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Studies on the Control of Exocrine Pancreatic Secretion in the Dog

A thesis presented in partial
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the degree of Doctor of Philosophy
at Massey University

Maureen Elizabeth Gaul Wichtel

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ABSTRACT

Conventional wisdom has held that, despite the close apposition of the proximal duodenum with the pancreas, the gut communicates with the pancreas only via "long" pathways involving the systemic arterial circulation, the central nervous system or a combination of both. This thesis examines the possibility of *local* avenues of communication, venous or neural, which take advantage of the developmental proximity of the pancreas to the gut and the veins of the hepatic portal system.

After carefully studying the anatomy, a venous latex casting technique was employed to more closely examine the venous drainage patterns of the canine pancreas in its area of close apposition with the duodenum. No clear evidence was found for a local vascular pathway of communication between the two organs, however tributaries of duodenal origin were sometimes observed to coalesce first with veins draining the pancreas prior to entering the cranial pancreaticoduodenal vein. An interesting observation concerned the presence of valves throughout the hepatic portal system, generally identified adjacent to primary, secondary and tertiary branch points relative to the main portal trunk. In all cases, the valve imprints directed blood towards the portal vein.

The results obtained from *histological* examination of the duodeno-pancreatic area were consistent with the results obtained from the latex casting study. Veins leaving the duodenum coursed between rather than through pancreatic lobules, and converged with progressively larger rather than smaller tributaries within interlobular septa. An unexpected observation was the presence of distinct inward-projecting folds in the walls of the veins of the portal vasculature that in some cases bore histological resemblance to sensory organelles. While these structures did not exhibit immunoreactivity to sensory neuropeptides, positive immunoreactivity was identified at the level of the endothelium in some of these veins. It was hypothesized that sensory structures in the portal vasculature might be involved in reflex regulation of the pancreas.

In order to test the hypothesis that components of a sensory mechanism exist within the hepatic portal system of the dog, and that such a sensory mechanism plays a role in the

control of exocrine pancreatic function, the latency of the pancreatic fluid secretory response to a bolus of secretin injected into the aorta was compared to that of secretin injected into selected veins of the portal system and systemic circulations in anaesthetized dogs. Overall, the results of two experiments suggested that the differences in latency between sites generally reflected expected differences due to circulation time. Additionally, the portal vein threshold dose was determined. The threshold dose was the smallest dose of secretin which elicited a detectable pancreatic response following injection into the portal vein site. When administered at each of the remaining non-portal vein sites, the threshold dose elicited a response in 7 of 16 cases. Collectively, the results of these studies provided no clear support for a sensory role for the portal vein or liver in the pancreatic response to secretin. The possibility that other local forms of communication exist that exert control over the exocrine pancreas await further investigation.

Dedicated to my grandmother, Ida Mills, who died of pancreatic carcinoma at Orillia Hospital in Ontario, Canada, August 17, 1977

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LIST OF ABBREVIATIONS

A	aorta
AUC	area under the curve
BSA	bovine serum albumin
CaVC	caudal vena cava
CCK	cholecystokinin
CGRP	calcitonin gene-related peptide
CNS	central nervous system
CMV	cranial mesenteric vein
EMG	electromyography
HR	heart rate
ID	internal diameter
IU	international units
GLM	general linear model
GLP-1	glucagon-like peptide-1
GRP	gastrin-releasing peptide
HCl	hydrochloric acid
HCO_3^-	bicarbonate
MABP	mean arterial blood pressure
MMC	migrating motor complex
MV	mesenteric vein
NaCl	sodium chloride
NKA	neurokinin A
OD	outer diameter
pH	potency of hydration
PDV	cranial pancreaticoduodenal vein
PP	pancreatic polypeptide
PV	portal vein
PYY	peptide YY
RR	respiratory rate
SAS	Statistical Analysis System
SD	standard deviation
SDMV	superficial dorsal metatarsal vein
Sub P	substance P
T	body temperature
TRH	thyrotropin-releasing hormone
VIP	vasoactive intestinal peptide