

Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

ETHANOL METABOLISM IN HUMANS

A thesis presented in partial  
fulfilment of the requirements  
for the degree of

Doctor of Philosophy

at

Massey University  
New Zealand

Kenneth George Couchman  
1979

ABSTRACT

This thesis outlines the development of breath alcohol measurement and investigations of the rate of absorption, equilibration and elimination of alcohol from the body using breath analysis. After a historical outline, the methods of alcohol detection are reviewed and a comparative study of some modern breath alcohol testing instruments detailed. The results show that the gas chromatograph Intoximeter was the most reproducible and accurate instrument. Of the fuel cell instruments, the Alcolimiter gave reproducible readings but with a higher frequency of mechanical breakdowns and the Alcometers failed to hold a calibrated value on repeated testing. The chemical analysis of the Borkenstein Breathalyzer offered portability and freedom from calibration but with a lowering of accuracy.

No instrument offered the degree of flexibility required for laboratory investigation of factors affecting breath alcohol concentrations. Consequently a gas chromatograph was modified for breath sampling at 30 second intervals. The partition coefficients for alcohol between air and blood were found to be related to the water content of the blood sample. Breath alcohol concentrations increased with expiration volume and were related to a rise in breath temperature. After correcting to a standard temperature of  $34^{\circ}$ , a linear increase in alcohol concentration remained which was greater with higher blood alcohol levels.

Equations for estimating the distribution volume of alcohol in the body were derived and the Widmark factor 'r' was found to be related to the ratio, body water over blood water. The blood alcohol time curves resulting from a fixed dose of alcohol given to semi-fasted subjects were analysed to determine the apparent distribution volumes in the body. Volumes exceeding physiological limits were found in some subjects and ascribed to either a faster rate of metabolism during the absorptive phase or to anomalies in equilibration. A markedly non-linear alcohol elimination curve was seen in one alcoholic. Faster rates of alcohol oxidation were discussed in relation to the Michaelis-Menten kinetics of enzymatic catabolism and it is suggested that some subjects

have a second enzyme for alcohol metabolism which operates at a higher  $K_m$  than normal.

The fluctuations of blood alcohol level during the absorptive phase were examined by measuring the abundance of a tracer dose of deuterated alcohol given orally after a loading dose of unlabelled alcohol. The fluctuations were ascribed to contractions of the pyloric sphincter releasing alcohol into the duodenum in an irregular fashion.

The studies were extended to subjects drinking in a private bar. The rate of alcohol absorption appeared to keep pace with the rate of drinking which was spread over at least a three hour period. The rates of alcohol elimination from the blood were faster than in a previous study with a lower dose of alcohol. This is explained by lower blood alcohol levels from a smaller dose and is consistent with the enzyme kinetics of alcohol catabolism. An equation was derived to enable the estimation of blood alcohol levels from amount consumed which compared favourably with traditional methods for this calculation.

The accuracy, rapidity and ease with which breath alcohol analyses could be made to determine alcohol concentrations in the body enabled its use with large groups of people consuming alcohol at party situations or in hotel bars and two examples of such studies are presented in the appendix.

## ACKNOWLEDGEMENTS

I am indebted to my supervisors, Professor R. D. Batt and Dr R. M. Greenway for their continuing interest in the study and help with the preparation of the manuscript for the thesis. I also wish to acknowledge the assistance of T. J. Braggins and Dr A. R. Stowell with the social drinking studies and Miss C. Veltman with measurements of breath volume effects on breath alcohol concentrations. My thanks are due to the Commanding Officer of the Ohakea Air Base for permission to conduct the social drinking studies, to the Medical Officer, Dr D. Stewart and the Officers and men of the Royal New Zealand Air Force at Ohakea and to students and staff of Massey University who willingly volunteered as subjects for study. My appreciation is also acknowledged to Mrs Katherine Newland for a considerable amount of skilful technical assistance. The thesis was typed by Miss Wendy Fairclough and I am indebted to her for her patience and care at all stages in preparing the final manuscript.

## TERMINOLOGY

Throughout the text, "alcohol" is used as synonymous with ethanol. All blood alcohol concentrations have been expressed in milligrams per 100 millilitres. This terminology is still commonly used by workers in the fields of medicine, alcohol abuse, psychiatry and alcohol and traffic safety to whom the present study could be of interest.

With the adoption and increasing use of SI units in recent years by the scientific community, blood alcohol levels expressed in millimoles per litre are becoming increasingly common. The equivalent value for 10 millimoles per litre (mmol/l) is 46 mg/100 ml. The results of breath alcohol analyses have, in the main, been expressed as blood alcohol concentrations based on the blood : breath distribution ratio of 1 : 2,100 as explained in the text. Recent legislation in New Zealand has made it an offence to drive a motor vehicle with a breath alcohol level greater than 500 µg per litre, and eventually it is expected that breath rather than blood alcohol concentrations will be widely used.

