

**The role of gastric and small  
intestinal mechanisms in  
postprandial hypotension**

*A thesis submitted by*

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*For the degree of*

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# **Thesis abstract**

Postprandial hypotension, defined as a fall in systolic blood pressure of  $\geq 20$  mmHg, within two hours of a meal, leading to syncope, falls, dizziness and angina, occurs frequently in the elderly and is now recognised as an important clinical problem. In healthy young and older individuals, meal ingestion is associated with a rapid rise in heart rate indicative of normal baroreflex function which appears to prevent a significant fall in blood pressure. However, in patients with postprandial hypotension, this response is inadequate to maintain blood pressure. Current approaches to the management of postprandial hypotension are suboptimal and there is a need for novel therapeutic strategies. Recent studies have established that the magnitude of the fall in blood pressure is dependent on the rate of delivery of nutrients from the stomach into the small intestine, while gastric distension attenuates the postprandial fall in blood pressure.

The overall aims of the studies described in this thesis were to investigate the pathophysiology of postprandial hypotension, with the particular focus on gastric and small intestinal mechanisms and their potential therapeutic relevance. In this thesis, studies were carried out in healthy older subjects (age 65 - 80 years) and were designed to evaluate the following: i) the effects of small intestinal glucose load on blood pressure, heart rate and superior mesenteric artery blood flow, ii) the comparative effects of two carbohydrates, glucose and xylose, on blood pressure, heart rate and gastric emptying, iii) the effects of gastric distension, using a barostat, on blood pressure, heart rate and superior mesenteric artery blood flow in response to intraduodenal glucose infusion, iv) the effects of variations in gastric volume, using a barostat, on blood pressure, heart rate and superior

mesenteric artery blood flow during intraduodenal glucose infusion, v) the effects of the oligosaccharide, alpha ( $\alpha$ ) – cyclodextrin, on blood pressure and heart rate, vi) the effects of acarbose on the blood pressure, heart rate and splanchnic blood flow responses to intraduodenal sucrose. All of the studies have either been published or manuscripts prepared and submitted for publication.

The effects of meal composition on the magnitude of the postprandial fall in blood pressure have been inconsistent. Of the macronutrients, the ingestion of carbohydrate, in particular glucose, was believed to have the greatest effect on blood pressure, with the effects of protein and fat being inconsistent. The fall in blood pressure following intraduodenal glucose appears to be load dependent rather than concentration dependent. A recent study demonstrated that when intraduodenal glucose is administered at a rate of 3 kcal/min, the fall in blood pressure and rise in heart rate were substantially greater compared to a 1 kcal/min glucose infusion. A limitation of this study was that there was no control arm, and because only two intraduodenal glucose loads were evaluated, it could not be determined whether the relationship between the fall in blood pressure and the duodenal glucose load is linear, this was addressed in **Chapter 5**.

There is relatively little information about the effect of different carbohydrates on postprandial blood pressure. Information relating to the effect of xylose on blood pressure is inconsistent, with previous studies showing xylose to have little or no effect. However, in these studies gastric emptying was not measured and it is known that differences in the rate of gastric emptying can affect the magnitude of



the fall in blood pressure. Blood pressure and the rate of gastric emptying of oral glucose and xylose was studied in healthy older subjects in the study reported in **Chapter 6**.

Previous studies have established that the magnitude of the postprandial fall in blood pressure is attenuated by gastric distension, however, it is unknown whether this effect is caused by the change in intragastric pressure (**Chapter 7**) or intragastric volume (**Chapter 8**). Gastric distension at predefined volumes and/or pressures can be achieved using a barostat device. Gastric distension at a pressure of 8 mmHg above minimal distending pressure using a barostat, increased mean arterial pressure, heart rate and total peripheral arterial resistance in healthy subjects. No studies have hitherto evaluated the effects of gastric distension, using a barostat, on the hypotensive response to small intestinal nutrients, and this was addressed in **Chapter 7**.

Intragastric distension with 500 ml water was shown to markedly attenuate the magnitude of the fall in systolic blood pressure in response to intraduodenal glucose. However, a limitation of this study was that during intraduodenal glucose infusion, gastric emptying was markedly attenuated, so that it reached a plateau at 300 ml and little information could be determined in relation to the minimum volume required to attenuate the hypotensive response to glucose, therefore, this was evaluated in **Chapter 8**.

