AUSTRALIAN NATIONAL ANTARCTIC RESEARCH EXPEDITIONS

ANARE RESEARCH NOTES 84

Cardiovascular Research in Antarctica

G.D. Deakin

ANTARCTIC DIVISION
DEPARTMENT OF THE ARTS, SPORT,
THE ENVIRONMENT AND TERRITORIES

ANARE RESEARCH NOTES (ISSN 0729-6533)

This series allows rapid publication in a wide range of disciplines. Copies of this and other *ANARE Research Notes* are available from the Antarctic Division. Any person who has participated in Australian National Antarctic Research Expeditions is invited to publish through this series. Before submitting manuscripts authors should obtain a style guide from:

The Publications Office
Antarctic Division
Channel Highway
Kingston
Tasmania 7050
Australia

Published March 1992
ISBN: 0 642 17102 5

CONTENTS

Figures

Tables

CARDIOVASCULAR RESEARCH IN ANTARCTICA*

by

Gillian D. Deakin
Clinical Research Unit
Baker Medical Research Institute
Melbourne, Australia

ABSTRACT

This *ANARE Research Note* examines the modification of major mutable cardiovascular risk factors in members of the Australian National Antarctic Research Expedition (ANARE), in isolation for a year at Davis, Antarctica.

The use of an ambulatory blood pressure monitor allowed for a detailed analysis of changes in blood pressure (BP) and heart rate during normal daily activities and during sleep, without the problems of observer error or the potentially stressful situation of clinic measurements.

A major part study examined the effects on BP and heart rate of varying levels of activity. The same ten subjects were studied over a year for three different seasons. Weights were kept constant throughout the study. During the active summer period, further increases in activity had no effect on BP. There was a decrease in heart rate, which correlated with the increase in fitness observed.

During the quieter and less active winter months, a significant rise in BP was noted following a period of minimal activity. This was returned to normal (summer) values following a period of increased activity.

Although the level of fitness increased with increased activity during both seasons, there was little correlation between changes in fitness and BP levels. That is, while fitness increased over the summer season, there was no change in systolic BP. However, following the winter period of minimal activity, the BP was greater than at any stage in the summer, although the fitness level was significantly greater than the summer.

The third part of the exercise study was done in the spring when there was a high level of stress and disruption on the station due to a demanding field program. Although maximal levels of fitness were noted, BP and heart rate were elevated and not affected by increased activity during the program. It was concluded that moderate exercise three to seven times weekly provides optimal benefits for BP, and further increases in activity levels may only reduce heart rate and increase fitness, with no evidence of further reductions in coronary heart disease (CHD) risk factors. In addition, any changes in BP due to exercise may be counteracted by the presence of psychological stress. In the absence of true exposure, there was no evidence that the cold climate can have any significant effect on the cardiovascular status.

Total and high-density lipoprotein (HDL) cholesterol, triglyceride and glucose tolerance were studied concurrently. No significant changes were seen in triglyceride levels; increased activity during the summer program led to raised concentrations of HDL cholesterol; increased activity did

*This note is based on a thesis submitted to Monash University for the degree of Doctor of Medicine. The Doctorate was awarded in 1991.

not alter total cholesterol levels although, from summer to winter, there was an increase in total cholesterol levels; as the varying levels of activity had no effect, the changes were attributed to an increase in dietary fat intake in the winter. All results were within normal limits and it was concluded that no stage of this study allowed the subjects to be sufficiently sedentary to demonstrate the effects of small increases in activity. That is, only a truly sedentary population would benefit from an increase in exercise in regard to their lipid profile and glucose tolerance.

A study was made of the acute and chronic effects of alcohol consumption on the diurnal pattern of BP and heart rate, in comparison to a control period. A triphasic response to alcohol was noted in systolic and diastolic BPs, while heart rates were increased throughout acute intoxication and withdrawal. However, by thirty-six hours following the cessation of alcohol consumption in regular drinkers, all circulatory variables had returned to normal, except diastolic pressure, which remained elevated during exercise. It was concluded that the major acute effect of alcohol was a fall in BP, with a compensatory tachycardia. Alcohol withdrawal was accompanied by a brief but significant pressor response. Recent alcohol consumption should be considered when assessing the hypertensive patient. Patients with limited cardiac reserves should be warned of the hazards of alcohol intoxication.

Ten healthy subjects participated in a study of the effects of regular alcohol consumption on glucose tolerance and lipid profile. The addition of dietary fish oil, containing omega-3 eicosapentaenoic acid, was also studied. The study confirmed the finding that alcohol caused an elevation of triglyceride in plasma, however, this adverse effect was successfully reversed by the addition of fish oil to the diet.

The increase in total plasma cholesterol following alcohol consumption was partly due to a rise in HDL cholesterol. There was zero effect of fish oil on total cholesterol, due to a concomitant increase in HDL- and decrease in low-density lipoprotein (LDL)- cholesterol. Therefore, the dietary supplementation of fish oil seems to have a net beneficial effect on plasma lipid levels.

However, this must be weighed against the finding that the addition of fish oil to the diet caused a significant elevation of plasma glucose, accompanied by increased plasma insulin levels.

PREFACE

Medical research in the Antarctic offers many advantages and a few disadvantages. The long isolation with a small community allows for great stability in the environment, both socially and individually. In general, all expeditioners experience the same daily lifestyle, with prepared meals and shared work and social activities. Routine is established and, particularly in winter, external influences are minimal. These are ideal conditions for clinical studies.

It is important not to overstate the significance of the climate on human physiology in the polar regions. While cold stress can be demonstrated on Antarctic field trips (Lugg 1973), there is little evidence that the prevailing temperatures have any consistent effects on humans within the station environment. It is my belief that clinical studies performed indoors have direct relevance to populations living in more temperate regions. Indeed, the temperatures experienced in the Antarctic are not dissimilar to those during winter in Northern Europe and America. However, there are many other factors, such as increased fitness levels, absence of urban stress and isolation itself, which require further investigation before their significance is fully understood.

Volunteers are recruited from among expeditioners selected to winter at the station. Research programs must be tailored to suit those expected to participate. This places some constraint on experimental design, which also must be able to cope with unforeseen events, such as emergency rescues or disrupted shipping schedules that are commonplace in the Antarctic. A good understanding of the seasonal changes in station activities and its effects on personnel is of great benefit. The author was able to take advantage of the predictable difference in the level of activity between summer and winter to design an exercise study using the same individuals over a period of a year.

Medical research done on Australian Antarctic stations is carried out by the medical officer (MO), whose prime responsibility is the provision of health care to the expeditioners. Research must not interfere with other duties, such as the maintenance of the single bed hospital, stock-taking of equipment and pharmacopoeia, provision of medical kits for field huts and expeditions, participation in search-and-rescue exercises or other events as well as the day-to-day provision of medical and dental care. Since both these duties and any proposed research are the sole responsibility of the MO, it is sometimes difficult to achieve research goals.

One of the disadvantages of Antarctic clinical studies is the difficulty in communication with colleagues and supervisors that is so vital to research work.

The work presented here is the result of three year's work. Much of 1985 was spent in preparation at the Australian Antarctic Division, Kingston, Tasmania, after the initial protocol was established at the Clinical Research Unit of the Baker Medical Research Institute, Melbourne, where the thesis was completed in 1987. The research program was carried out on the Antarctic Continent, where the author was a member of the Australian National Antarctic Research Expedition (ANARE), under the auspices of the Antarctic Division now part of the Department of the Arts, Sport, the Environment and Territories.

Most biochemical assays were performed by the author while in the Antarctic, with the final program's analysis carried out at the Baker Institute. Insulin levels were measured by Kerin O'Dea at Melbourne University. (refer Chapter 2).

This *ANARE Research Note* is divided into five chapters. After the Introduction and a chapter of methods used in the collection of data, the third chapter is dedicated to the main study, which

examined the effects of varying levels of exercise on coronary heart disease (CHD) risk factors. The experiment was repeated twice during the year to determine the effects of various environments.

Chapter 4 examines the role of alcohol in the development of CHD risk factors and, specifically, compares the effects of acute versus chronic alcohol use on BP and heart rate, both at rest and during normal daily activity. Chapter 5 also looks at alcohol, and examines its effects on the blood lipids and glucose tolerance. Marine fish oil is administered to the same subjects to study what effects eicosapentaenoic acid can have in the presence of alcohol use.

NOMENCLATURE

Exercise study

The exercise study is divided into three similar blocks, to be referred to as 'programs': 'summer', 'winter' and 'spring'. Each of these programs lasted approximately ten weeks and each were divided into three separate 'periods': 'minimum', 'medium' and 'maximum'. These names refer to the prescribed amount of activity the subject was to achieve on a weekly basis over the three week period.

At the end of each period, each subject wore a blood pressure (BP) monitor for a 24 hour period, during which he performed his normal activities. A record was kept of what activity immediately preceded the BP recording. These data were used to divide the 42 or so BP readings taken over the day into, ultimately, four different 'levels of activity': 'sleep', 'sit', 'stand' and 'work'. The number and ratio of each level of activity varied between subject, period and program, so it was necessary to calculate the 'mean values' of systolic, diastolic pressure and heart rate.

Alcohol study

The terms 'alcohol' and 'ethanol' are used interchangeably.

In general, Standard International (SI) units were used. The conversion of lipid values is as follows:

Cholesterol mg/dl = mmol/litre x 38.6

TG mg/dl = mmol/litre x 88.5

1. INTRODUCTION

A major role in the pathogenesis of many diseases of modern society is lifestyle; there is a growing awareness of this fact today. Data from the National Cooperative Pooling Project (NCPP) in the USA suggest the 70% of coronary heart disease (CHD) is attributable to three of the primary risk factors: cigarette smoking, hypertension and hypercholesterolaemia and each are equally important. For cerebrovascular disease the risk factors are the same, but hypertension is the most significant factor. The effects of less prominent risk factors, such as obesity, hypertriglyceridaemia and glucose intolerance, may be confounded by their frequent coexistence with major factors.

While all these risk factors remain prevalent in most industrialised communities, there is encouraging evidence both that they can be modified and that such intervention is associated with a reduction in risk. It is generally accepted that modification of risk factors needs to occur on a broad scale if real progress is to be seen in disease prevention and control.

There is no serious controversy over whether these risk factors affect the incidence of CHD. However, difficulties arise in determining the mechanism of the action, methods of their modification and the benefits that such modification can bestow on the individual.

According to the National Heart Foundation of Australia Risk Factor Prevalence Study (1983), 19% of men and 14% of women had BP >160/95. Unless otherwise stated, the figures quoted hereafter are taken from the latter survey and relate to urban Australians aged 25-64 years in 1983. With hypertension defined as a diastolic pressure above 90 mm Hg, there was a prevalence of 25% in the US adult population (Kaplan 1983). The use of the 90 mm Hg level to define hypertension has come largely from long-term epidemiological studies that have related initial BP levels to the development of coronary disease, strokes, and other cardiovascular complications (The Pooling Project Research Group 1978). The 20 year actuarial experience of almost 4.5 million persons examined for life insurance showed a significant increase in mortality for those with readings in the 138-147 mm Hg range for systolic and in the 88-92 mm Hg range for diastolic BP (Society of Actuaries and Association of Life Insurance Medical Directors of America 1979).

However, data from the Framingham study (Kannel and Sorlie 1975) showed that the risk from any given level of BP was unevenly distributed and closely tied to the degree of concomitant risk factors. The difference in risk was compared for two groups of 40 year old men. For example, in those with very high systolic pressure (195 mm Hg) but otherwise low risk factors (serum cholesterol 4.7 mmol/l; nonsmoker; normal glucose tolerance; no left ventricular hypertrophy shown by electrocardiogram), the chance of a major cardiovascular event in the next 8 years was 4.6%. For the group with the same systolic pressure of 195 mm Hg, but with other risk factors present (serum cholesterol 8.4 mmol/l; smoker; abnormal glucose tolerance; and left ventricular hypertrophy shown by electrocardiogram) the chance of a major cardiovascular event was 70.8%.

The Australian National Blood Pressure Study (1980) showed that definite benefits followed the treatment of even mild hypertension (95-109 mm Hg). Effective therapy caused a decrease in the incidence of cardiovascular events by 5 per 1000 person-years' exposure to risk. The benefits of treatment became progressively greater with higher initial diastolic pressures, within the range of 95-109 mm Hg.

The prevalence of glucose intolerance was rated at 2% for the Australian adult community. Abnormal glucose tolerance is usually referred to as a secondary risk factor, although its role in the

pathogenesis of cardiovascular disease is uncertain. Some have postulated that insulin itself is atherogenic and the raised levels found in insulin resistant patients accelerates plaque formation (Stout 1981). The Whitehall study showed that subjects with even marginal levels of glucose intolerance (at the 95th percentile of blood sugar distribution), have double the population's mortality rate for CHD (Fuller et al. 1980).

Thirty-two per cent of men and 25% of women studied in 1983 were current cigarette smokers. In a prospective study of 7735 men, it was found that smokers and ex-smokers had more than twice the risk of a major CHD event than men who had never smoked. In both smokers and ex-smokers, the number of years a man had smoked cigarettes was the clearest indicator of CHD risk due to cigarettes. It was concluded that the major benefit of giving up smoking may lie in halting the accumulation of 'smoking years' (Cook et al. 1986).

Hypercholesterolaemia (plasma cholesterol > 6.5 mmol/l) was present in 20% of the Australian population. Framingham studies have shown a linear increase in coronary risk with increments in total plasma cholesterol from 4.7 mmol/l upwards (Connor and Connor 1972). LDL cholesterol, which approximates 75% of total cholesterol, has a major role in the transport of cholesterol from plasma to peripheral cells. Evidence suggests that LDL cholesterol causes direct damage to arterial endothelium and causes proliferation of smooth muscle cells and accumulation of lipid, which may ultimately lead to the formation of atheromatous plaques (Scow et al. 1980).