## LIST OF CONTENTS

	<u>Page</u>
Abstract	ii
Acknowledgements	iv
Terminology	v
List of Contents	vi
List of Figures	x
List of Tables	xii
 Chapter 1	
<u>INTRODUCTION</u>	1
 Chapter 2	
<u>BREATH ALCOHOL TESTING INSTRUMENTS</u>	8
2.1	MEASUREMENT OF ALCOHOL IN BREATH 8
2.2	TESTING PROCEDURES 10
2.2.1	Breath volume 10
2.2.2	Tests with a breath alcohol simulator 10
2.2.3	Maintained reliability 14
2.2.4	Linearity of response 14
2.2.5	Breath tests on subjects 14
2.3	RESULTS 15
2.3.1	Alcolimiter 15
2.3.2	Alcolimeters and Alco-Sensor 16
2.3.3	Intoximeter Mk IV 20
2.3.4	Breathalyzer 21
2.3.5	Results on subjects 24
2.4	DISCUSSION AND CONCLUSIONS 27
 Chapter 3	
<u>BREATH ALCOHOL ANALYSIS</u>	31

3.0	INTRODUCTION	31
3.1	METHODS	31
3.1.1	Alcohol measurement by gas chromatography	31
3.1.2	Alcohol measurement <u>in vitro</u>	33
3.1.3	Partition coefficients	35
3.1.4	Respiration measurements	42
3.1.5	Breath alcohol levels in drinking subjects	42
3.2	RESULTS	46
3.2.1	Breath temperature	46
3.2.2	Breath alcohol levels	46
3.3	DISCUSSION	62
Chapter 4	<u>STUDIES ON THE ABSORPTION, DISTRIBUTION AND ELIMINATION OF ALCOHOL IN THE BODY WITH VOLUNTEERS STUDIED UNDER LABORATORY CONDITIONS</u>	70
4.1.1	INTRODUCTION	70
4.1.2	Body water compartmentation	70
4.1.3	Measurement of the water compartment sizes using alcohol	71
4.1.4	Derivation of the Widmark equation	73
4.1.5	The kinetics of alcohol metabolism	76
4.1.6	Experimental investigations	78
4.2	METHODS	78
4.2.1	Studies on normal volunteers	78
4.2.2	Studies on alcoholics undergoing detoxication	78
4.3	RESULTS	80
4.3.1	Normal volunteers	80
4.3.2	Alcoholics	80



4.4	DISCUSSION	95
Chapter 5	<u>STUDIES ON THE ABSORPTION OF ALCOHOL THROUGH THE GUT WITH TRACER DOSES OF DEUTERATED ALCOHOL</u>	106
5.1	INTRODUCTION	106
5.2	METHODS	106
5.3	RESULTS	108
5.4	DISCUSSION	108
Chapter 6	<u>ABSORPTION, DISTRIBUTION AND ELIMINATION OF ALCOHOL UNDER NORMAL SOCIAL DRINKING CONDITIONS</u>	115
6.1	INTRODUCTION	115
6.2	METHODS	115
6.3	RESULTS	116
6.3.1	The "mouth alcohol" effect	116
6.3.2	Rate of drinking	116
6.3.3	Rate of alcohol absorption	116
6.3.4	Rate of alcohol elimination	121
6.3.5	Widmark ratios	121
6.4	DISCUSSION	127
Chapter 7	<u>ESTIMATIONS OF BLOOD ALCOHOL LEVELS AFTER DRINKING</u>	130
7.1	INTRODUCTION	130
7.2	CALCULATIONS	130
7.3	RESULTS	131
7.4	DISCUSSION	135

Chapter 8	<u>GENERAL DISCUSSION</u>	137
-----------	---------------------------	-----

REFERENCES		141
------------	--	-----

APPENDIX 1.	Joint Project, Department of Biochemistry and Department of Sociology, Massey University. "Blood Alcohol Levels in Young Adults After Free Drinking". Prepared for a Rotary Youth Leadership Course.	
-------------	--	--

APPENDIX 2.	Breath Testing for Alcohol with Hotel Patrons. A report prepared for the Liquor Advisory Council.	
-------------	---	--

## LIST OF FIGURES

		<u>Page</u>
2.1	A range of fuel cell instruments	12
2.2	The gas chromatograph Intoximeter Mk IV with mixed hydrogen/nitrogen gas supply and breath simulator.	
2.3	The Breathalyzer 900A and 1000 with a mark IIA breath alcohol simulator.	13
2.4	Correlations between breath test results obtained from a digital Alcolmeter and a gas chromatograph.	26
3.1	A plan view of the modified Carle gas chromatograph to show the interior.	32
3.2	Alcohol and acetone peaks obtained with the Carle gas chromatograph.	34
3.3	A plot of the logarithmic transformation of partition coefficients for alcohol between air and water at various temperatures.	37
3.4	A plot of the water content of blood against haematocrit.	40
3.5	A plot of the partition coefficients for alcohol between air and blood at 34° against the water content of the blood.	43
3.6	The modified gas chromatograph with a spirometer, mercury manometer and chart recorder.	45
3.7	Frequency diagram of breath temperatures at various expiration volumes.	48
3.8	The change of alcohol concentration with breath temperature.	51
3.9 a-f	Breath alcohol curves from all subjects showing the effect of temperature correction.	52
3.10	The regression of mean temperature corrected breath alcohol concentration against expiration volume for each subject.	60
3.11	A plot of the regression coefficients of breath alcohol concentration on expiration volume against the mean breath alcohol concentration from each subject.	61

