  (table I). There was no significant difference between the first and the second 40 min periods. The amplitude of the terminal antral pressure events was not significantly different from that of the phasic pyloric pressure events but was about twice that of duodenal ones ( $49.8 \pm 3.93$ ,  $51.1 \pm 4.24$  and  $26.2 \pm 1.34 \text{ mmHg}$  for the

**Table I.** Basal pyloric pressure and characteristics of isolated pyloric pressure events recorded by the sleeve sensor before (–40 to 0 min), during (0 to 40 min) and immediately after (40 to 80 min) small intestinal saline, dextrose, Intralipid and casein infusions.

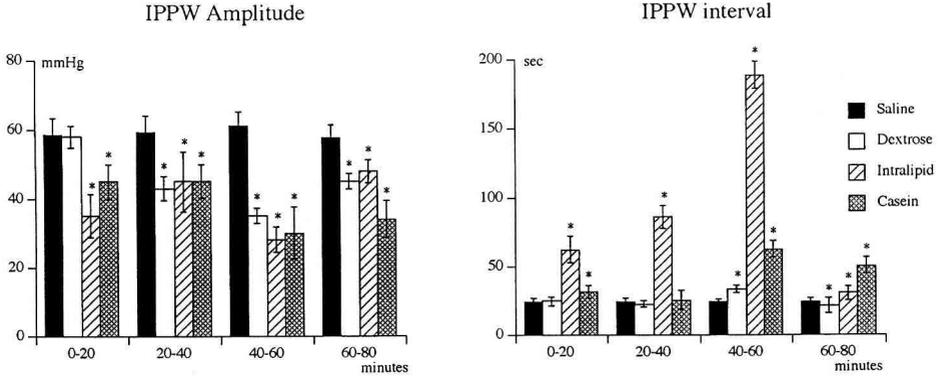
	<i>Time (min)</i>	<i>Test saline</i>	<i>Dextrose</i>	<i>Intralipid</i>	<i>Casein</i>
Basal	– 40,0	$21.0 \pm 2.99_a$	$21.4 \pm 3.52_a$	$22.9 \pm 2.28_a$	$22.1 \pm 1.26_a$
Pressure (mmHg)	0,40	$23.5 \pm 2.00_a$	$18.4 \pm 0.89_b$	$12.6 \pm 0.48_d$	$15.7 \pm 0.30_c$
	40,80	$24.0 \pm 2.10_a$	$15.9 \pm 0.34_c$	$11.5 \pm 0.34_d$	$12.9 \pm 0.08_d$
IPPW	– 40,0	$62.1 \pm 2.70_a$	$65.5 \pm 3.52_a$	$60.4 \pm 3.93_a$	$58.8 \pm 2.39_a$
Amplitude (mmHg)	0,40	$59.2 \pm 4.69_a$	$50.7 \pm 3.51_a$	$39.6 \pm 8.74_b$	$45.1 \pm 4.80_c$
	40,80	$61.0 \pm 4.21_a$	$40.4 \pm 2.24_b$	$38.4 \pm 3.58_b$	$32.3 \pm 7.66_d$
IPPW	– 40,0	$22.4 \pm 4.06_{a''}$	$21.2 \pm 3.20_{a''}$	$19.7 \pm 3.20_{a''}$	$24.9 \pm 3.35_{a''}$
Interval (seconds)	0,40	$23.6 \pm 2.58_{a''}$	$22.0 \pm 2.37_{a''}$	$74.7 \pm 8.40_{c''}$	$29.3 \pm 6.62_{b''}$
	40,80	$23.4 \pm 2.36_{a''}$	$29.2 \pm 3.03_{b''}$	$111.4 \pm 9.61_{d''}$	$56.3 \pm 6.00_{e''}$

Mean  $\pm$  SE for eight pigs. Values with different subscript letters were significantly different from each other at  $P < 0.05$  (two-way repeated measures Anova).

antral, pyloric and duodenal pressure events, respectively). The mean interval between consecutive pyloric pressure events was  $25.0 \pm 0.27$  s (fig 2). IPPW represented 75% of the recorded pyloric pressure events (fig 3).