In the studies carried out to date, the ratio of total cholesterol to HDL cholesterol appeared to be the best predictor of atherosclerosis progression (Miller et al. 1981). Brensike et al. (1984) found that each HDL cholesterol increment of 10 mg/l was associated with a 50% reduction in CHD risk. HDL cholesterol is believed to participate in cholesterol removal from cells by initiating the process of reverse cholesterol transport (Gotto 1984). It appears to be the reciprocal of cholesterol delivery to the cell by the LDL particle. Another important function is its role in initiating the catabolism of very low density lipoproteins (VLDL) (Nikkilä 1978). These alleged functions of HDL are consistent with clinical findings of an inverse relationship between HDL cholesterol and CHD (Gordon et al. 1980). However, there is no evidence that this represents a causal relationship.

The current concept of the pathogenesis of atherosclerosis has been termed the modified response to injury hypothesis (Ross 1986). The process may be viewed as proliferative rather than degenerative and is believed to begin in early life. Stary (1983) has reported accumulation of monocytes and lipid-filled macrophages in coronary arteries before the age of ten. This accumulation increases during adolescence. Therefore, early intervention in pre-symptomatic youth would appear rational.

The population in the present study had a mean age of 31 years and were in good health (Chapter 2 details the medical examination prior to selection). One aim of the present study was to demonstrate the presence of coronary risk factors, that could be modified in an apparently healthy population. Such intervention may retard or reverse the possibly already present atherosclerotic process. It is theoretically more likely to effect regression of the atheromatous process while the disease is in its early stages, rather than when ulceration and plaque formation are already established.

Although there has been good documentation of the reversibility of atherosclerosis in animal studies for some time (Wissler and Vesselinovitch 1975), there has been difficulty documenting the regression of atherosclerosis in humans with reduction of plasma cholesterol. Several intervention studies have been successful in showing the deceleration of atheromatous disease: the NIH Type II hyperlipidaemia study (Brensike et al.1984) used diet and cholestyramine to halt progression of

coronary disease; and Duffield et al. (1983) have documented regression of atherosclerosis in femoral arteries. However, there is criticism of these studies in that angiographic techniques are relatively crude and further studies are being conducted using sophisticated computerised methods.

Nevertheless, there is good evidence from the Lipid Research Clinic (1984) which showed that a 1% fall in plasma cholesterol was associated with a 2% fall in CHD. And a recent study, Blankenhorn et al. (1987), using film pairs showing identical coronary artery views, showed a reduction in size of luminal deposits in the coronary arteries of patients who previously had undergone coronary artery bypass surgery. These subjects had succeeded in lowering plasma cholesterol by diet and drugs for the year study period.

Whether or not raised triglyceride levels independently promote CHD has been controversial. Although a number of studies have failed to show hypertriglyceridaemia as a primary risk factor for CHD, there is evidence to suggest that a plasma triglyceride level greater than 1.70 mmol/l is associated with increased cardiovascular mortality, independent of cholesterol levels (Simons and Gibson 1980). The degree of angiographically demonstrable disease and the extent of electrocardiographic ST segment depression during exercise was found to correlate significantly with the subjects' triglyceride levels (National Heart Foundation of Australia 1974). Carlson and Bottiger (1972) found the incidence of CHD linearly increased with elevations in triglyceride concentration, independent of fasting cholesterol. They also noted that an increase in both triglyceride and cholesterol levels resulted in a higher risk of coronary disease than did elevation of either lipid alone.

Triglyceride concentration may be directly influenced by ethanol consumption (Nestel and Hirsch 1965), oestrogen therapy (Moritch et al.1974), per cent body fat (Grundy et al. 1979) and diet (Fry et al. 1973). Modification of these factors can reduce triglyceride levels; however, the benefits regarding CHD risk are unknown.

There is a lower prevalence of hypertriglyceridaemia than of hypercholesterolaemia in the population: 12% of men and 6% of women not taking contraceptives had plasma triglyceride ≥ 2.0 mmol/l. In both, the prevalence increased with age.

There is a growing interest in alcohol consumption and its effects on CHD. Mathews (1976) examined the epidemiological data from a study in an Australian town, and claimed that 'up to 30% of hypertension in affluent countries may prove to be attributable to the use of alcohol', but MacMahon (1987) sets the figure for hypertension caused by alcohol at 11%. Much is still unknown about the risks versus the benefits of alcohol consumption, 'acceptable' quantities, the reversibility of effects and its mechanism of action. The relationship between alcohol and CHD is discussed in detail in Chapters 4 and 5.

Over the last two decades, studies of the diets of peoples with low incidences of CHD have led to major modifications in western eating habits, with an emphasis on less salt, less fat, less refined carbohydrate and more fibre and polyunsaturated oils were found to lower cholesterol levels.

However, the risk of a high fat diet was challenged by the work of Bang and Dyerberg (1972), who found a very low incidence of CHD in the Eskimo population, despite a very high intake of fat, protein and cholesterol. It was hypothesised that the high intake of omega -3 polyunsaturated fatty acids, present in marine fish oils, gave 'cardioprotection'. This subject is discussed in detail in Chapter 5.

Leeder and MacMahon (1985) have reported a decline of 45% in death rates from coronary heart disease in Australia since the peak in the mid 1960s. Similar findings in New Zealand were attributed almost entirely due to a reduction in the numbers of sudden deaths (Beaglehole 1986). Heller (1986) claimed that 60% of this decline in mortality can be ascribed to changes in serum cholesterol levels and cigarette smoking, and the other 40% to changes in medical interventions, and especially the increased use of beta-blockers over this time.

A frequent criticism of much clinical and epidemiological work in this area has been the failure to properly control all factors that influence the outcome of the studies. As well, there are problems with selection bias, and inadequate methods of assessing both the intervention and their effects.

All the cardiovascular risk factors measured in the present study are known to be affected by many factors other than those tested. For example, Table 1 lists a number of factors that are relevant to HDL cholesterol levels (Goldberg and Elliot 1985).

Table 1. Some of the factors known to affect plasma HDL cholesterol levels. For reference see Goldberg and Elliot (1985).

HDL Cholesterol:	is increased by	is decreased by
	low body weight index	high body weight index
	ethanol consumption	high carbohydrate diet
	nicotinic acid use	zinc supplements
	oestrogens	androgens
	phenytoin	cigarette smoking
	terbutaline	atenolol, phenothiazines

Factors affecting LDL cholesterol levels include age, saturated fat ingestion, and per cent body fat. Triglyceride levels are altered by ethanol consumption, oestrogen therapy, per cent body fat, diet (Goldberg and Elliot 1985). Similar lists could be compiled for BP, other lipids and glucose tolerance. On this basis, all subjects in the present study were requested to maintain their usual lifestyles, smoking habit, diet, alcohol consumption and body weight during the studies.

There is clinical and epidemiological work to support the popular belief that regular exercise is beneficial to health, although which factors are improved remain uncertain. The effects of exercise on CHD risk factors are discussed in detail in Chapter 3.

The objective of this publication has been to demonstrate a modification of some of the major CHD risk factors, both by specific alterations in diet and by increased levels of activity. In particular, the changes in BP, heart rate lipids and glucose tolerance was studied three times over the year of a polar expedition, following periods of varying levels of activity. The repetition of the same study during different phases of the year was planned so that the effects of different 'background' levels of activity could be determined.

This research also investigated the effects of moderate doses of alcohol consumption on the CHD risk factors specified above, and to examine whether those effects were altered by the use of eicosapentaenoic acid, present in high concentrations in marine fish oil. The relationship of fish oil to the modification of CHD risk is discussed in Chapter 5.

All expeditioners, including those who did not partake in any research project, attended for monthly physiological measurements (described in Chapter 2). These results were analysed, with the aim of discovering the presence of any selection bias in the volunteers for clinical studies, and to study the existence of any seasonal variation in BP, heart rate and weight during the polar year.

The exercise study was performed at three different levels of activity with the aim of determining the threshold of beneficial effect on CHD risk. On the basis of a study by Jennings et al. (1984), it was hypothesised that only moderate exercise is required to achieve maximum benefit: this is discussed in detail in Chapter 3.

1.1 ANTARCTICA

In 1947, the Australian Government established the Australian National Antarctic Research Expeditions (ANARE). Since that time, Australia has continuously maintained stations on the Antarctic Continent and subantarctic islands. Ninety-eight per cent of Antarctica is covered with ice, the mean thickness being 1800 m . The ice in general flows from the centre of the continent to the sea, where it breaks off to form the characteristic 'tabular' icebergs, which float northwards. When the sea freezes during winter, ice is present for many hundreds of kilometres off-shore. During summer this breaks up to form pack ice. Only then is it possible for polar vessels to penetrate to the Antarctic coastal stations to transport expeditioners and resupply stocks for the following winter.

1.2 CLIMATE

Rubin and Weyant (1965) have described the climate of Antarctica. It is the coldest on earth, with temperatures decreasing with altitude and distance from the coast. Temperatures as low as -88°C have been recorded. Antarctica is a continent of high winds. Due to the slope of the ice, the cold air flows outwards towards the coast . As it accelerates down the steeper slopes it may reach gale force. These winds are known as katabatic winds. Wind speeds often exceed hurricane force (120 km/heart rate) for several days at a time, with maximum gusts of more than 250 km/heart rate.

The length of daylight hours varies markedly throughout the polar year. At midsummer, the region experiences 24 hours of daylight. Six months later at midwinter, there is continual darkness for six weeks, with a glimmer of 'dawn' light for a few hours at midday.

1.3 HUMAN POPULATIONS

Antarctica is unique in having no industrial or commercial activities, and no indigenous peoples inhabit the area. Many nations, including Australia, lay claim to territory on the Antarctic Continent. However, with the signing of the Antarctic Treaty (1961), the sixteen treaty nations have cooperated with its charter, which includes the condition that no territorial claim is recognised nor disclaimed.

1.4 DAVIS STATION

Davis (68°35'S, 77°58' E) is situated in the Vestfold Hills on the east side of Prydz Bay in Princess Elizabeth Land, Antarctica. The station was comprised of two parts: the 'old' section, which had been chiefly established from 1957-1960, was chiefly used as sleeping accommodation, surgery, gymnasium, biology and upper atmospheric physics laboratories, meteorological office and radio room. The buildings were separated, where possible, to diminish the risk of fire. The flat-topped

boxlike buildings were constructed by clamping together prefabricated wall panels of plywood, steel or aluminium with a core of insulating polystyrene. The buildings rested on wood stumps or scaffold piping and were firmly tied to the rock by cables rigged to roof brackets. This type of construction had been used for rapid erection by the expeditioners.

The new section has been under construction over recent years and using prefabricated aluminium panels constructed over concrete foundations, with steel framework. The buildings were heated by an integrated-energy central heating system, which utilised the waste heat from the four diesel-electric generators. Most buildings had a porch which acted as a trap to prevent the entry of wind and snow, or loss of heat when the inner door was opened.

The Antarctic station environment has changed considerably since the early days of settlement, and were now considered comfortable and secure by normal Australian standards. Williams (1986) has written an excellent account of life on an Australian Antarctic station.

1.5 RESEARCH IN ANTARCTICA

Antarctic research stations are ideal for certain clinical studies: the isolation guaranteed a fixed study population for a full year, provided the expeditioners could be persuaded to comply; the lifestyle is simple and routine, with little variation possible; when variables occurred, they were known and accountable; all subjects shared the same food, living and climatic conditions; diet is provided by the same chef throughout the year and is limited to certain foodstuffs; the selection of expeditioners is broad-based, from all socio-economic levels, the only exclusions being those with pre-existing ill-health discovered on the routine medical examination prior to departure.

The simple, basic social environment allowed most to develop a predictable daily routine for the year, making it an ideal situation for longitudinal studies. There was a considerable amount of background information on all the expeditioners. All had undergone a full medical and psychological examination prior to selection, and had a monthly check of BP, heart rate, weight, skin fold thicknesses (x 4) and arm circumference.

The MO was also the messing officer, who was responsible, with the chef, for rationing, correct storage and reordering of food. This ensured the MO was well acquainted with the expeditioner's diet.

Nevertheless, there are a number of constraints on polar research which must be considered before planning a protocol: the expedition's MO was primarily responsible for the health of the expedition, and for the maintenance of the surgery and its equipment; ensuring field trips had adequate first-aid training and supplies was also important; limited numbers make cross-over trials a preferred method; subject compliance is affected by occupational and station demands; some expeditioners will arrive late or leave the station early, making a full year program difficult; isolation from professional support staff, facilities and replacement equipment means thorough preparation is mandatory and every contingency considered; the protocol must be able to be modified to accommodate major, unpredictable events on the station; investigations must be kept as noninvasive as possible to avoid the possibility of complications and because all work must be done by a single operator.

1.6 THE ANTARCTIC YEAR

The marked variations in both the climate and station life over the year is unique to polar regions. Furthermore, each station and each wintering group are distinct and, in many ways, resist generalisation.

Because Australian stations were only accessible by ship, and then only when the sea-ice broke up, the brief summer period was inevitably hectic. After a month's voyage, most of the 1986 wintering expeditioners arrived at Davis in mid December 1985. During the summer, up to 80 expeditioners lived on the station to take advantage of the 24 hour daylight and relatively mild conditions, to carry out field research, surveying, and the construction of new buildings.

Most of the new arrivals had left sedentary jobs and were relatively unfit after a month of very restricted activity on board ship. However, a heavy work schedule, which involved most expeditioners, commenced immediately. There was an eight hour day, working on a new building site, in subzero temperatures and, at times, high winds. Much of the work was steady, moderately heavy manual labour.

The summer was the time of greatest biological activity for Antarctic wildlife. Most expeditioners took advantage of the 24 hour daylight to walk several kilometres in the evening to the penguin rookeries or seal colonies. Recreation took the form of other outdoor sports, such as soccer, cricket and jogging which were possible before the arrival of the snow in autumn.