		<u>Page</u>
4.1	The expected blood alcohol curve resulting from a rapid intravenous injection of alcohol.	72
4.2	Blood alcohol curves generated from the results in table 4.2 illustrating the effect of Michaelis-Menten kinetics.	79
4.3	Blood alcohol curves from 20 volunteers given an alcohol dose of 1.0 g/kg.	81
4.4a	Rapid fluctuations in blood alcohol concentration during the absorptive phase in subject 5.	90
4.4b	Rapid fluctuations in blood alcohol concentration during the absorptive phase in subject 8.	91
4.5	A blood alcohol curve in the elimination phase showing the absence of rapid fluctuations.	92
4.6	A blood alcohol curve from an alcoholic showing marked non-linearity.	96
4.7	A blood alcohol curve from an alcoholic which suggests non-linear elimination.	97
4.8	Unexplained fluctuations in the blood alcohol curve from an alcoholic.	98
4.9	Unexplained fluctuations in the blood alcohol curve from an alcoholic.	99
5.1-5.4	Blood alcohol and isotope abundance curves from subjects who had consumed alcohol followed by a tracer dose of deuterated alcohol.	109-112
6.1	A representative sample of the rates of alcohol consumption before and after a meal.	117
6.2 a & b	The rate of increase in blood alcohol level before a meal.	118-119
6.3	The rate of increase in blood alcohol level after a meal.	120
6.4	The rate of decrease in blood alcohol levels.	122
6.5	A frequency diagram of calculated Widmark ratios.	125
7.1	Observed blood alcohol levels 3 hours after drinking began against alcohol consumption.	134

## LIST OF TABLES

	<u>Page</u>
2.1 Breath alcohol testing instruments	11
2.2 Results of ten consecutive tests with a simulated breath alcohol standard corresponding to 100 mg/100 ml of blood.	17
2.3 Deviations in mg/100 ml from a standard simulator test of 100 mg/100 ml at various intervals during a one month period.	18
2.4 Linearity of instruments. Results of standard alcohol vapours from the simulator.	18
2.5 Absorbance at 440 nm of dichromate solutions prepared in the Breathalyzer 900A from breath alcohol standards and read in a Hitachi spectrophotometer.	23
2.6 Absorbance at 440 nm of dichromate solutions prepared by pipetting 50 µl alcohol solution into 3.0 ml ampoule solution and read in a Hitachi spectrophotometer.	23
2.7 Comparative tests on consecutive breath samples.	25
2.8 Results of simultaneous breath samples taken with a gas chromatograph and a digital Alcolmeter.	28
3.1 The alcohol concentration of simulator solutions and the resulting peak heights from the gas chromatographic analysis of the vapour phase.	36
3.2 The range of alcohol concentrations in the vapour phase from simulator solutions.	36
3.3 Alcohol peak heights obtained from gas chromatographic analysis of the vapour phases from alcohol concentrations in the simulator of 1.216 g/litre of water, plasma or blood at three different haematocrits.	39
3.4 Partition coefficients for alcohol between air and water, plasma and blood at three haematocrit values.	41
3.5 The calculated values of water content, alcohol partition coefficients and distribution ratios for blood with a normal range of haematocrit.	44
3.6 Breath temperatures at the end of various expiration volumes.	47
3.7 Alcohol concentrations in the breath at the end of various expiration volumes.	49

	<u>Page</u>
3.8 Breath alcohol concentrations after correcting for temperature differences from 34°.	50
3.9 Mean breath alcohol concentrations at each expiration volume.	59
3.10 Distribution ratios at various expiration volumes.	63
3.11 The re-equilibration of alcohol between aqueous and vapour phases in a simulated upper respiratory tract.	64
4.1 Widmark ratios (r) calculated from known body water and blood water values.	75
4.2 The velocities of alcohol elimination for two values of Km and various substrate (blood alcohol) concentrations.	77
4.3 Alcohol distribution concentrations and estimated absorption times for subjects given alcohol at 1.0 g/kg body weight.	89
4.4 Alcohol elimination rates in subjects given alcohol at 1.0 g/kg body weight.	93
4.5 Correlation coefficients for regressions of blood alcohol level on time before and after logarithmic transformation.	94
6.1 Alcohol distribution concentrations and elimination rates for beer drinkers.	123
6.2 Alcohol distribution concentrations and elimination rates for spirit drinkers.	124
6.3 A comparison of beta slopes and Widmark ratios obtained by analysing selective portions of the blood alcohol curve.	126
7.1 Calculated and observed blood alcohol levels in subjects after the consumption of 0.4 or 1.0 g alcohol/kg body weight.	133