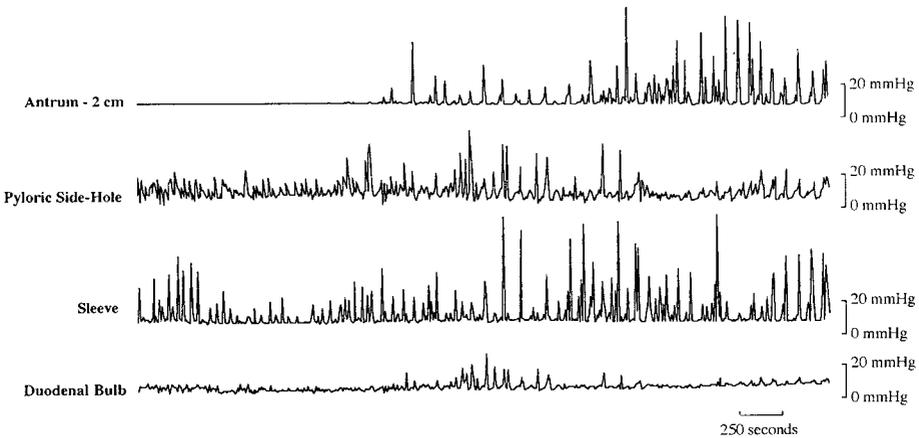
**Nutrient infusions**

Nutrient infusions, irrespective of their nature, reduced basal pyloric pressure compared to test saline infusion (table I).



\* indicates a significant difference from test saline at  $P < 0.05$ .

**Fig 2.** Effects of jejunal nutrient infusion on the characteristics of isolated pyloric pressure events. The amplitude and frequency of IPPWs were significantly decreased by small intestinal nutrients. These effects were observed 40–60 min after the onset of dextrose infusion but occurred earlier with Intralipid and casein infusions.



**Fig 3.** Raw antro-pyloro-duodenal motility tracing in chloralose–urethane anaesthetized pig during gastric infusion of saline. Note the presence of antral and duodenal pressure events and the large proportion of IPPW accounting for 75% of the pyloric pressure events.

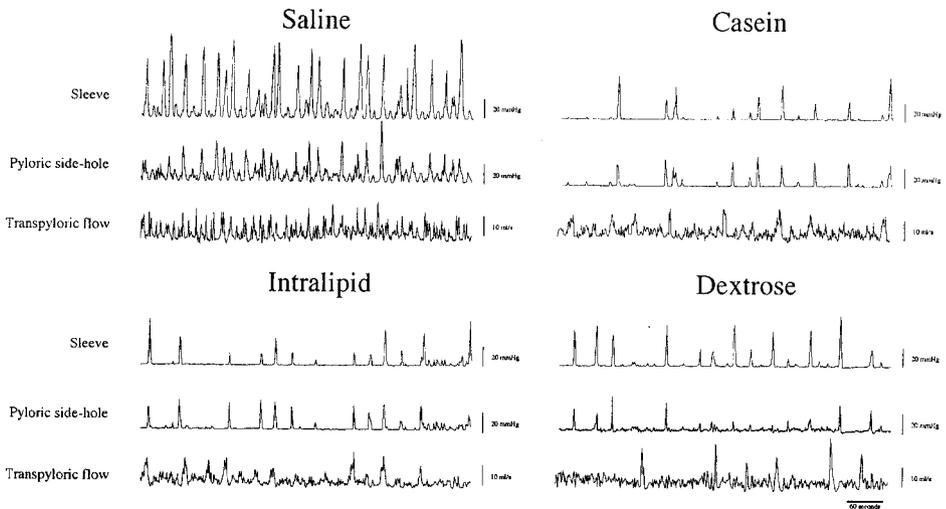
Intralipid and casein infusions resulted in a greater decrease in basal pyloric pressure than in dextrose ( $P < 0.05$ ) with a pressure reduction of about 50% for 80 min. Antral and duodenal pressure events were abol-

ished during all nutrient infusions. They recurred during the subsequent 40 min of saline infusion at various intervals related to the nutrient:  $15 \pm 4$  min,  $17 \pm 6$  min and  $29 \pm 8$  min after the termination of dextrose,

**Table II.** Characteristics of the transpyloric flow before (-40 to 0 min), during (0 to 40 min) and immediately after (40 to 80 min) small intestinal saline, dextrose, Intralipid and casein infusions (see text for definitions of pulsatile and non-pulsatile flow).