By March, the last ship had removed the summer population and the wintering population numbered 20, with the author the only woman, work routines were well established and, in general, there was good social harmony. There was more time for leisure. Sporting tournaments were organised. With the arrival of the snow, several expeditioners were regularly involved in winter sports such as cross-country or downhill skiing, ice-skating or skidooing. Although skidoos were available for long distance (20-60 km) day trips, they were not used on the station; this meant frequent walks for all expeditioners, several hundred metres through snow, as part of the daily routine.

With each month, the days grew shorter, until June when the sun did not rise at all for six weeks. There was complete darkness except for a few hours around midday when there was a 'dawn' glow. Station activity reached a minimum over winter, although most expeditioners sought regular exercise in the gymnasium.

With the vernal equinox in September, there was a heightened level of activity on the station. Major field trips were planned and executed with the involvement of all expeditioners. With the pressure to complete allotted tasks before the year's end, combined with increasingly unreliable conditions (sea-ice used for travel was beginning to break up and the vehicles were occasionally a problem), there was a fair degree of psychological stress. This was compounded by the imminent arrival of the ship, when the new group arrived and inevitably disrupted the social order of the small and closely knit wintering group. A late and unexpected request from the Antarctic Division to establish a new station at a remote location with whatever was available put a large strain on both supplies and personnel. As many expeditioners were absent from the station over the spring period, the final phase of the medical research project was severely curtailed.

The arrival of the polar vessel MV *Icebird* in the early summer marked the end of the year.

1.7 STRESS, LIFESTYLE AND HEALTH

It is generally accepted that psychological stress plays a significant role in the health of an individual, although the mechanisms remain poorly understood. Part of the reason for this difficulty lies in the varying degree to which each individual is affected by life events, and also, the effect such stress has on physical health.

A wintering year in isolated Antarctic communities is widely regarded as stressful. The development of acute psychosis or anxiety states have not been infrequent in the past, although with improved psychological screening, these are less common (Williams 1986). Godwin (1983) questioned a large number of expeditioners and identified fairly consistent sources of stress. Highest rated were: separation from immediate family and friends; lack of privacy; problems in group compatibility; and pressure to conform to the wishes of the majority. Concern about the hazardous and inhospitable environment were less common.

Nevertheless, the fact that a high percentage (24%) of expeditioners who return for second or more winters supports the author's view that a well organised and harmonious station can provide an environment remarkably free from daily stress, except for those specific periods described above.

1.8 DIET

The MO played an active role in the victualling on Antarctic stations. Although there was no formal analysis of food intake, the following observations were made.

While the quality and variety of food available on Antarctic stations has improved greatly over the years, the problem of lack of fresh food remained. During the summer, the frequent arrival of ships ensured that some fresh fruit and vegetables arrive in edible condition, and, with care, these remained edible for a number of weeks. The summer diet, therefore, was more similar to the mainland diet than at other times of the year. It was usual in the summer for most to attend five eating times: a cooked breakfast; morning tea with cake or scones; a hot lunch, such as pizza, hamburgers, spaghetti bolognese, or steak; afternoon tea with biscuits; and an evening meal, generally with more red meat and roasted vegetables. The cooked breakfast was rare in the winter. However, when the fresh items ran out, there was a heavier dependence by all on the meat dishes. What vegetables were available (in dried, tinned or frozen form) were frequently fried, rather than boiled. Full cream powdered milk was supplied, and there was a regular supply of chocolate blocks and biscuits.

Due to shipping problems in 1986, there was a very limited supply of lean meats and fish, so these items were rationed to one meal a month. The meals were chiefly red meats, such as lamb, beef or ham.

The combination of increased cold exposure and physical exertion, and the lack of other forms of gratification combined with the effect that most expeditioners had high energy intakes, with a likely proportionate increase in saturated fat content.

The 1986 MO was also responsible for issuing the monthly supply of alcohol for each expeditioner, which amounted to 24 cans of beer (5% alcohol/vol). As well, there was occasionally available wine and spirits, but limited supplies restricted their use to celebrations or special occasions. Some expeditioners brought with them plentiful supplies of alcohol, which enabled them to have up to five-eight drinks on a regular basis (say, three-four times a week). Drinking habits were reasonably consistent throughout the year and despite a high alcohol intake in some individuals, there were no overt signs of alcoholism.

In order to attempt to quantify cholesterol and fat intake, two representative menus for a week each for summer and winter were supplied to a dietitian on return to Australia for estimations. Daily cholesterol intakes were averaged at 540 mg and 715 mg for summer and winter, respectively. Total fat intakes were estimated at 45-50% energy intake for summer and 50-55% for winter.

1.9 POLAR HEALTH

There are now several studies on the peculiar health conditions at Antarctic stations (Williams 1986; Dick 1985): although not unique to Antarctica, the risk of cold injury, snowblindness, and carbon monoxide poisoning, and the absence of most infective illnesses are inherent in polar living. Insomnia frequently is aggravated by the photoperiodicity, especially during the summer months. However, the relative incidences of other health problems are difficult to quantify.

There is much anecdotal evidence of the development of hypertension on Antarctic stations: Fletcher (1980) reported seven new cases of high BP during routine monthly examinations of a population of 31; two of these required pharmacological treatment by the year's end. Williams (1986) reported three cases of essential hypertension, which developed during the two years spent on polar stations (total population 54), and Bodey (1971) discovered four new cases of hypertension out of a wintering party of 24.

In 1972, at the end of an uneventful year at Macquarie Island (a subantarctic territory of Australia), a 33 year old radio operator developed left arm pain and sweating shortly after the evening meal. Within one hour, he suffered a cardiac arrest and died despite attempts at resuscitation. Autopsy revealed occlusion of the left main artery by thrombus. The MO had collected monthly fasting blood samples over the year and recorded a total cholesterol concentration of 11.12 mmol/l, ß lipoprotein 1208 mg/100ml. His BP during the physical examination prior to departure had been 140/92 and during the year his monthly casual BP reading had been normotensive; his Quetelet body mass index was 25.7.

The question was raised whether the polar environment initiated the development of, or aggravated the previously subclinical presence of cardiovascular problems. Psychological, social and environmental stresses do exist in Antarctica and may be considered potential health hazards. Do restrictions on diet in an isolated station have adverse effects? Furthermore, if individuals avail themselves of such activities as outdoor sports with the aim to reduce their cardiovascular risk, are there factors such as cold stress and cold adaptation that counteract any potential benefit?

As will be described in Chapter 3, past research work has suggested that one sign of cold adaptation is the reduced metabolic response to cold. However, Keatinge (1961) found the fall in metabolic response to cold correlated with fitness levels and no further change was noted following prolonged time in polar regions. It is not known whether other changes attributed to cold exposure may be attributed to increased physical fitness.

The present study was undertaken to test what effect living in a polar environment had on BP and heart rate over the period of a year, and to determine whether these changes were modified by increases in physical activity.

In 1971, Dr Alan S. Bodey submitted a thesis of his work on human acclimatisation to cold in Antarctica. He measured changes in basal and casual BP readings in relation to adrenaline and noradrenaline 24 hour urinary excretion rates of all expeditioners, prior to departure and then at monthly intervals for a year on the Antarctic continent.

Initially, the mean noradrenaline level rose significantly on arrival in Antarctica, then it fell slightly to a level still greater then the pre-departure mean value. Bodey attributed these changes to cold acclimatisation, inducing increased non-shivering thermogenesis by means of raised noradrenaline.

Adrenaline excretion rates did not increase on arrival and, therefore, it is likely that some non-climatic factor may have influenced the rise in adrenaline excretion in the latter half of the year. Bodey cited previous studies that indicate that adrenaline is the catecholamine most likely to be increased by anxiety. Furthermore, anticipation (in this case, thoughts of the approaching home-coming) may be more anxiety-provoking than the event itself.

The low adrenaline excretion during the early Antarctic months excludes anxiety or anticipation as causes of the high noradrenaline excretion. Bodey concludes that noradrenaline plays an important part in adult human cold acclimatisation.

BP studies by Bodey showed casual systolic BP to decrease gradually over the winter then increase towards the end of the year. However, as this is not a consistent finding in other Antarctic studies (Budd and Warhaft1970, Boriskin 1973, Godwin 1983), it is again suggested that, non-climate factors may also have varying influence on BP changes over the Antarctic year.

2. METHODS

2.1 24 HOUR BLOOD PRESSURE MONITORING

The impetus for the development of ambulatory BP monitoring (ABPM) arose from the recognition that BP was exquisitely sensitive to situational and emotional factors, and that BP determinations in the clinic were often poorly related to measures taken in the home and workplace (Brown 1930, Ayman and Goldshine 1940). As the adverse effects of BP on the circulation are thought to depend on the average level of pressure over time, or possibly also on the peak levels of pressure, there is a sound theoretical reason for thinking that multiple measurements of BP will be better predictors of pressure-related morbid events than single measurements (Armitage et al. 1966). To quote one of the pioneers of ABPM,"the identification and measurement of the influence of environment in determining arterial pressure is the most important field to be explored, if we wish to know precisely the factors concerned with the aetiology of hypertension" (Pickering 1961).

The discrepancy between pressures recorded in the home and the clinic has been repeatedly confirmed (Julius, et al. 1974). A study in The Lancet reported that twenty out of fifty-nine subjects, who were classified as hypertensive by cuff measurements, had awake ambulatory pressures of less than 140/90. Pickering and Harshfield (1982) found this difference to be greatest in patients diagnosed as borderline hypertensives.

It is generally agreed that intra-arterial recordings are the most accurate method for ABPM. Because of their inconvenience, cost and potential risk, however, they are unlikely ever to be of practical clinical value. Di Rienzo et al. (1983) found that BP readings taken every 30 minutes or so provided an accuracy similar to evaluation of mean BP composed with beat-to-beat monitoring.

ABPM reduces the influence of BP variability, by averaging up to forty readings over a 24 hour period. While it is accepted practice to repeat BP measurements over a number of clinic visits, before the diagnosis of hypertension is made, there may be a role in this area for ambulatory BP monitoring.

Another important consideration is the placebo effect on BP. There is evidence to suggest that administration of a placebo, or participation in a clinical trial, significantly reduces BP of hypertensive patients, when measured in the clinic. However, Gould et al. (1981) found the administration of placebo had no effect on the BP recording obtained outside the clinic setting with ambulatory monitoring. Similarly, a study using transdermal clonidine (Schaller et al. 1984) showed a negligible fall in BP when measured in the office, but a 23/21 mm Hg in BP when using ABPM.

The prognostic value of ABPM was studied by Perloff et al. (1983). They found a greater degree of predictability of both fatal and non-fatal cardiovascular events, using non-invasive ABPM, compared to office BP measurements.

Perhaps more significantly, Sokolow et al. (1966) showed a higher correlation ($r = 0.68$) between severity of hypertensive complications and the average ambulatory BP, compared to a correlation found using repeated casual clinic readings ($r = 0.52$). The ambulatory readings explained 26% of the variance not accounted for by the casual pressures.

However, because BPs taken during exercise are likely to be higher than sedentary values, the use of 24 hour mean BPs in more active populations would skew data to falsely high levels, not representative of usual BP levels. The variability in the amount of exercise done daily would be another confounding factor.

The ambulatory BP monitor (ICR, Squibb, Spacelabs) used in the present study was based on the Korotkoff sound technique, with oscillometry as a back-up method of monitoring. It therefore, had the same physiological limitations common to all sphygmomanometric techniques, although it had the advantage of avoiding such problems as observer bias and the 'white coat' effect (Beckman et al. 1981). The ICR monitor has been validated against mercury sphygmomanometer readings (Harshfield et al. 1984, Dembrowski and MacDougall 1984). Correlations between ABPM and intra-arterial monitoring were 0.98 for both systolic and diastolic pressure.

The reproducibility of ABPM has also been studied. Pessina et al. (1984) found that BP readings were lower on the second of two 24 hour recordings, while others (Fitzgerald et al. 1984, Drayer et al. 1984) did not find appreciable changes. To avoid the potential for first-use bias, all subjects wore the monitor for a 24 hour familiarisation period prior to testing.

The ICR ambulatory BP monitor used in the present study was programmed to record systolic, diastolic BP and heart rate at specified times throughout the 24 hour period. A 15 x 51 cm cuff (12 x 22 cm bladder) was applied to the right arm and the monitor was worn under outer clothing to protect against cold and accidental damage. Each reading was preceded by a warning sound, which signalled the subject to stop for 45-60 seconds to allow for an undisturbed measurement. After each measurement, the subject recorded his posture, activity and any relevant comment on the sheet. A sample is shown in Figure 1.

On completion of each 24 hour period, the monitor was returned and the data transferred from the Epson HX-20 computer via a ROM Baselink to a Macintosh 512K computer (Apple Computer, Inc. USA) for analysis. A 24 hour period yielded about forty-two readings of BP and heart rate and time of reading. Artifactual readings, as a result of movement during recording, were indicated by a error code, such as EO1, and deleted from the record. The author then used Table 2 to code each reading with the appropriate activity level. As the daily activities of each subject were well known to the author, it was possible to code quite accurately each reading.

To test the reproducibility of data, one subject was asked to wear the monitor for two 24 hour periods, and to record activities on a Daily Activity Record sheet (Figure 1). The two recordings of systolic pressure are shown (Figure 2). Each day yielded thirty-eight readings. Apart from the apparent lower nocturnal readings, a comparison of the 2 days on a temporal basis was not possible. Both days showed frequent and marked variations in systolic pressure. Similar variations were noted in diastolic pressure and heart rate.

Table 2. Activity level code given to each BP and heart rate reading.

