NON-INVASIVE ASSESSMENT OF GASTROINTESTINAL FUNCTION USING BREATH TEST TECHNOLOGY: INVESTIGATIONS IN HEALTH AND DISEASE

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A thesis submitted for the degree of Doctor of Philosophy

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December 2002
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ABSTRACT

Assessment of gastric emptying in animals is hampered by the lack of a technique that is non-invasive and does not involve sacrificing the animal. The primary aims of these studies therefore were to develop the breath test for the mouse and then investigate gastric emptying rates in physiological, pathological and pharmacological studies. After an overnight fast, mice were fed a solid or liquid meal that contained a $^{13}$C-labelled substrate, and placed in breath collection chambers. Breath samples collected at intervals were analysed for levels of $^{13}$CO$_2$, with the rate of appearance in the breath giving a measure of the gastric emptying rate. The breath testing technique was shown to be reproducible and sensitive enough to be able to detect induced alterations to gastric emptying, with results comparable to those obtained from other techniques. The breath test was used to assess gastric emptying in mice and showed that: (1) *H. pylori* infection accelerated gastric emptying in the initial weeks of infection, whilst a more severe stomach inflammation caused dysmotility; (2) baclofen (a potential reflux therapy) accelerated gastric emptying of solids and delayed liquid emptying in a dose-dependent manner; and (3) mice with a high daily food intake had faster emptying compared to those with low intake, which resulted in the same weight gain of the two groups. Breath testing was also used in adults and children and showed that: (1) increasing the caloric content of a solid meal delayed the emptying of the solid, but not of a liquid given simultaneously; (2) gastric emptying rate is correlated to the amount of colonic gas produced; and (3) improvement in pancreatic lipase activity with pancreatic enzyme replacement is inversely related to the gastric emptying time. Breath testing was also used to show that substrates with a natural $^{13}$C-enrichment can be used to assess small intestinal enzyme activity. Breath testing is a sensitive and reproducible tool to investigate gastric emptying in mice. Its non-invasive nature allows it to be repeated within each subject which is useful for follow-up investigations. It can now be applied further to a range of disease, pharmacological and nutritional investigations.