	Time (min)	Test saline	Dextrose	Intralipid	Casein
Total volume emptied (mL)	-40,0	$179 \pm 11.1_a$	$159 \pm 10.3_a$	$165 \pm 9.5_a$	$166 \pm 7.8_a$
	0,40	$168 \pm 10.8_a$	$160 \pm 9.5_a$	$156 \pm 10.4_a$	$164 \pm 10.0_a$
	40,80	$171 \pm 9.1_a$	$165 \pm 10.1_a$	$161 \pm 9.9_a$	$168 \pm 10.5_a$
Pulsatile volume (mL)	-40,0	$130 \pm 5.5_a$	$131 \pm 9.0_a$	$129 \pm 5.9_a$	$135 \pm 7.5_a$
	0,40	$134 \pm 7.4_a$	$126 \pm 6.8_a$	$112 \pm 5.2_b$	$123 \pm 6.7_c$
	40,80	$135 \pm 6.9_a$	$129 \pm 6.5_a$	$113 \pm 8.0_b$	$124 \pm 5.7_c$
Pulsatile/non pulsatile	-40,0	$4.3 \pm 0.29_a$	$4.4 \pm 0.13_a$	$5.3 \pm 0.24_a$	$4.5 \pm 0.29_a$
	0,40	$4.0 \pm 0.58_a$	$3.7 \pm 0.49_a$	$2.5 \pm 0.22_b$	$3.0 \pm 0.17_c$
	40,80	$3.9 \pm 0.26_a$	$3.6 \pm 0.30_a$	$2.3 \pm 0.15_b$	$3.1 \pm 0.21_c$

Mean  $\pm$  SE for eight pigs. Values with different subscripts were significantly different from each other at  $P < 0.05$  (two-way repeated measures Anova).



**Fig 4.** Examples of the effects of jejunal nutrient infusion on pyloric motility and transpyloric flow recorded 30 min after the onset of the infusions. The reduced amplitude and frequency of pyloric pressure events induced by nutrient infusion were associated with a reduction in the frequency of the flow pulses. Apart from the well-defined flow pulses, small fluctuations in transpyloric flow were apparent.

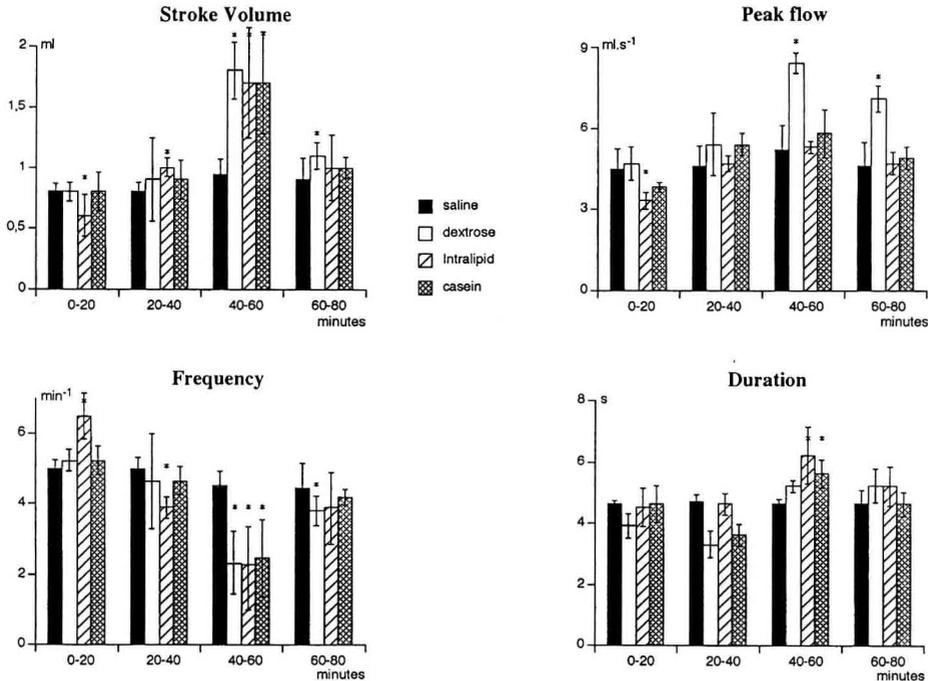
casein and Intralipid infusions, respectively. The IPPWs recorded during and after nutrient infusions were of reduced amplitude and frequency compared to test saline infusion ( $P < 0.05$ , table I). The amplitude and frequency of pyloric pressure events were lowest during small intestinal intralipid infusion ( $P < 0.05$ , fig 2).