Activity	Code
Sleep	1
Lie awake	2
Sit	3
Stand	4
Light work	5
Moderate exercise, work/fast walk	6
Heavier exercise, work/fast walk	7

DAILY ACTIVITY RECORD

Name: DICK Date: 16-4-86 ARM: (R) L

Test: ALCOHOL

* Start on hour monitor beings
* Tick ONE average position and ONE activity
* Note any reason for abnormal reading or error

	Position				Activity						
Time	Sit	Stand	Reclining	Moving	Talk	Eat	Relax	Stress	Physical	Desk Work	Comments
1 am			1				1				
2 am			1				1				
3 am			1				1				
4 am			1				1				SLEEP
5 am			1				1				
6 am			1				1				
7 am			1				1				
8 am	1 2					1	2				BREAKFAST READING
9 am				1 2					1 2		CLIMBING LADDER MOVING LIGHTING
10 am				1 2					1 2		SWEEPING FLOOR CLIMBING LADDER
11 am	1			2			1		2		SMOKING CIGAR USING AIRGUN ON LADDER
midday	2			1		2			1		USING AIRGUN ON LADDER LUNCH
1 pm		1 2			1				2		TALKING WITH RUSSELL SAWING
2 pm				1 2					1 2		WORKING ON LADDER DRILLING HOLES
3 pm	1	2					1		2		SMOKING 5TH LAST CIGARETTE SAWING
4 pm		1		2	1				2		TALKING MOVING PLANKS
5 pm	2			1					1	2	WALKING READING MANUAL
6 pm		1 2			1		2				AT BAR AT BAR
7 pm	1 2					1 2					DINNER COFFEE
8 pm	1 2						1 2				WATCHING VIDEO
9 pm	1 2						1 2				WATCHING VIDEO
10 pm			1 2				1 2				IN BED
11 pm			1 2				1 2				IN BED
midnight			1 2				1 2				SLEEP

Figure 1. Sample of a daily activity record. The numbers 1 and 2 indicate the first and second readings of the hour, respectively.

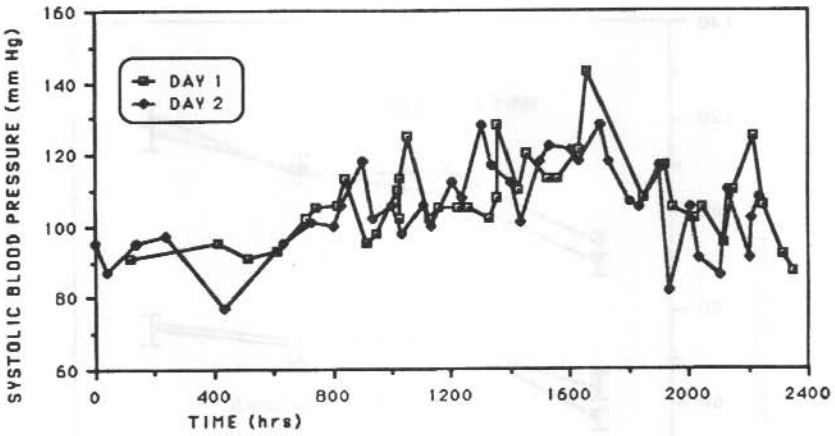


Figure 2. A comparison of the diurnal variations in systolic BP of two 24 hour periods in one subject. The ambulatory monitor was initially checked against a mercury sphygmmanometer at the time of fitting. Mean systobic pressure (F SD) for day 1 and day 2 were 107 (F 11.6) mm Hg and 105 (F 12.11)mm Hg, respectively.

The daily activity records kept by the subject showed the amount of activity varied on the different test days. As expected, posture and activity level proved major factors in determining BP and heart rate. Consequently, differences in the daily means, range, maxima or minima from the test periods were difficult to interpret.

The monitor broke down twice during the year, and was repaired by the electronics engineer. The monitor was checked against a mercury sphygmomanometer and no recalibration was necessary.

However, by dividing the data into the eight activity levels shown in Table 1, it was possible to compare the 24 hours of results in a useful fashion. Figure 3 shows the mean and standard error (SE) of the readings of the 2 days, grouped by activity level. The graph represents systolic and diastolic pressure readings for four levels of activity. T-tests on systolic, diastolic pressure and heart rate for each activity level showed no significant difference between the 2 days.

The categories of activity above were chosen as a semi-quantitative means to analyse otherwise unwieldy data. Since they did not distinguish isometric or isotonic activity and a broad range of activity was allotted to each category, it was not possible to use a unit measure such as mets for each level. Nevertheless, the graph is representative of the expected changes in BP with posture and activity: systolic pressure shows an increase from sleeping to sitting, when a further increase is seen with higher levels of activity.

Diastolic pressure also showed a physiological response, with an initial increase from rest to sedentary activity, then little further increase seen with escalating activity.

There was a reasonable degree of correlation in these equations, ($r = 0.70$). However, since there was no control for the many other factors affecting haemodynamic function, including emotional state, ambient temperature, time of day, preceding activity, state of psychological stress and relationship to meals, some variance was to be expected.

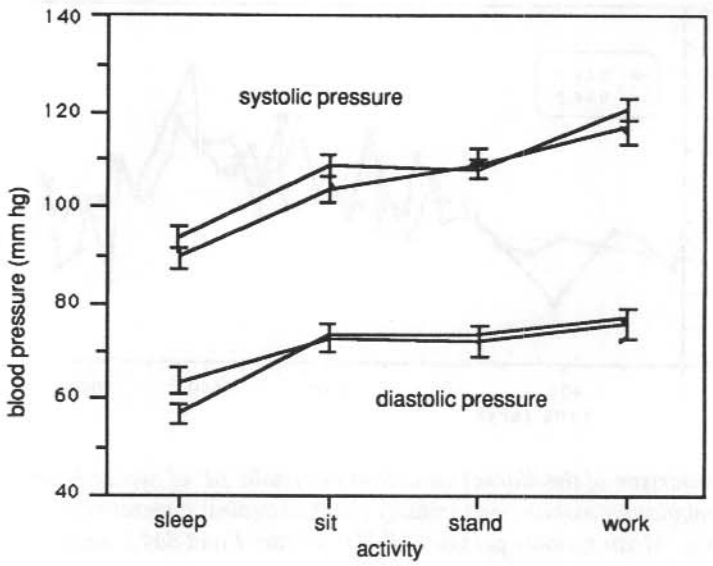


Figure 3. A comparison of the systolic and diastolic pressure in relation to activity level, of one subject over two similar days. Mean values and standard errors are indicated.

2.2 EXERCISE TESTING

All subjects were familiarised with the following procedure a number of days prior to testing. The subject was warm, relaxed and fasted, for 2 hours. Baseline heart rate, BP and weight were taken. Room temperature and barometric pressure were measured and equipment calibrated. (Equipment is described on the following page).

The subject mounted the Monarck cycle ergometer, and positioned the heart rate monitor, mouthpiece and nose clip. He commenced cycling at 60 rpm, with minimal load.

The load was increased by 100 kilopond metres per minute (kpm/min), every minute. When the subject indicated that maximal effort was being made, the ventilation metre was set to zero, time was noted and the expired gases were collected for the final minute. The gas sample was saved in a Douglas bag and the oxygen partial pressure was immediately analysed after mixing (vide infra).

Maximal heart rate was recorded by the Exersentry exercise heart rate monitor applied to the chest of the subject. After exactly one minute on maximal exertion, the subject removed mouthpiece and nose clip and cycled for a further 5 minutes 'cool down' stage at 30 rpm, 300 kpm/min.

Minute volume and maximal respiration rate were recorded on the Morgan Ventilometer Mark II Model PCB, large turbine ventilation meter.

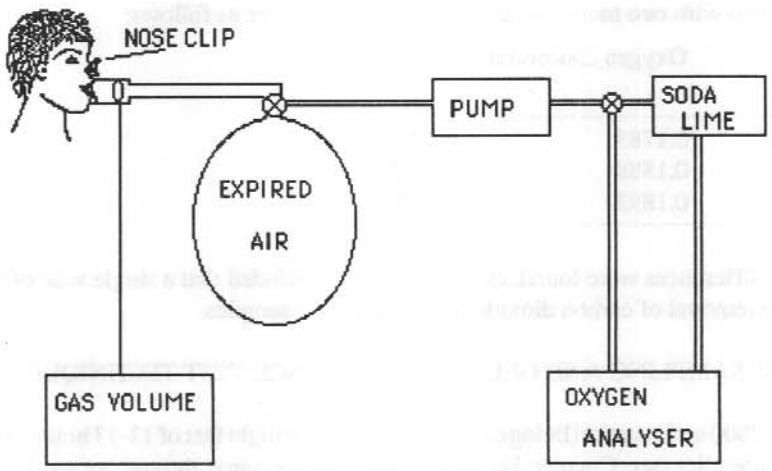


Figure 4. Schematic representation of the measurement of VO_2max.

2.3 TECHNIQUE FOR OXYGEN ANALYSIS

The Servomex 570A oxygen analyser was turned on for at least 45 minutes. Having warmed to operating temperature, the analyser was calibrated at zero with high purity, 99.9% nitrogen (CIG, Australia). Using dry air, the scale was set at 20.94% oxygen. This step was repeated daily or whenever the barometric pressure varied. The operation of the analyser was checked several times weekly with a known nitrogen-oxygen mixture. A voltage surge protection device was used. The apparatus was arranged as in Figure 4.

At the end of the fitness test, the expired air was pumped from the bag which was constantly being mixed. The air was dried by being passed through a tube of calcium chloride. The sample then entered the Servomex oxygen analyser and the pump was turned off to prevent disturbance. The concentration of oxygen was noted. A second reading was then taken after the sample had passed through a tube of soda lime and all carbon dioxide was removed.

The formula used to calculate VO_2max is set out in Appendix I.

2.4 SODA LIME EFFICIENCY

To determine the efficiency of carbon dioxide absorption by the tube of soda lime used in determining the increase in oxygen concentration, the following experiment was performed: a sample of exhaled gas was analysed after being passed through:

a) one tube of soda lime

b) two tubes of soda lime in series.

This was repeated with two more gas samples. The results were as follows:

Sample	Oxygen concentration (F_iO_2)	
	a	b
1	0.1783	0.1780
2	0.1888	0.1890
3	0.1892	0.1892

No significant differences were found, therefore it was concluded that a single tube of soda lime suffices for the removal of carbon dioxide from expired air samples.

2.5 PLASMA SAMPLING AND GLUCOSE TOLERANCE TEST TECHNIQUE

Tests started at 0800 in the station living quarters, after an overnight fast of 12-13 hours. All subjects were on the same diet (see Chapter 1), which remained the same throughout each season and contained the 150 g of carbohydrate recommended to precede a glucose tolerance test (Klimt 1969). Drinking water was allowed.

All subjects walked the same distance to be tested and during the test sat quietly in a warm room (15-18°C). A 21 gauge winged intravenous cannula was inserted in the forearm and a 15 ml sample of venous blood collected without a tourniquet,in a plastic syringe. The cannula was flushed with a saline solution and cappedten millilitress of the blood was then mixed with EDTA for lipids and 5 mL were mixed with potassium oxalate/sodium chloride for glucose. These glass Vacutainer tubes with rubber stops were immediately placed in the centrifuge for 10 minutes at 3000 rpm.

Plasma was then stored in plastic containers with screw-top lids to prevent moisture loss. Samples were immediately frozen to -20°C until just prior to analysis. One ml of EDTA plasma was taken for HDL cholesterol levels. Before freezing, the plasma was mixed with a heparin/mangenous chloride solution to precipitate lipoproteins other than high density lipoprotein (see this page for details). After centrifuge, the supernatant was collected. The plasma samples for lipid determination were stored in two vials, one to be analysed at the end of the test period in Antarctica, and the second to be analysed automatically on return to Australia. Only total cholesterol was compared on return at the Alfred Hospital, Melbourne. Cholesterol is considered acceptably stable over a 12 month period (Dr Abe Wan, Alfred Hospital, Melbourne, personal communication, 1985).

Seventy-five grams of D-glucose were dissolved in water and the solution drunk over a maximum of three minutes and timing was commenced.

Further blood samples (for glucose only) were taken at 30, 60, 90 and 120 minutes. During this two hour period the subjects remained seated and resting.

The samples were immediately centrifuged and plasma collected in labelled plastic tubes for freezing. One millilitre of EDTA plasma was kept for high density lipoprotein (HDL) cholesterol precipitation, using the heparin-manganous chloride method (Warnick et al. 1985), which was done during the test period.

2.6 ANALYSIS OF SERUM SAMPLES

Due to the months' delay in returning specimens to a laboratory for analysis, it was necessary for me to do the sampling and analysis in loco. All samples were frozen at -20°C until analysis at the end of each program (a maximum of 6 weeks) to avoid inter-assay variation.

2.7 METHODOLOGY

2.7.1 Instrumentation

Equipment used in Antarctica included an MSE centrifuge and a Beckman spectrophotometer (Junior II, Model 6/20).

Prior to departure, the author received training from Professor Zen Meglo, Director of the Biochemistry Department of the Repatriation Hospital in Hobart, in the use, calibration and maintenance of the Beckman spectrophotometer to be taken to Antarctica.

Dr Abe Wan, Deputy Director of the Department of Biochemistry, Alfred Hospital, Melbourne, provided instruction in analysis of serum samples. All techniques were practised under supervision to guarantee precision and accuracy.

2.7.2 Reagents

Water was collected from melted snow and purified using a Millipore Deionizer (two passes).

2.7.3 Glucose

Glucose was measured by the GOD-PAP (Boeheart rateinger Mannheim Diagnostica, France) method. The test principle was as follows:

GOD

glucose + O2 + H2O ———> gluconate + H2O2

POD

2H2O2 +4-aminophenazone + phenol ——> 4-(p-benzoquinone-mono-imino) phenazone + 4H2O

2.7.4 Cholesterol

Total cholesterol analysis was made by the enzymatic CHOD-iodide method (Merckotest, E Merck Diagnostica, France). Cholesterol and its esters were released by detergents from lipoproteins.

2.7.5 Cholesterol esterase hydrolysed the esters

H2O2 was formed in the subsequent enzymatic oxidation due to cholesterol oxidase. H2O2 converted iodide to iodine which was determined by photometric method.