Cyclodextrins inhibit pancreatic amylase activity and are poorly digested in the small intestine.  $\alpha$ - and beta ( $\beta$ )- cyclodextrins have been reported to reduce the postprandial glycaemic and insulinaemia responses to a starch meal. However, a limitation of these studies was that the rate of gastric emptying was not measured, hence it remains to be determined whether the observed effects were related to gastric emptying and/or intestinal glucose absorption. In the study reported in **Chapter 9**, the effects of  $\alpha$ -cyclodextrin on the rate of gastric emptying and hypotensive response to an oral sucrose drink were evaluated.

Acarbose has been used in the treatment of type 2-diabetes for many years by suppressing postprandial glycaemia and slowing of small intestinal digestion and absorption of carbohydrate. Previous studies have illustrated that acarbose has the capacity to slow gastric emptying and attenuate the hypotensive response to carbohydrate meals. The effects of acarbose on postprandial blood pressure and heart rate when administered intraduodenally i.e. in the absence of an effect on gastric emptying, have not been evaluated. Intraduodenal infusion allows the 'intra-gastric' mechanisms related to changes in gastric emptying to be 'bypassed', which have been evaluated in **Chapter 10**.

## **Declaration of originality**

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Lora Vanis and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Lora Vanis

September 2010

# **Dedication**

*To my dear family,  
Thank you for your continual love and support,  
You have been truly inspirational,  
I couldn't have done this without you*

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## **Publications arising from thesis**

**Vanis L**, Gentilcore D, Hausken T, Pilichiewicz A, Lange K, Rayner CK, Feinle-Bisset C, Meyer JH, Horowitz M, Jones KL (2010). “Effects of gastric distension on blood pressure and superior mesenteric artery blood flow responses to intraduodenal glucose in healthy older subjects.” *Am J Physiol Regul Integr Comp Physiol* 299:R960-967.

**Vanis L**, Hausken T, Gentilcore D, Rigda RS, Rayner CK, Feinle-Bisset C, Horowitz M, Jones KL. “Comparative effects of glucose and xylose, on blood pressure, gastric emptying and incretin hormones in healthy older subjects.” *BJN* (accepted).

**Vanis L**, Gentilcore D, Rayner CK, Horowitz M, Feinle-Bisset C, Jones KL. “Effects of small intestinal glucose load on blood pressure, splanchnic blood flow, glycemia and GLP-1 release in healthy older subjects.” *Am J Physiol Regul Integr Comp Physiol* (submitted).

Accepted in abstract form: *JNHA*, 2009;13(Suppl 1):S478 and *JNHA* 2009;13(Suppl 2):S17.

**Vanis L**, Gentilcore D, Hausken T, Rayner CK, Feinle-Bisset C, Meyer JH, Horowitz M, Jones KL. “Effects of variations in intragastric volume, on blood pressure and superior mesenteric artery blood flow during intraduodenal glucose infusion in healthy older subjects.” *Am J Physiol Gastrointest Liver Physiol* (submitted).

Gentilcore D, **Vanis L**, Teng JC, Wishart JM, Buckley JD, Rayner CK, Horowitz M, Jones KL. “Effects of the oligosaccharide, alpha (a)-cyclodextrin, on gastric emptying of, and the glycemic and blood pressure responses to, oral sucrose in healthy older subjects.” *BJN* (submitted).

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Gentilcore D, **Vanis L**, Wishart JM, Rayner CK, Horowitz M, Jones KL. “Effects of intraduodenal acarbose on blood pressure, heart rate and splanchnic blood flow in healthy older subjects.” *J Hypertens* (submitted).

Accepted in abstract form: *JAGS*, 2010; 58(Suppl 1):S280.

### **Other manuscripts**

Gentilcore D, Nair NS, **Vanis L**, Rayner CK, Meyer JH, Hausken T, Horowitz M, Jones KL (2009). “Comparative effects of oral and intraduodenal glucose on blood pressure, heart rate and splanchnic blood flow in healthy older subjects.” *Am J Physiol Regul Integr Comp Physiol* 297:R716-722.

Gentilcore D, Nair NS, Kuo P, **Vanis L**, Buckley JD, Rayner CK, Horowitz M, Jones KL. “Effects of aerobic exercise on gastric emptying of, and the glycemic and cardiovascular responses to, oral glucose in healthy older subjects.” (manuscript in preparation).

Accepted in abstract form: *Neurogastroenterol Motil* 2008;20:83.