## Transpyloric flow

### Test saline infusion

The mean gastric emptying rate was  $4.2 \text{ mL} \cdot \text{min}^{-1}$  about 90 min after the begin-

ning of intragastric instillation. Emptying of saline was mostly pulsatile with  $6.3 \pm 0.41$  flow pulses per minute (fig 4) and non-pulsatile flow amounted to 20% of the total gastric emptying ( $0.2 \pm 0.05 \text{ mL} \cdot \text{min}^{-1}$ , table II). Flow pulse duration was  $4.6 \pm 0.15 \text{ s}$  and the mean stroke volume  $0.8 \pm 0.23 \text{ mL}$  (fig 5). In 31% of flow pulses, backflow events were recorded immediately upon the cessation of forward flow. The volume of the backflow episode amounted to 15% of the forward flow ( $0.1 \pm 0.03 \text{ mL}$ ). There were no significant differences in the characteristics of flow pulses between the first and the second 40 min of the experimental period (see fig 5).



\* indicates a significant difference from test saline at  $P < 0.05$ .

**Fig 5.** Effects of jejunal nutrient infusion on the characteristics of flow pulses. All nutrient infusions reduced flow pulse frequency. The stroke volume of flow pulses was increased between 40 and 60 min after the onset of dextrose, Intralipid and casein infusions. This increased stroke volume reflected an increased peak flow rate (dextrose) and a longer duration of the flow pulses (Intralipid and casein).

### Nutrient infusions

Nutrient infusions did not alter the overall gastric emptying rate of saline (table II) but did modify the individual characteristics of the transpyloric flow pulses. Intralipid and to a lesser extent casein infusions, but not dextrose, increased significantly the amount of non-pulsatile transpyloric flow.

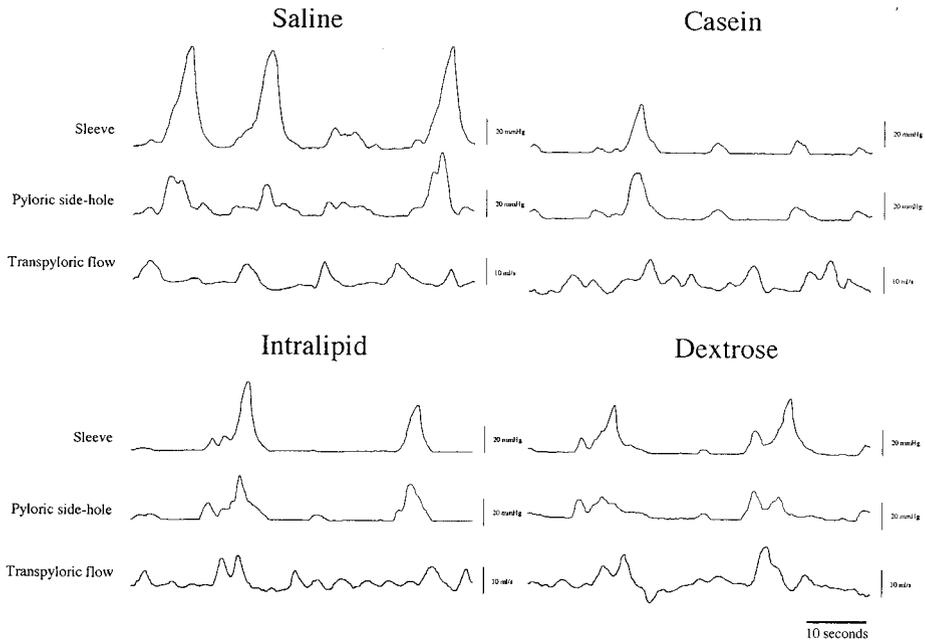
All nutrient infusions were associated with flow pulses of significantly greater stroke volume (fig 5) and reduced frequency. In all cases, these effects were observed 40 to 60 min after the onset of the infusions and there was no significant difference between nutrients. The cause of the increased stroke volume of flow pulses differed between nutrients. For dextrose, the increased stroke volume reflected greater peak flow compared to test saline infusion