2.7.6 High density lipoprotein cholesterol

Low density lipoprotein cholesterol was precipitated by a mixture of heparin : Manganese chloride, 4 : 5 v : v. 1.0 ml of plasma was added to 100 µl of heparin/MnCl2. The mixture gave a final concentration of manganese of 92 mM and heparin of 202 units/ml. After mixing, it was left for 60 minutes, then spun at 3000 rpm for 30 minutes. The supernatant was then analysed for cholesterol content as above. The assay was corrected for a dilution factor of 1.1

2.7.7 *LDL cholesterol*

LDL cholesterol was calculated using the Friedewald formula (Frieldewald et al. 1972) as follows:

LDL = triglycerides /5 + HDL cholesterol -total cholesterol.

2.7.8 *Triglycerides*

Triglycerides were measured by the fully enzymatic GPO-PAP (Merckotest, E Merck Diagnostica, France) method. Triglycerides were enzymatically hydrolysed to glycerol and free fatty acids by special lipases. Glycerol reacted further according to the following reaction scheme:

GK

Glycerol + ATP <————> L- a - glycerol - 3- phosphate + ADP

GPO

L- a - glycerol - 3- phosphate + O2 <———> dihydroxyacetone phospsphate + H202

POD

H2O2 + 2 - chlorophenol + 4 - aminoantipyrine <———> 4 -(o-benzoquinone monoimido) phenazone + 2H2) +HCl

1000 µl of plasma was mixed with 10 µl of the reaction solution and incubated at 20-25°C for 10 minutes. The absorbance of the samples and standards (described below) were measured within an hour.

A further plasma sample was kept frozen and, on return to Australia, analysed for gamma- glutamyl transferase.

2.7.9 *Quality control*

The purpose of quality control is to ensure both precision and accuracy. This was done by using a minimum of two concentrations of standards and a control solution for each assay. Reaction solutions, standards, and controls that required reconstitution were made each morning using deionised water.

2.7.10 *Precision*

Within-run precision was monitored between each subject's sample, using a single sample of Australian Lipid standardisation Program Serum standard for total and HDL cholesterol and for triglyceride, and Precimat -D glucose (Boeheart rateinger Mannheim Diagnostica, France) for glucose. Throughout the year's program, the Coefficient of Variation for within-run precision monitoring was between 1.5% —1.7% of the mean for total and HDL cholesterol, 1.4% — 1.7% for triglyceride, or 1.5% —1.6% for glucose measurement.

Similarly, inter-assay precision was monitored by comparing the mean values of each run's quality control. The coefficient of variation never exceeded 3.5% of the mean, which was within acceptable limits.

2.7.11 *Accuracy*

Accuracy was monitored by the use of Seronorm Lipid (Nyegaard Diagnostica, Norway) for cholesterol and triglyceride. Seronorm Lipid is a lyophilized reference serum which was reconstituted with 3.00 ml of deionised water. Seronorm (Boeheart rateinger Mannheim Diagnostica, France) was reconstituted with 5.00 ml of deionised water and was used as the reference serum for glucose. The

values given by the manufacturer (a concentration of 6.90 mmol/l for cholesterol, 2.15 mmol/l for triglycerides and 5.88 mmol/l) were compared to quality control results and and found to be within acceptable limits.

2.7.12 Subject selection

All subjects were chosen from the Australian National Antarctic Research Expedition (ANARE), based at Davis station. Medical standards for expeditions have been discussed by Lugg (1982) and Bachelard (1982). Before departing Australia, the selection process included a complete medical history and physical examination, electrocardiogram, chest X-ray, urinalysis, Mantoux testing, haematological examination and serological screening for hepatitis B, syphilis and Acquired Immune Deficiency Syndrome, which were all normal. All subjects were deemed in good health, normotensive, with normal hepatic enzyme levels.

Psychological suitability screening tests were conducted by the Australian Army Psychological Research Unit. The preferred selection of adaptable, cooperative individuals worked in favour of a successful research program.

2.7.13 Statistical methods

Since each subject served as his own control, statistical analysis was made using paired methodologies. Comparisons of haemodynamic variables and plasma levels in the exercise study were performed using paired t-test.

Data in the alcohol and fish oil studies were analysed by two-way analysis of variance and partitioning the treatments sum of squares. Standard error of the differences was obtained from the analysis of variance (Snedecor and Cochran 1967). The null hypothesis was rejected at $p<0.05$.

3. THE EFFECT OF VARYING LEVELS OF ACTIVITY ON BLOOD PRESSURE, HEART RATE, PLASMA LIPIDS AND GLUCOSE TOLERANCE

3.1 INTRODUCTION

There has been much controversy about whether exercise has an independent effect on the improvement of cardiovascular risk factors. Eichner (1983, 1985) has reviewed many epidemiological studies and found a negative association between physical activity and incidence of mortality and morbidity from cardiovascular disease. However, studies have frequently been hampered by the possibility of selection bias, imprecise objective measures of physical activity, poor quantification of the exposure and failure to separate fitness and activity levels (Kannel 1985).

There has also been a failure to adequately control for other important factors such as diet, weight and smoking. Unresolved issues remaining include the precise level and duration of exercise required, the need to achieve 'a trained state', the impact of leisure versus work activity, the exact mechanism of benefit and the net effect of exercise, taking other risk factors into account. The duration of cardiovascular benefits of exercise, once achieved, in contrast to the persistence of training effect, is unclear. Furthermore, there have been no previous studies of the effects of increasing levels of exercise on ambulatory BP.

In the Framingham study (Kannel and Sorlie 1979), 4220 subjects were followed over 14 years; mortality and morbidity from cardiovascular disease was found to be inversely related to (self-reported) physical activity, despite low correlations between physical activity and the major risk factors of systolic BP, serum cholesterol and cigarette consumption. Self-assessment is likely to be imprecise and would blunt any relationship found. As well, the population was skewed heavily towards the levels of lowest activity and hence may not have been appropriate to display a true association.

Cooper et al. (1976) studied 3000 men and showed a consistent inverse relationship among physical fitness categories and resting heart rate, body weight, percent body fat, serum levels of cholesterol and triglyceride, glucose, and systolic BP. However, their conclusion was that the association between physical fitness and lower cardiovascular risk factors could not be proven, only implied.

In a prospective study using 6039 normotensive subjects, Blair et al. (1984) compared the level of fitness to the development of hypertension for a period of up to 12 years. After adjustment for sex, age, follow-up interval, baseline BP and baseline body-mass index, the physically unfit group (72% of the population) had a 1.52 relative risk of becoming hypertensive. However, no causality could be assumed.

Some clinical studies have recently paid attention to each individual risk factor and its modification by exercise. Jennings et al. (1986) have examined the effects of varying levels of exercise with careful control of all other variables, and have shown that improvement in cardiovascular function with training is accompanied by falls in BP, total peripheral resistance and sympathetic activity.

An important aspect of this study was that most improvements in BP and heart rate were seen after a month of exercise bouts lasting 30 minutes, occurring only three times a week. Daily bouts of exercise bestowed very limited further improvements, despite an improvement in fitness (VO_2 max). They concluded that there may be an optimal level of exercise for each individual, beyond which no further cardiovascular benefit and possible detrimental effects may be seen.

The present study was designed to test whether the hypotensive effects of increasing levels of activity was a low-threshold phenonemon, that is, whether the benefits of exercise are operative only for sedentary subjects or whether there are ongoing improvements with further increments in exercise in the already active. As will be discussed below, a protocol similar to that used by Jennings et al. (1984) was used. The study was repeated three times throughout the polar year to take advantage of the varying levels of background activity (see Chapter 1). The aim of the study was to test whether identical increases in activity achieved the same benefits in subjects when active as sedentary.

Furthermore, BP measurements in the present study were made using a 24 hour ambulatory BP monitor. This avoided the problem of laboratory-induced stress and placebo effect of casual BP measurements, as described in Chapter 2. There are no previous studies into the effects of increased levels of exercise on ambulatory BP readings. The present study used 24 hour BP monitoring in order to determine the effects of exercise during normal daily activity and during sleep. As it was impossible to blind subjects in regard to exercise levels, it was considered mandatory to limit as much as possible the potential for measurement biases.

The present study examined the changes in BP over the period of a year on the Antarctic Continent, and monitored the effect of varying levels of activity on these changes. Many previous polar researchers have made monthly measurements of casual and basal BP, but few have attempted to control those factors affecting BP.

In 1971, Dr Alan S. Bodey submitted a thesis of his work on human acclimatisation to cold in Antarctica. He measured changes in basal and casual BP readings in relation to adrenalin and noradrenalin 24 hour urinary excretion rates of all expeditioners, prior to departure and then at monthly intervals for a year on the Antarctic Continent.

Initially, the mean noradrenalin level rose significantly on arrival in Antarctica, then it fell slightly to a level still greater than the pre-departure mean value. Bodey attributed these changes to cold acclimatisation, inducing increased non-shivering thermogenesis by means of raised noradrenalin.

Adrenalin excretion rates did not increase on arrival and, therefore, it is likely that some non-climatic factor may have influenced the rise in adrenalin excretion in the latter half of the year. Bodey cited previous studies that indicate that adrenalin is the catecholamine most likely to be increased by anxiety. Furthermore, anticipation (in this case, thoughts of the approaching home-coming) may be more anxiety-provoking than the event itself.

The low adrenalin excretion during the early Antarctic months excludes anxiety or anticipation as causes of the high noradrenalin excretion. Bodey concludes that noradrenalin plays an important part in adult human cold acclimatisation.

BP studies by Bodey showed casual systolic BP to decrease gradually over the winter then increase towards the end of the year. However, as this is not a consistent finding in other Antarctic studies (Budd and Warhaft 1970, Boriskin 1973, Godwin 1983), it is again suggested that, non-climatic factors may also have varying influence on BP changes over the Antarctic year.

The effects of increased activity on plasma cholesterol levels is controversial: most studies claim there is no direct relationship between total cholesterol and exercise (Goldberg and Elliot 1985). However, earlier research may have failed to consider that HDL cholesterol consistently increases with exercise (Nakamura et al. 1983, Haskell et al. 1980). A reduction in LDL cholesterol with a concomitant HDL cholesterol elevation might occur without an observed change in total cholesterol,

although such changes would considerably alter cardiovascular risk. HDL cholesterol levels have a potent inverse relationship with CHD (Kannel 1983, Rhoads et al. 1976). Refer to Chapter 1 for more details.

Some prospective studies have documented decreased triglyceride levels after training both normal and hyperlipidaemic subjects. Holloszy et al.(1964) found a significant decrease in serum triglyceride after training, however, these changes were greatest immediately after an exercise bout and persisted for only two days after the exercise session. This finding was repeated by Thompson et al.(1980), who found reductions in triglyceride of trained men after a 42 km race, which persisted for at least 2 days after the event. However, other studies have failed to show exercise can lower plasma triglyceride levels. Lipson et al. (1980) followed a group of sedentary men for a year and failed to show reductions in plasma triglyceride after exercise conditioning. Exercise studies using hypertriglyceridaemic subjects have shown significant reductions in total triglyceride levels, however, final levels are frequently still greater than the recommended maximum of 2.0 mmol/l (Gyntelberg et al. 1977).

Alexander (1984) documented the effects of aerobic training on carbohydrate metabolism as follows: lower fasting insulin levels; lower insulin levels in response to carbohydrate load; increased insulin binding to cells; earlier shift to free fatty acids during exercise; improved carbohydrate tolerance in diabetics. Glucose tolerance remains normal despite lower fasting insulin levels. As for other risk factors, the degree of benefit and duration of effect is yet to be determined.

Jennings et al. (1986) found that insulin sensitivity rose by 27% following exercise three times a week, but declined to sedentary levels with daily exercise. They concluded there may be an optimal level of activity, and there may be a need for rest days.

Interest has rekindled in recent years in the seasonal variation seen in BP. The Medical Research Council (1982) studied the BP and heart rate changes of 17 000 men and women with mild hypertension over a five year period. A distinct seasonal pattern emerged with BP higher in the winter than the summer. Heart rate showed no consistent seasonal variation.

However, Antarctic researchers have found inconsistent seasonal trends in the Antarctic. Lugg (1973) recorded casual and basal BP over the polar year and found a significant decrease over the winter months. Similar observations have been made under constant conditions by Soviet physicians (Boroskin 1973) in the Antarctic.

This study examined the effects of varying amounts of physical activity in a randomised controlled study repeated three times over the polar year with its consequent varying levels of background activity; the changes in BP, heart rate, plasma lipids and glucose tolerance were compared with increases in physical fitness.

Casual systolic and diastolic BP and pulse rate measurements were made monthly to be compared with those of expeditioners not participating in the study.

3.2 METHOD

Thirteen volunteers from the Australian National Antarctic Research Expeditions (ANARE) volunteered for a three part study to be done during their year at Davis Station (66°35'S, 77°58'E). The subjects were Australian Caucasian males; their mean age was 36 years (range 24-49), mean height 181 cm (173-186), mean weight 83 kg (59-106), mean Quetelet index 25 (22-31) (Table 3).

The non-participators are the 10 expeditioners who did not volunteer for the exercise study. They underwent no structured exercise regimen. They in no way participated in the study, however they did undergo monthly physiological examinations, described above. This is summarised in Figure 5 and 5a.

Prior to the start of the study, the 10 subjects underwent a familiarisation period, during which the BP monitor (see Chapter 2) was worn for 24 hours. On arrival in Antarctica, each subject carried out three different levels of activity for three weeks each, successively.

Table 3. Physical details of the 10 subjects, the 10 non-participators and each groups' means. The non-participators are the 10 expeditioners not involved in the study.

Subjects code	Age yrs	Height cm	Total weight kg	Quetelet body Mass index $wt/(ht)^2$
1	42	178	88	24
2	28	186	106	31
3	38	175	79	28
4	42	184	79	23
5	32	173	59	20
6	27	184	92	27
7	44	183	93	28
8	24	175	81	26
9	51	186	76	22
10	35	182	77	23
Mean:	36	181	83	25
Non-participators				
11	41	172	69	23
12	26	180	69	21
13	40	177	81	26
14	36	184	95	28
15	49	183	87	26
16	35	182	77	23
17	28	167	60	22
18	36	171	79	27
19	53	173	85	28
20	27	178	71	22
Mean:	37	177	77	25

A randomised balanced method was used. The order in which the activity levels were done was determined by a 3 x 3 Latin square. The activity levels were: 'minimum', during which subjects added no exercise to their usual level of activity; 'medium' required 40 minutes of aerobic exercise at 60-70% of maximum work capacity (Wmax) to be done three times a week; and 'maximum' required the same bout of exercise to be performed daily.

