

**Role of the Gastrointestinal Tract in  
Postprandial Blood Pressure Regulation**

**Role of the Gastrointestinal Tract in  
Postprandial Blood Pressure Regulation**

*A thesis submitted by*

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*For the Degree of*

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## **Summary**

This thesis presents studies relating to the role of the gastrointestinal tract in postprandial blood pressure regulation. The areas that have been addressed include: (i) the methodological approaches to the evaluation of gastric emptying, blood pressure, splanchnic blood flow, intraluminal manometry and gut hormones and (ii) the pathophysiological mechanisms underlying postprandial hypotension, with a particular focus on 'gastric' and 'small intestinal' mechanisms and their potential therapeutic relevance. All of the studies have been either published or manuscripts have been prepared for publication.

While scintigraphy represents the 'gold standard' for the measurement of gastric emptying, recent studies suggest that three-dimensional (3D) ultrasonography may also allow a precise measure of gastric emptying. Concurrent scintigraphic and ultrasonographic measurements of gastric emptying of liquids were performed in healthy young volunteers. There was a good correlation and agreement between scintigraphic measurements of gastric emptying and 3D ultrasonography after ingestion of both low- and high- nutrient drinks, indicating that 3D ultrasonography, provides a valid measure of gastric emptying of liquid meals in normal subjects.

Postprandial hypotension, defined as a fall in systolic blood pressure of  $\geq 20$ mmHg, occurring within two hours of a meal is now recognised as an important clinical problem, particularly in the elderly and in patients with type 2 diabetes. The mechanisms mediating postprandial hypotension are poorly understood. The effects of variations in concentration of intraduodenal glucose on the magnitude of the fall in

blood pressure were evaluated in healthy elderly subjects. Blood pressure fell, and heart rate and blood glucose increased over time during infusions, however, there was no difference in blood pressure, heart rate or blood glucose concentrations between the study days. These observations suggest that glucose induced postprandial hypotension is a load rather, than concentration, dependent phenomenon.

The effect of meal composition has been reported to influence the hypotensive response to a meal and information relating to the effects of triglyceride and protein on blood pressure is inconsistent. The comparative effects of isocaloric and isovolaemic intraduodenal infusions of glucose, triglyceride and protein on the magnitude of the postprandial fall in blood pressure and rise in heart rate and superior mesenteric artery blood flow were evaluated in healthy elderly subjects. There were comparable falls in systolic blood pressure and rises in heart rate, however, the maximum fall in systolic blood pressure occurred later after triglyceride and protein and the stimulation of superior mesenteric artery blood flow was less after protein. These observations suggest that the relatively slower systolic blood pressure response after triglyceride and protein may potentially reflect the time taken for digestion of triglyceride to free fatty acids and protein to amino acids.

Acarbose is an antidiabetic drug that slows both gastric emptying and small intestinal glucose absorption. The effects of acarbose, on blood pressure, heart rate, gastric emptying of, and the glycaemic, insulin, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic-polypeptide (GIP) responses to, an oral sucrose load were

evaluated in healthy elderly subjects. Acarbose attenuated the fall in blood pressure and increase in heart rate induced by oral sucrose. Acarbose slowed gastric emptying and was associated with increased retention in the distal stomach. Stimulation of GLP-1 may contribute to the slowing of gastric emptying and suppression of postprandial glycaemia by acarbose. These findings suggest that acarbose may represent a therapeutic option for the treatment of patients with postprandial hypotension.

Recent studies indicate that gastric distension attenuates the postprandial fall in blood pressure. The effects of gastric distension on blood pressure and heart rate during intraduodenal infusion of glucose at a constant load and concentration were evaluated in healthy elderly subjects. Intra-gastric administration of water markedly attenuated the falls in systolic and diastolic blood pressure induced by intraduodenal glucose. Heart rate increased, with and without gastric distension, in response to intraduodenal glucose infusion but not after intraduodenal saline infusion. This study suggests that gastric distension may potentially be used as a simple adjunctive treatment in the management of postprandial hypotension.

Studies employing nitric oxide synthase blockers have established, in animals, that nitric oxide mechanisms are important in the regulation of splanchnic blood flow and, hence, may effect postprandial blood pressure. The role of the nitric oxide synthase inhibitor, NG-nitro-L-arginine-methyl-ester (L-NAME), on gastric emptying, postprandial blood pressure, plasma insulin concentration and incretin hormone (ie GIP and GLP-1) release, following an oral glucose load, were evaluated in healthy elderly

subjects. L-NAME attenuated the postprandial fall in blood pressure and increase in heart rate but had no effect on gastric emptying of glucose. L-NAME attenuated the glucose-induced rise in plasma insulin but had no effect on the incretin (GIP and GLP-1) hormone response to oral glucose. The study indicates that the magnitude of the fall in blood pressure and increase in heart rate and stimulation of insulin secretion induced by oral glucose in healthy elderly subjects are mediated by nitric oxide mechanisms by an effect unrelated to changes in gastric emptying, or the secretion of GIP and GLP-1.

Studies utilising 5-hydroxytryptamine (5-HT) infusions in animals have demonstrated regional variations in intestinal blood flow suggesting a role for 5-HT in postprandial haemodynamic responses. The effects of the 5-hydroxytryptamine 3 (5-HT<sub>3</sub>) antagonist, granisetron, on the blood pressure, heart rate, antropyloroduodenal motility and glycaemic responses to intraduodenal glucose infusion were assessed in healthy elderly subjects. Granisetron had no effect on blood pressure, heart rate or antral and pyloric motor responses but modulated the duodenal motor response, to intraduodenal glucose. This study indicates that while the cardiovascular response to intraduodenal glucose does not appear to be influenced by the stimulation of 5-HT<sub>3</sub> receptors, this receptor may be involved in the modulation of the duodenal motor activity.

## **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 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.

I give consent to this copy of my thesis being made available in the University Library. The author acknowledges that copyright of published works contained within this thesis resides with the copyright holder/s of those works.

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Diana Gentilcore

December 2006

# **Dedication**

*For my husband Laurie  
Your courage is inspirational.*

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## **Publications arising from this thesis**

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**Gentilcore, D**, O'Donovan, D, Jones, KL & Horowitz, M 2003, 'Nutrition therapy for diabetic gastroparesis', *Curr Diab Rep*, vol. 3, no.5, pp. 418-426.

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