( $8.4 \pm 0.37 \text{ mL}\cdot\text{s}^{-1}$  versus  $4.6 \pm 0.92 \text{ mL}\cdot\text{s}^{-1}$ ,  $P < 0.05$ ) while for Intralipid and casein infusions, flow pulses were of longer duration ( $6.2 \pm 0.93$  and  $5.6 \pm 0.46 \text{ s}$  for Intralipid and casein, respectively, versus  $4.6 \pm 0.15 \text{ s}$  for test saline infusion,  $P < 0.05$ ) without any change in peak flow. Backflow episodes amounted to 24% of the forward flow for dextrose and were absent for Intralipid and casein infusions (see fig 6). Forty minutes after the onset of Intralipid and casein infusion, backflow was less than 1% of the forward flow.

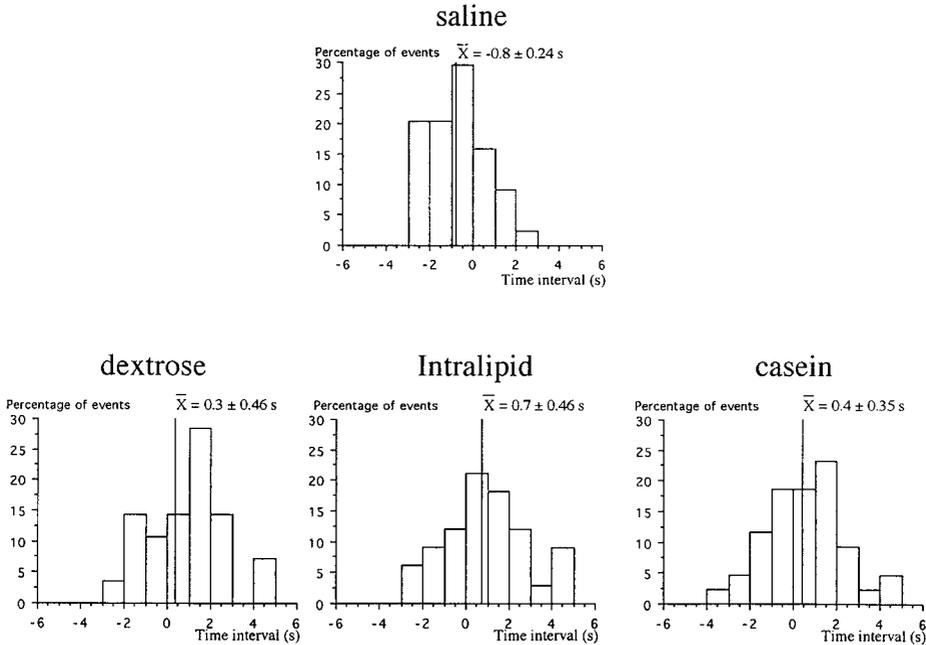
### Pressure–flow relationships

#### Test saline infusion

Transpyloric flow pulses occurred  $0.8 \pm 0.24 \text{ s}$  before the onset of a pyloric pressure



**Fig 6.** Example of effects of jejunal nutrient infusion on the relationship between pyloric pressure events and flow pulses at 30 min after the onset of the infusions. During test saline infusion, the transpyloric flow pulses occurred before or during the onset of pyloric pressure events whereas most flow pulses occurred after pyloric pressure events during nutrient infusions.