Subjects were allowed to use their preferred method of aerobic exercise, which included cross-country skiing, vigorous back-packing in snow, jogging or aerobics. However, most chose to use the cycle ergometer, exercising for 30 minutes at 60-70% of Wmax, with a 5 minute warm-up and a 5 minute cool down.

Subjects were asked to keep all factors other than physical activity constant. All food was prepared by the same chef throughout the year and the author was present at most meals. All subjects were remarkably constant in their dietary habits for any one season. Despite the gradual changes in station activity over the year, described below, the physical and social limits of a small and isolated research station ensured minimal disruption to daily routines (with the exception of the 'spring' program).

In order to determine the effects of different levels of background activity, three identical nine week programs were performed in 'summer', 'winter' and 'spring'. The Antarctic environment was ideal for this purpose, because the extreme variations in climate dictated, to a large degree, the level of activity possible. Refer to Chapter 1 for details of the changing lifestyle on a polar station. The design of the program is schematically represented (Figures 5 and 5a).

The 'summer' program commenced immediately on arrival on the Antarctic Continent, after a four week voyage on a polar vessel with very little opportunity for exercise. As the Antarctic summer is very brief, all expeditioners were expected to assist in the completion of outdoor projects.

Long and demanding working days were frequently followed by further outdoor activities late into the evening, to take advantage of the 24 hour daylight to explore on foot the numerous wildlife colonies that proliferate in the relatively mild summer weather. Walking 8-10 km in the evening was not unusual.

The 'winter' program commenced in May, when the polar winter was well advanced. Most work was confined to indoors with little need for regular physical exertion. The working day was shorter and the leisure time extended. This meant that both work and leisure activities were relatively less physically demanding during the winter. Nevertheless, all subjects chose to maintain some regular exercise as part of their routine. A major field expedition was planned for after the 'winter' study and all members were keen to be fit for field conditions and exercise daily, lasting 30-60 minutes. The colder weather (mean minimum temperature for July -23.1°C) necessitated that heavier clothing (up to 10 kg) was worn during outdoor activity.

In order to fulfil the criteria of differing the levels of activity during the 'winter' study, most subjects opted to maintain their usual activity as the 'medium' period and to decrease their activity during 'minimum' (explained above). This resulted in the winter minimum period being a time of truly sedentary behaviour, as opposed to the summer minimum period which necessitated a continuance of the moderately heavy work program. Relative increases in activity from minimum to maximum was the same for both summer and winter.

Month	Subjects	Non-participators
December	E.S.	
January	E.S. plus P.S.	P.S.
February	P.S.	P.S.
March	P.S.	P.S.
April	P.S.	P.S.
May	P.S.	P.S.
June	E.S. plus P.S.	P.S.
July	E.S. plus P.S.	P.S.
August	P.S.	P.S.
September	P.S.	P.S.
October	P.S.	P.S.
November	E.S. plus P.S.	P.S.
December	E.S.	P.S.

Figure 5. Plan of exercise study program.

P.S. = monthly physiological studies: BP, pulse rate, weight, temperature, skinfold thicknesses and arm circumference.

E.S. = exercise study as represented in Figure 5a.

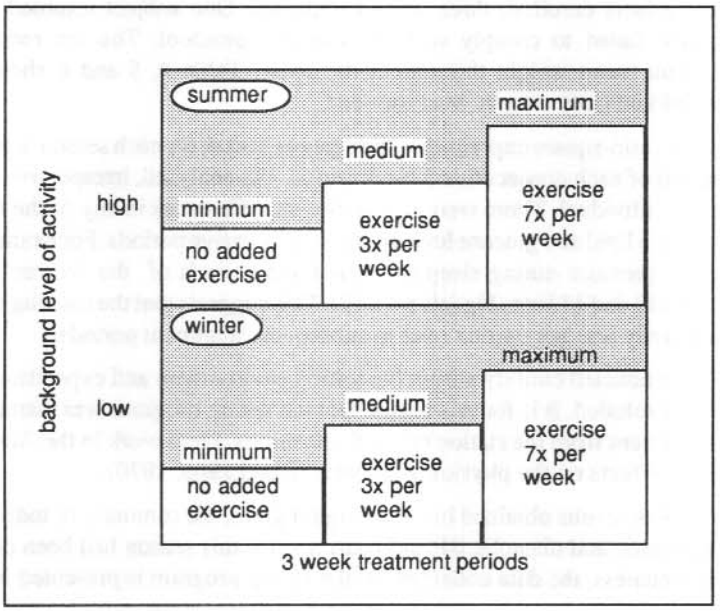


Figure 5a. Schematic representation of the exercise study design.

With the lengthening of daylight hours, outdoor activity during the spring season increased, and many expeditioners launched major field excursions for research or recreation. Due to a late re-scheduling of the station activities (see Chapter 1), the 'spring' study program had to be curtailed, as many of the subjects were absent from the station. Those that managed to complete part of the exercise program satisfactorily have been included in the study. However, the increase in cold stress and psychological stress known to affect field parties in polar conditions (Gunderson 1968) may be considered as confounding factors.

At the end of each three week period, subjects underwent a glucose tolerance test after a 12-13 hour fast overnight. Extra blood was taken in the fasting sample for plasma total cholesterol, HDL cholesterol and triglyceride (refer to Chapter 2 for method). No alcohol was consumed for 24 hours prior to the test. Following the test, breakfast was eaten and the 24 hour BP monitor was applied and recordings of systolic, diastolic BP and pulse rate were measured every half hour during the day, and hourly from midnight to 0600 h, giving a total of about 42 readings. The use of the monitor is described in Chapter 2. Weight was measured prior to exercise testing (VO_2max), which was measured after the other tests to avoid affecting results. The method of exercise testing is described in Chapter 2. Measurements were made 24 hours after the last exercise bout.

Throughout the year, monthly physiological measurements were taken of all twenty expeditioners, (i.e. including those not involved in the study) under constant conditions (see Chapter 2 for details). After a 30 minute rest, sitting BP and heart rate were measured. Body weight was recorded with subjects in underclothing only; arm circumference, and skinfold thicknesses were measured at four sites: biceps, triceps, subscapular and supra-iliac, according to Durnin and Womersley (1974).

3.3 RESULTS

Of the thirteen subjects enrolled, three were withdrawn. One subject returned prematurely to Australia, and two failed to comply with the exercise protocol. The ten remaining subjects maintained constant mean weight throughout the study. Table 4, 5 and 6 shows the monthly variations in individual body weight over the year.

The efficacy of the Latin-square experimental design was tested; for each season's program, BP and heart rate at the end of each consecutive 3 week period was analysed, irrespective of the period of activity in a given individual. There were no significant differences in any of the mean values for BP, heart rate, plasma lipid and glucose levels over the successive periods. For example, the average values for systolic pressure during sleep over the three periods of the 'winter' program were, respectively, 112, 112 and 113 mm Hg (all $\pm$ 4 S.E.). This suggests that the training effect of periods with increased activity was not carried over to subsequent treatment periods.

The studies were conducted entirely within the station environment and expeditioners involved in field studies were excluded. It is for this reason that the spring program was disrupted, as most of the subjects were absent from the station on field operations. Field work in the Antarctic is known to have significant effects on the physiological state (Budd 1965, 1970).

Due to the incomplete results obtained in the spring program, the summary of individuals' 24 hour mean values of systolic and diastolic BP and heart rate for this season had been omitted from the results. For completeness, the data collected for the spring program is presented in Table 7.

Table 4. Twenty-four hour mean values of all subjects for minimum, medium and maximum levels of activity for summer and winter systolic pressure.

SYSTOLIC PRESSURE						
	Summer			Winter		
Subject	Minimum	Medium	Maximum	Minimum	Medium	Maximum
1	122 ± 3	123 ± 3	140 ± 3	138 ± 3	116 ± 3	124 ± 3
2	149 ± 2	147 ± 3	144 ± 4	141 ± 4	141 ± 4	150 ± 3
3	119 ± 4	124 ± 2	134 ± 3	132 ± 3	132 ± 3	131 ± 4
4	117 ± 2	118 ± 3	116 ± 3	116 ± 3	127 ± 3	131 ± 3
5	126 ± 2	125 ± 3	126 ± 2	131 ± 4	117 ± 2	123 ± 3
6	131 ± 3	136 ± 3	132 ± 3	143 ± 3	142 ± 5	120 ± 3
7	126 ± 2	123 ± 3	118 ± 2	117 ± 3	118 ± 3	115 ± 3
8	131 ± 3	127 ± 2	130 ± 4	134 ± 3	135 ± 4	136 ± 3
9	100 ± 2	104 ± 3	108 ± 2	120 ± 3	111 ± 3	104 ± 3
10	134 ± 3	126 ± 2	126 ± 3	124 ± 3	130 ± 3	146 ± 4
Mean ± SE	126 ± 3	125 ± 3	127 ± 3	130 ± 3	127 ± 3	128 ± 3

within each season: † - Significant at 0.05 ; * - Significant at 0.02; **- Significant at 0.01

Table 5. Twenty-four hour mean values of all subjects for minimum, medium and maximum levels of activity for summer and winter diastolic pressure.

DIASTOLIC PRESSURE						
	Summer			Winter		
Subject	Minimum	Medium	Maximum	Minimum	Medium	Maximum
1	80 ± 2	81 ± 2	93 ± 3	85 ± 3	75 ± 3	76 ± 5
2	105 ± 2	83 ± 2	80 ± 2	80 ± 4	86 ± 4	82 ± 4
3	77 ± 2	75 ± 2	81 ± 2	86 ± 3	77 ± 3	81 ± 3
4	81 ± 2	76 ± 2	77 ± 2	80 ± 3	85 ± 3	85 ± 3
5	82 ± 2	76 ± 2	77 ± 2	78 ± 4	70 ± 2	75 ± 3
6	81 ± 2	80 ± 2	78 ± 2	91 ± 3	93 ± 5	75 ± 3
7	89 ± 2	82 ± 2	83 ± 1	82 ± 3	81 ± 3	77 ± 6
8	80 ± 3	80 ± 2	78 ± 3	78 ± 5	77 ± 5	75 ± 3
9	74 ± 2	75 ± 2	75 ± 2	81 ± 3	78 ± 3	70 ± 3
10	82 ± 2	77 ± 2	76 ± 2	91 ± 3	93 ± 5	75 ± 3
Mean ± SE	83 ± 3	78 ± 3†	80 ± 2	83 ± 3	82 ± 4	77 ± 4**

within each season: † - Significant at 0.05; * - Significant at 0.02; ** - Significant at 0.01

Table 6. Twenty-four hour mean values of all subjects for minimum, medium and maximum levels of activity for summer and winter heart rate.

	HEART RATE					
	Summer			Winter		
Subject	Minimum	Medium	Maximum	Minimum	Medium	Maximum
1	84 ± 4	69 ± 2	87 ± 3	73 ± 3	74 ± 3	79 ± 3
2	80 ± 1	72 ± 2	74 ± 3	72 ± 4	74 ± 4	81 ± 4
3	67 ± 4	61 ± 2	67 ± 3	72 ± 3	69 ± 3	73 ± 3
4	78 ± 2	76 ± 3	76 ± 2	76 ± 3	77 ± 3	84 ± 3
5	80 ± 3	81 ± 3	71 ± 2	75 ± 4	73 ± 2	68 ± 3
6	73 ± 3	73 ± 4	61 ± 4	80 ± 3	74 ± 5	70 ± 3
7	96 ± 3	87 ± 3	80 ± 2	80 ± 3	75 ± 3	75 ± 3
8	69 ± 2	84 ± 3	65 ± 4	69 ± 3	72 ± 4	66 ± 3
9	87 ± 3	82 ± 3	85 ± 4	76 ± 3	71 ± 3	58 ± 3
10	87 ± 2	58 ± 1	77 ± 2	60 ± 3	63 ± 3	65 ± 4
Mean ± SE	80 ± 3	73 ± 3*	74 ± 3**	73 ± 3	72 ± 3	72 ± 3

within each season: * - Significant at 0.02; ** - Significant at 0.01

Table 7. Twenty-four hour mean values of all subjects for minimum, medium and maximum levels of activity for summer and winter systolic and diastolic pressures and pulse rate during the spring program.

	SYSTOLIC PRESSURE			DIASTOLIC PRESSURE			PULSE RATE		
	Min	Med	Max	Min	Med	Max	Min	Med	Max
1	126 ± 2	130 ± 2		82 ± 2	80 ± 3		77 ± 3	78 ± 4	
2	145 ± 3	147 ± 4		85 ± 2	83 ± 3		85 ± 4	78 ± 4	
3		169 ± 3	141 ± 3		98 ± 3	86 ± 3	64 ± 3	73 ± 4	
4		137 ± 3	147 ± 4		76 ± 2	85 ± 3	59 ± 2	71 ± 3	
5		124 ± 2	142 ± 3		75 ± 2	94 ± 3	70 ± 3	93 ± 4	
6		132 ± 3			88 ± 4			90 ± 3	
7		129 ± 2			78 ± 3			69 ± 3	
8		124 ± 3	135 ± 3		75 ± 3	86 ± 2		85 ± 4	88 ± 3
9		121 ± 3	112 ± 2		84 ± 3	75 ± 2		74 ± 3	74 ± 3
10	138 ± 3	133 ± 2		81 ± 3	79 ± 2		66 ± 4	68 ± 3	
Mean ± SE	136 ± 3	135 ± 3	135 ± 3	83 ± 3	82 ± 3	85 ± 3	76 ± 4	74 ± 3	80 ± 3

3.3.1 *Blood pressure*

The 24 hour BP monitor produced an average of forty-two readings per subject for each period. A sample of the daily readings for one subject is shown in Chapter 2. A facsimile of one subject's daily activity record is also shown in Chapter 2. It was seen that BP and heart rate recordings were taken throughout the subject's normal working day, and included readings from all activity levels from sleeping to walking to heavy work.

