The Effect of Alcohol on Pancreatic Blood Flow.

An Experimental Study.

Glen Benveniste MB BS, FRACS

ACKNOWLEDGEMENTS:

I am most grateful to the late Professor Ronald Elmslie for his offer to spend a research year (1984) in the Department of Surgery at the Queen Elizabeth Hospital and for his stimulation and encouragement throughout that year.

My thanks also go to my supervisor, Mr. Tony Slavotinek for his untiring support during not only my research year but throughout the period of preparation of this thesis.

I wish to thank Miss Elaine Deakin, the late Mrs. Sue Nance and Mr. Ken Porter for their expert technical assistance, the late Mrs. Esther Mazel for her secretarial support, Mr. Basil Popwicz for his photographic expertise and Mr. Peter Tyler for advice regarding statistical analysis of the results.

Finally my thanks to Professor Guy Maddern for his help in enabling the thesis to be presented following the long delay since the original work was carried out.

DECLARATION:

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, 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. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

Glen L. Benveniste.

ABSTRACT:

The reference sample method using 15 micron diameter radionuclide labelled carbon microspheres was used to establish a rat model of pancreatic blood flow which was then used to follow up previously reported studies in dogs which showed that intravenously administered alcohol lead to a fall in pancreatic blood flow. In addition, the oral administration of alcohol alone and in combination with glucose was studied.

The literature regarding pancreatic blood flow was reviewed with special emphasis on techniques of measurement and the effect of intravenously administered alcohol.

While the rat model proved highly successful, it was not possible to use a dual injection technique as had been previously carried out in the larger experimental animal. This meant that instead of carrying out a control measurement on each animal it was necessary to have separate control and experiment groups.

The major findings of the study were of difference in pancreatic blood flow between fasted (105 \pm 9, mean \pm s.e.) and non-fasted animals (134 \pm 11) which was significant at the 0.025 level using the unpaired t test (t=2.14, df 18, p<0.025). No significant changes in pancreatic blood flow were observed with alcohol administered via intravenous or via gastric infusion compared to control groups.

The major finding of the study was that a combination of alcohol and glucose administered via gastric infusion was found to produce a rise in pancreatic blood flow (161 \pm 19) which was greater than that seen with either intravenous alcohol alone

(111 \pm 9) or glucose alone (90 \pm 6). This change was highly significant (t=2.70, df 10, p<0.0125).

It is concluded that the rat is a suitable experimental model for studying pancreatic blood flow with the microsphere method, that fasting significantly lowers pancreatic blood flow, and that the combination of alcohol and glucose is a potent stimulator of pancreatic blood flow.

Table of contents

PART 1. BACKGROUND AND LITERATURE REVIEW	
CHAPTER 1. INTRODUCTION, OBJECTIVES, HYPOTHESES	
1.1 Introduction	
a. Pancreatic blood flow	9
b. Alcohol and pancreatitis.	10
1.2 Objectives.	12
1.3 Hypotheses	13
CHAPTER 2. THE PANCREAS	
2.1 Morphology	14
2.2 Hormonal control	15
2.3 Blood supply	15
a. Arterial supply	16
b. Venous drainage	16
c. Microcirculation	17
2.4 Pancreatic blood flow.	18
a. Introduction.	18
b. Historical overview.	18
2.5 Pancreatitis.	34
a. Introduction.	34
b. Pathogenesis of pancreatitis	
CHAPTED 2 DI COD EL OW ME ACHDEMENT TECHNIQUES	
CHAPTER 3. BLOOD FLOW MEASUREMENT TECHNIQUES	40
3.1 Introduction	
3.2 Indicated transport methods.	
1	
b. Indicators used to measure blood flow	
3.3 Venous outflow	
3.4 Electronic flow meters	49

PART 2. METHODS: MICROSPHERE MEASUREMENT OF BLOOD

CHAPTER 4. THE EQUIPMENT	
4.1 Introduction.	55
4.2 The microspheres	55
4.3 Arterial and venous cannulae	56
4.4 Monitoring equipment	57
4.5 Injection / withdrawal pump	58
4.6 Scintillation counting tubes	58
4.7 Gamma counter	58
4.8 Microcomputer.	59
CHAPTER 5. PRELIMINARY STEPS	
5.1 Experimental animals	60
5.2 Quality control of microspheres.	60
5.3 Microsphere standard	60
5.4 Calibration of gamma counter.	61
5.5 Laboratory	61
5.6 Radiation safety	61
CHAPTER 6. DETAILS OF EXPERIMENT METHOD	
6.1 Preparation of the animals.	63
6.2 Preparation and injection of the microspheres	67
6.3 Preparation of samples for counting	69
6.4 Calculation of blood flow	70
6.5 Disposal of radioactive tissue	71

PART 3. RESULTS

CHAPTER 7. VALIDATION EXPERIMENTS	
7.1 Microspheres	81
7.2 Effect on cardiovascular function.	91
7.3 Double injection series.	96
7.4 Blood alcohol / glucose levels	98
CHAPTER 8. PANCREATIC BLOOD FLOW	
8.1 Controls	101
8.2 Intravenous alcohol	105
8.3 Intragastric alcohol	110
CHAPTER 9. GASTROINTESTINAL BLOOD FLOW	117
PART 4. DISCUSSION AND CONCLUSIONS	
Discussion	125
Conclusions	
Bibliography	151
Appendices	173