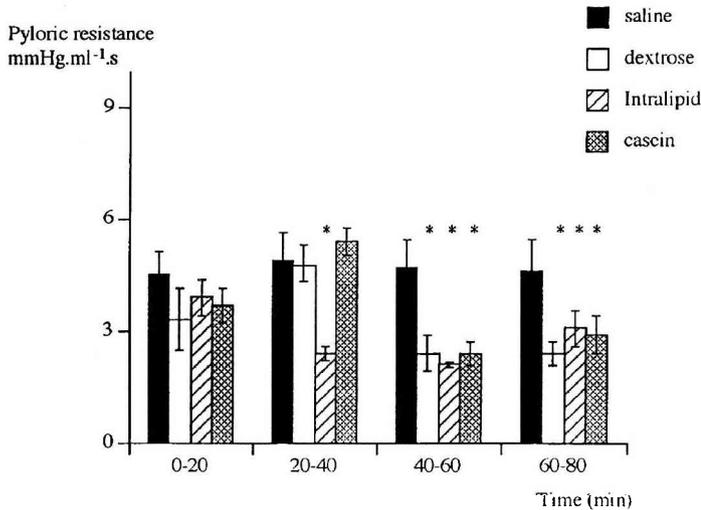
**Fig 7.** Time interval between the onset of a pyloric (sleeve) pressure event and a flow pulse during test saline, dextrose, Intralipid and casein infusions. Data are expressed as a percentage of the pyloric events. The vertical grey lines represent the mean  $\pm$  SEM of the time interval. During all nutrient infusions, the distribution of the time interval was shifted to the right indicating the occurrence of a pyloric pressure event before the onset of a flow pulse.

event (fig 7). The end of the flow pulse was always associated with the onset of this pyloric pressure event (fig 6). Sixteen percent of the flow pulses were not associated with a pyloric pressure event. The stroke volume of these pulses was less ( $0.6 \pm 0.19$  versus  $0.8 \pm 0.23$  mL,  $P < 0.05$ ) than that of flow pulses associated with pyloric pressure events.

The relationship between flow and transpyloric pressure difference was ellipsoidal so that flow rate and pressure difference increased and then decreased simultaneously. Mean pyloric resistance was  $4.6 \pm 0.54$  mmHg.mL<sup>-1</sup>.s<sup>-1</sup> (0–80 min).

### *Nutrient infusions*

All nutrient infusions altered the temporal relationship between the onset of a transpyloric flow pulse and a pyloric pressure event so that most flow pulses occurred after the onset of a pyloric pressure event. The mean intervals between the flow pulses and the pyloric pressure events were  $0.3 \pm 0.46$ ,  $0.7 \pm 0.46$  and  $0.4 \pm 0.35$  s for dextrose, Intralipid and casein infusion, respectively (fig 7). For all three nutrients, the number of flow pulses unassociated with a pressure event was not significantly different from that observed during test saline infusion



\* indicates a significant difference from test saline at  $P < 0.05$ .

**Fig 8.** Time course of pyloric resistance during test saline, dextrose, Intralipid and casein infusions. Pyloric resistance was lowered by all three nutrients 40–60 min after the onset of the infusion.

(18% versus 16% for test saline infusion,  $P > 0.05$ ).

Pyloric resistance was reduced ( $P < 0.05$ ) by all nutrient infusions compared to test saline, with a maximum decrease at 40 to 60 min (fig 8). The decrease in pyloric resistance occurred earlier (20 to 40 min) after intralipid infusion but after this time (40 to 80 min) there was no significant difference between nutrients ( $P > 0.05$ ). Indicative of a reduction in pyloric resistance, the slopes of the pressure–flow relation decreased but remained ellipsoidal during nutrient infusions.

## DISCUSSION

The main findings of this study are three fold. First, the overall gastric emptying of saline was not modified by intestinal infusion of nutrients while the fundic pressure was held at 980 Pa. Second, the pattern of

transpyloric flow was modified drastically by the intestinal nutrient infusions. The flow pulses were of larger stroke volume but less frequent and the amount of non-pulsatile flow was increased. Third, these changes in the pattern of transpyloric flow were accompanied, for all nutrients, by a marked decrease in pyloric resistance related to changes in the temporal relationship between pyloric pressure events and flow pulses.