All ten subjects completed the summer and winter programs. However, due to a rescheduling of the expedition activities, only two of the three periods were completed in the spring program. All completed the 'spring' medium period, seven of the ten subjects did the maximum period, and three did the minimum period. Due to inadequate data, during the 'spring' program, most comparisons were done using only the summer and winter programs.

3.3.2 *24 hour means*

The effects of increasing amounts of exercise on systolic, diastolic pressures and heart rate were analysed. Table 8 shows the 24 hour mean values of all subjects for minimum, medium and maximum periods of activity for summer and winter. In general, there is a decrease in all three variables with increasing activity, with some exceptions.

There was no significant change in systolic pressure for both summer and winter programs. Significant falls were seen in diastolic pressure for both summer and winter. Only in summer were decreases seen in heart rate. Table 4 and 5 show the individual 24 hour mean values for the ten subjects for summer and winter.

There was marked variation in the range of activity over the 24 hour period, for the same subject on different test days and between subjects. There was also a marked difference in the range of activity between different programs. Consequently, subjects who wore the BP monitor on active days, or subjects who were habitually more active would have higher 24 hour mean values than their more sedentary counterparts.

The author used the activity records taken by the subject during the test to group the readings of BP and heart rate into eight levels of activity (described in Chapter 2). For convenience, these have been grouped to four levels of activity: 'sleep', 'sit', 'stand' and 'work'. These correspond to activity levels 1, 3, 4/5 and 6/7, respectively (as described in Chapter 2). Activity levels 2 ('lie awake') and 8 ('maximal exercise') have been excluded for insufficient data. BP and heart rate readings showed the expected increases over the activity levels of 'sleep', 'sit', 'stand' and 'work'.

3.3.3 *Effects of posture and activity*

In Figure 6, the three graphs show the effect of different levels of activity ('sleep', 'sit', 'stand' and 'work') on the mean values of systolic, diastolic pressures and heart rate. The periods designated 'medium' from the summer, winter and spring programs were used to compare the seasonal changes.

Between levels of activity, the rate of increase was greatest from sleeping to waking ('sit') with an average increase of 18 mm Hg and 16 mm Hg in systolic and diastolic pressures respectively, and 8 beats/minute in heart rate. With further increases in activity, the increase in systolic pressure and heart rate was reasonably linear, but diastolic pressure showed little further increase.

*Table 8. Twenty-four hour mean values of systolic, diastolic pressure and heart rate all subjects for minimum, medium and maximum levels of activity for summer and winter. Significant falls of the medium and maximum periods compared to the minimum period are denoted * ($p < 0.05$) and ** ($p < 0.02$) for summer and winter. In general, there is a decrease in all three variables with increasing activity, with some exceptions.*

	Systolic		Diastolic		Heart	
Period	Summer	Winter	Summer	Winter	Summer	Winter
Minimum	126 ± 3	130 ± 3	83 ± 3	83 ± 3	80 ± 3	73 ± 3
Medium	125 ± 3	127 ± 3	78 ± 3	82 ± 4	73 ± 3**	72 ± 3
Maximum	127 ± 3	128 ± 3	80 ± 2	77 ± 4**	74 ± 3**	72 ± 3

Between the seasons, there was an increase in most measurements from summer to winter and especially, spring. For both BP and heart rate, the differences between seasons were accentuated at the higher levels of activity. The 'sleep' values are consistently low with diastolic showing the least variation over the seasons.

Since level of activity was the strongest determinant of BP and heart rate, all data has been categorised into four levels of activity, as described in above. All further analysis is done within a given activity level.

3.3.4 Systolic pressure

Figure 7 compares the effects of periods of increasing exercise on the systolic pressure means for all subjects. Data from both summer and winter are represented. Separate graphs represent the four different levels of activity: 'sleep', 'sit', 'stand' and 'work'. The 24 hour means of each activity level for all subjects following the three test periods (minimum, medium and maximum) were compared.

Compared to the winter program, the summer program showed lower mean values at all levels and periods. Summer periods of higher activity, (medium and maximum) failed to lower further the systolic values.

At all levels of activity, systolic values following the winter minimum period were markedly higher than the summer minimum period.

Winter systolic values at all levels of activity showed falls following the medium and maximum periods, reaching significance for activity levels 'stand' and 'work'.

The winter periods of increased exercise (medium and maximum) achieved mean systolic values similar to those of all the summer program. For example, 'sleep' systolic pressure following the maximum period was 110 mm Hg (±4 SE) for both summer and winter.

Winter systolic values taken during higher levels of activity ('stand' and 'work') showed a greater absolute fall in mean values following periods of increasing exercise (i.e 'medium' and 'maximum'). For example, mean systolic pressure fell an average of 8 mm Hg (±3.2 SE) during 'stand' activity, when comparing the minimum and medium periods of the winter program. For 'work' activity, the fall in systolic pressure between minimum and medium periods was 20 mm Hg (±5.3 SE).

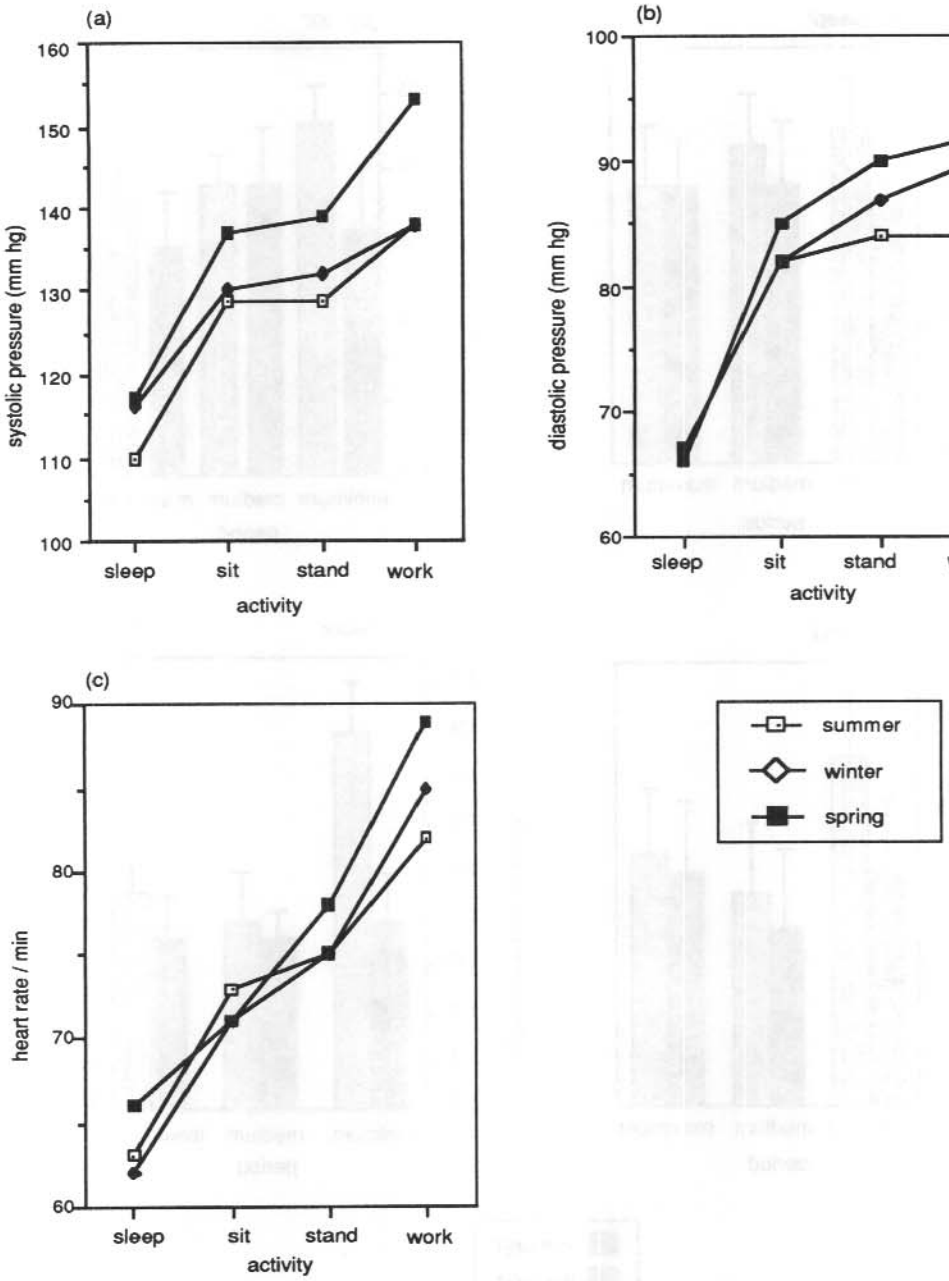


Figure 6. Changes in a) systolic pressure b) diastolic pressure and c) heart rate with increasing levels of activity. The results of the medium periods of summer, winter and spring are compared.

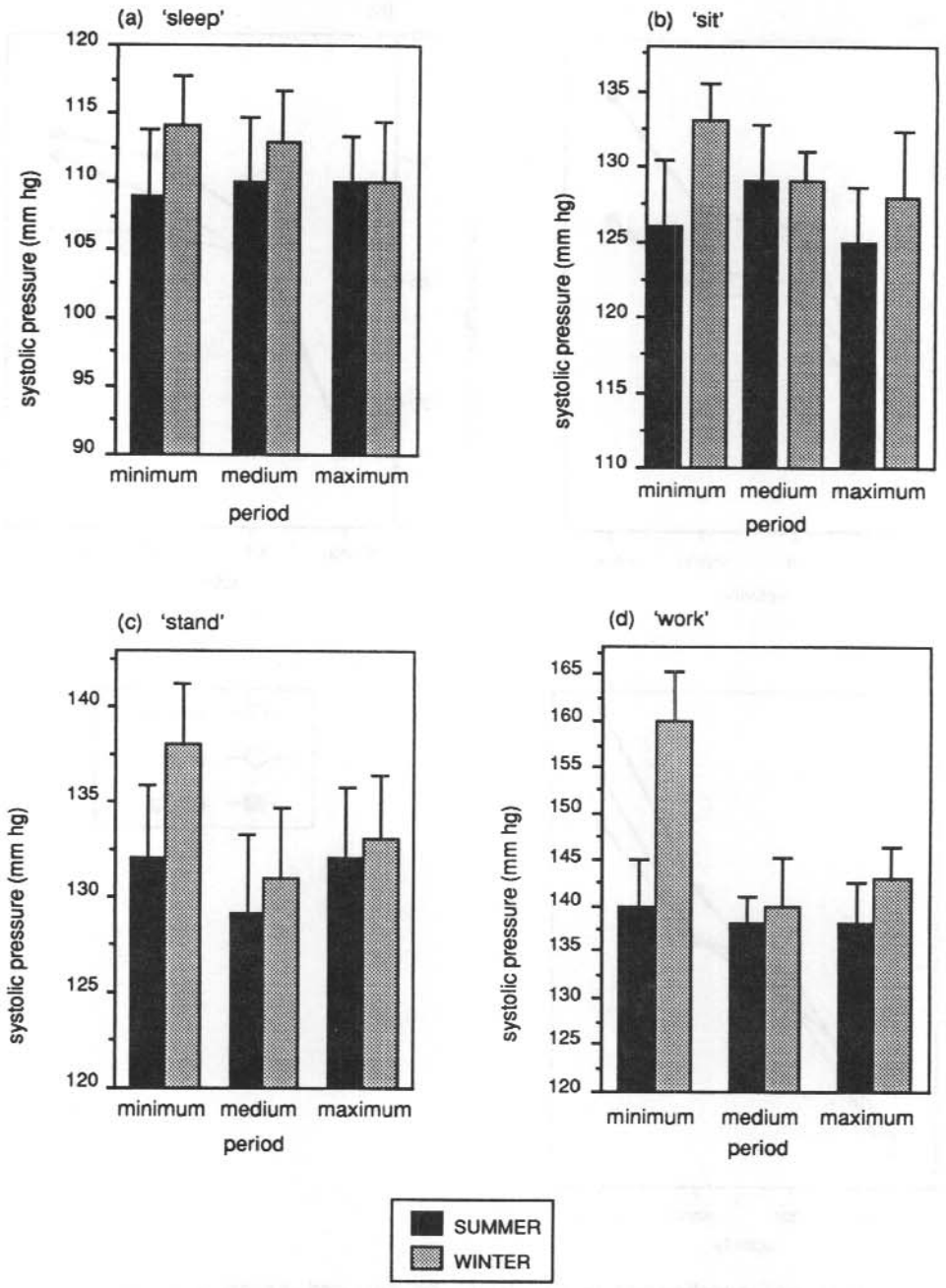


Figure 7. Effects of increasing levels of exercise on systolic blood pressure during a) sleep b) sit c) stand and d) work activities. Summer and winter programs are compared.

3.3.5 *Diastolic pressure*

At all levels of activity, the winter minimum diastolic mean values tended to be higher than those of the summer minimum period, but only reached significance ($p < 0.05$) for the 'work' level (Figure 8).

The summer diastolic values fell significantly following periods of higher activity (medium and maximum) for 'sit' and 'work', however, for both 'sleep' and 'stand' levels, the periods of increased exercise had no effect.

The winter readings showed a significant decrease from minimum to maximum periods at all levels of activity, except 'sleep'. The most significant decrease occurred between minimum and medium periods, with a small further decrease in maximum. There was no significant difference between medium and maximum at any level.

With the periods of greater exercise (medium and maximum) the difference between the summer and the winter decreased, with both seasons achieving similar low mean values following these periods. For example, the mean diastolic values for 'stand' were 84 ± 2 and 84 ± 1 (mm Hg $\pm$ SE) for summer and winter, respectively.