One important issue is the appropriateness of the anaesthetized pig model used. We have previously shown that the present model exhibits (i) the pattern of gastric and duodenal occlusive motor events and (ii) the transpyloric flow pattern observed in awake animals (Malbert et al, 1995). Extrinsic and intrinsic nervous control of motor and flow patterns was also present in this model (Malbert and Mathis, 1994). The concentration of nutrient infused in the small intestine was within the range of that known to slow gastric emptying in the pig (Gre-

gory and Rayner, 1987; Landers et al, 1990). The length of the nutrient exposed jejunal segment was about equal to 2/10th of the total small intestine length; a value within the range of those explored by others (Lin et al, 1989). Furthermore, the inhibition of phasic antral motility and the exclusive presence of isolated pyloric pressure events observed after the infusion of nutrients were identical to those already described in humans, dogs and pigs (Hedde et al, 1988a, b; Treacy et al, 1990).

The overall gastric emptying rate was not diminished by nutrient infusions in our preparation where the fundic pressure was held constant. Similar absences of gastric emptying retardation with nutrient meals have been already observed in dogs under controlled fundic pressure (Miller et al, 1981). Using an hydraulic barostat, Miller et al (1981) found that while the gastric pressure was held at 980 Pa, gastric emptying rate of nutrient containing solutions was not significantly different from saline itself. However, the same authors also found that barostat pressures higher than 980 Pa generated a slower gastric emptying rate for nutrient meals versus saline. Similarly, in conscious pigs, a reduction of gastric emptying of dextrose was observed only when the barostat pressure was over 1 470 Pa (Treacy et al, 1994). Therefore, it is likely that the fundic barostat was at the origin of the preservation of gastric emptying rate, observed in our study. This steady outflow was a priority for the continuous measurement of pyloric resistance because this measurement involved an evaluation of the pressure/flow ratio and hence the presence of pulsatile emptying. The unchanged overall gastric emptying was nevertheless associated with major variations of transpyloric flow pattern. During nutrient infusions, the stroke volume of flow pulses was increased, a feature identical to that already observed after surgical removal of the fundic influences (Malbert and Mathis, 1994). Therefore, it cannot be excluded that the increased

stroke volume might be related to a reduced (barostat bag) or an absent (fundectomy) receptive capability of the proximal stomach (Azpiroz and Malagelada, 1986).

The present finding of a decreased pyloric resistance during nutrient infusions is controversial because other studies have suggested that increased pyloric resistance might be involved in the reduced gastric emptying rate of nutrient meals (Schulze-Delrieu and Brown, 1985; Mearin et al, 1986; Williams et al, 1986). Using a pair of coils acting as an inductograph for the pylorus, Ehrlein (1992) showed that, in conscious dogs after nutrient administration, the lowest diameter of the pylorus was either unchanged or slightly diminished. However, because the changes of the pyloric diameter between the open and closed states were of lower amplitude, Ehrlein postulated an increased pyloric resistance. On the contrary, the reduced basal pyloric pressure observed in our study after nutrient infusions was consistent with a decreased resistance. This decreased pyloric resistance after jejunal nutrient infusions agrees with the conclusions of Miller et al (1981) who found that 'the dominant regulator of gastric emptying of nutrient containing liquids is a resistance or series of resistance to outflow beyond the pylorus' (Miller et al, 1981). They further suggest that the main resistance regulating gastric outflow of nutrient is located beyond the second portion of the duodenum.

It is clear that under the present experimental conditions, IPPWs were ineffective in generating pyloric resistance because of their irregular time-relationship to the onset of the flow pulses. On the contrary, during test saline infusion, pyloric pressure events occurred on a regular basis (when the flow rate was maximal). Isolated pyloric pressure events have always been described in situations of decreased gastric emptying rate, ie, during intragastric, duodenal or jejunal infusions of macronutrients (Hedde et al,

1988a, b), acidification of the duodenum (Allescher et al, 1989) and duodenal cold stress (Fone et al, 1990). In our study, their ineffectiveness in reducing gastric emptying might be related to the presence of the fundic barostat that maintained the fundic pressure, thus avoiding the possible fundic distension generated by the inhibition of gastric emptying (Fone et al, 1990; Edelbroek et al, 1993). The linear relationship, found in conscious pigs, between the frequency of IPPWs and the degree of gastric distension strongly supports this view (Treacy et al, 1994).

In conclusion, under controlled low fundic pressure, gastric emptying rate of saline was not significantly modified by jejunal nutrients. However, the mechanisms of gastric emptying were altered, the transpyloric flow pulses being more propulsive but less frequent. The origin of this increased stroke volume was a decreased pyloric resistance.

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