3.3.6 *Heart rate*

For both summer and winter programs, there was a fall in heart rates between the minimum and maximum periods at all levels of activity (except for winter sleep values, which did not change) (Figure 9). The most significant decreases occurred between minimum and medium periods, with a small further decrease in maximum. There was no significant difference between medium and maximum at any level.

In general, the winter values were lower than the summer values, without reaching significance. However, the fall in heart rate from minimum to maximum periods, is greater in the summer program than winter (9 versus 4 beats/min, respectively).

3.3.7 *VO_2 max*

Maximal oxygen uptake (VO_2 max) was measured following each test period to assess the effects of the varying levels of exercise, and to study the changes in VO2 max over the year. VO_2 max was estimated, using the method described in Chapter 2.

The range in VO_2 max for all individuals for the year was 2.19-4.58 litres O2/min. There was no correlation between age and VO_2 max.

There was a significant increase in VO_2 max from minimum to maximum periods in both summer and winter (Figure 10). Baseline VO_2 max levels, taken before departure in Australia were the lowest values recorded in the study. Winter VO_2 max values were significantly higher than summer levels for minimum and medium periods, but following the maximum period, summer approached the winter mean VO_2 max values.

Due to inadequate data, a full comparison of the three programs was not possible. However, by using results from the medium period, it was seen that VO_2 max improved markedly throughout the year, from a mean summer value of 3.59 ± 0.16 (litres O_2/min $\pm$ SE) reaching a peak in the spring program with 4.04 ± 0.12 (Figure 10a). The range of VO_2 max values between individuals was marked and the changes seen with increasing levels of exercise relatively small.

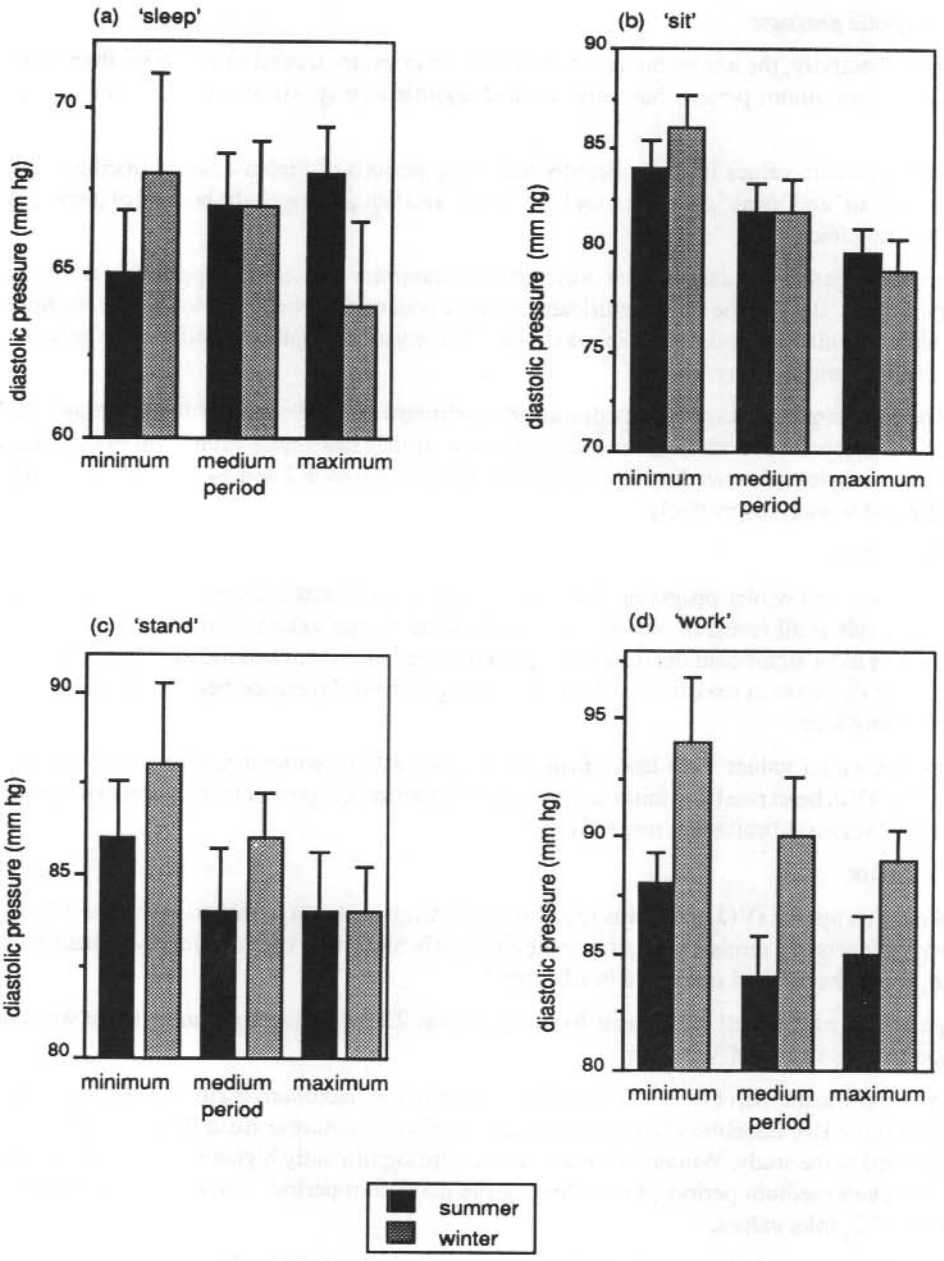


Figure 8. Effects of increasing periods of exercise on diastolic blood pressure during a) sleep b) sit c) stand and d) work activities. Summer and winter programs are compared. SEM are indicated by error bars.

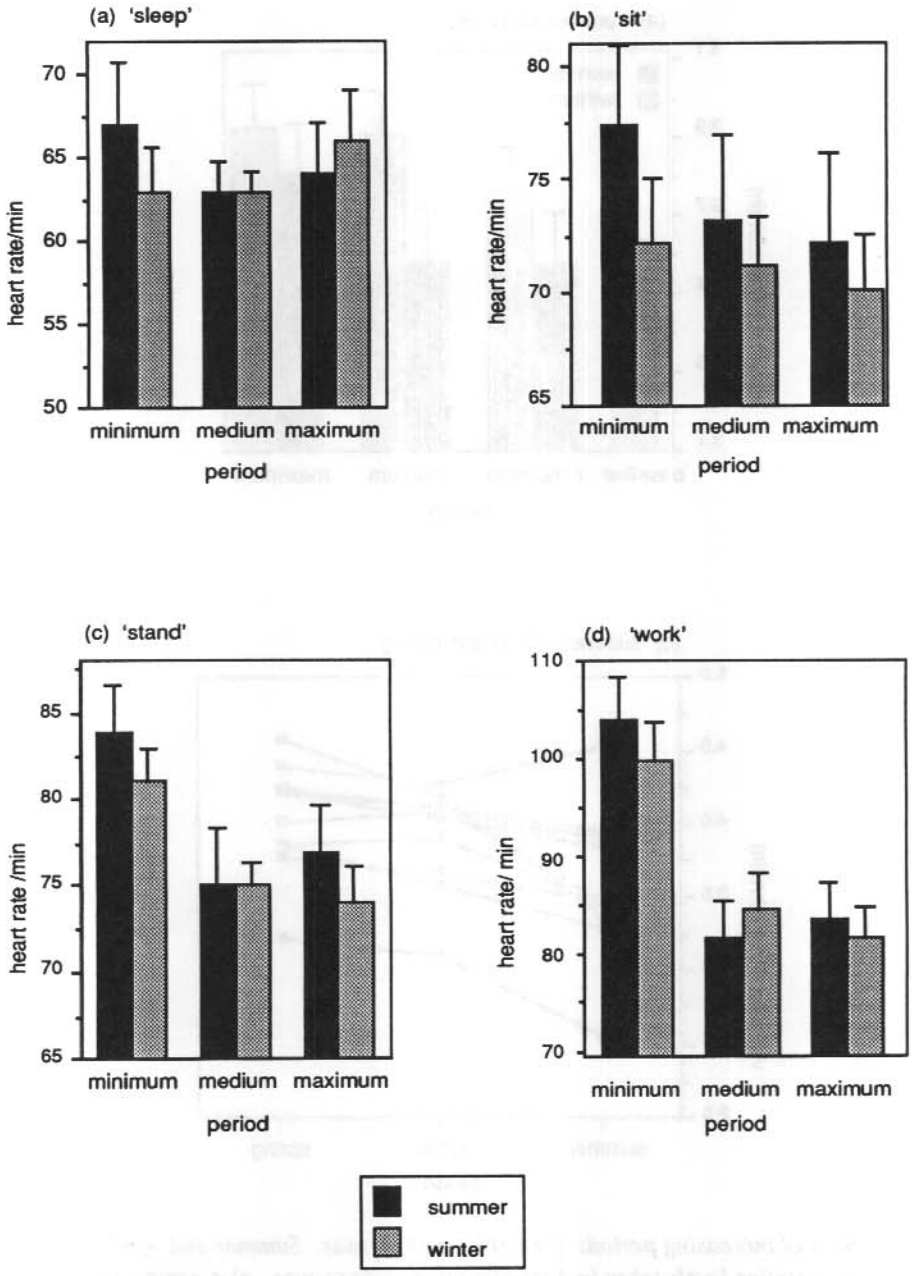
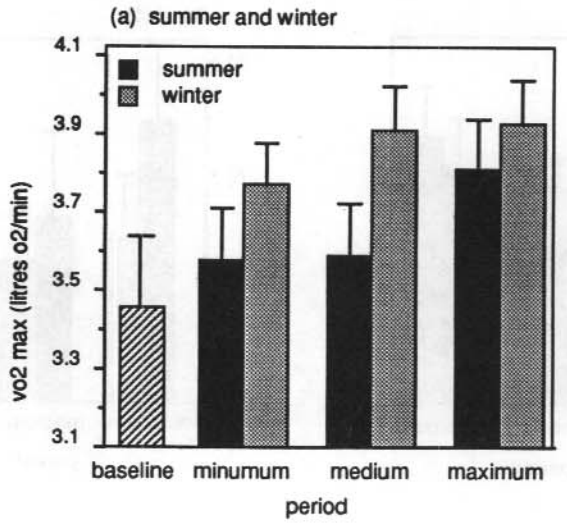


Figure 9. Effects of increasing periods of exercise on heart rate during a) sleep, b) sit, c) stand and d) work activities. Summer and winter programs are compared. SEM are indicated by error bars.



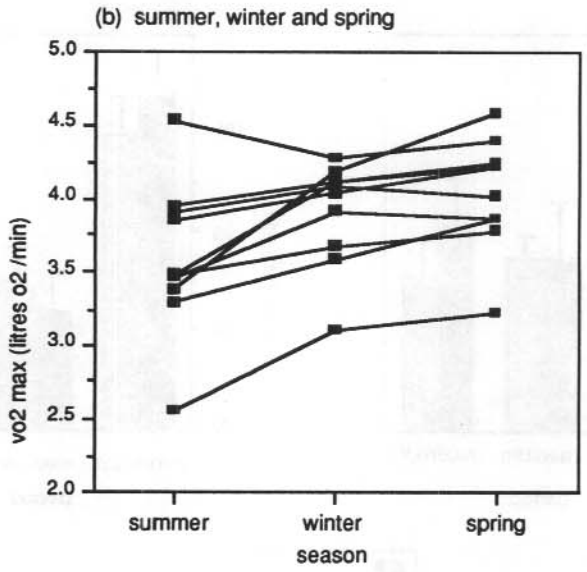


Figure 10. Effects of increasing periods of exercise on VO_2 max. Summer and winter programs are compared to baseline levels taken in Australia prior to departure. a) A comparison of the mean VO_2 max. for the medium periods of summer, winter and spring.

3.3.8 *Glucose tolerance*

All subjects maintained glucose tolerance within normal limits throughout the year. Mean fasting glucose levels ranged from 4.52 ± 0.16 to 4.90 ± 0.21 (mmol/l ± SE). Peak glucose levels occurred at 30 minutes during the summer program and for winter medium and maximum periods, however, for the winter minimum period, was delayed to 60 minutes.

Figures 11a and 11b showed the mean results of GTTs for the three periods of summer and winter, respectively. For both seasons, the mean values of the three periods were similar. The winter minimum period showed a peak mean value of 7.45 ± 0.79 delayed to 60 minutes and a retarded fall to a final value of 4.83 ± 0.46. Final values were similar following all three periods. The differences in area under the curves (∂AUC) analysis (Figure 11c) showed no significant difference over the summer program. During the winter program, minimum peak values were the highest for the year, but failed to reach significance.

Using the data of the medium periods, it was possible to compare the glucose tolerance over the entire year. Figure 11d shows the ∂AUCs of the medium periods. The first two programs were similar, while the lower value for the spring program failed to reach significance.

3.3.9 *Lipids*

Varying levels of exercise had no significant effect of plasma total cholesterol and triglyceride levels in the present study. Figure 12a shows the mean values of total plasma cholesterol for the summer and winter programs. Overall, the winter cholesterol level were significantly higher than summer, ($p<0.02$). The increasing levels of exercise in the minimum and maximum periods of both programs had no significant effect.

There was a 15% increase in plasma HDL cholesterol from the summer minimum period mean of 0.95 ± 0.06 mmol/l ± SE to the summer maximum period mean of 1.09 ± 0.09 mmol/l ± SE. No significant difference occurred between mean HDL values for the three winter periods (Figure 12b),. which, however, were significantly ($p<0.007$) higher than the summer mean. The maximum periods approached a similar value, the winter mean value being 1.10 ± 0.09. The resulting total cholesterol: HDL cholesterol ratio remained within a small range of values: 5.07-5.81 mmol/l, and showed no significant difference.

Triglyceride levels remained within normal range throughout the year; the range of mean values were 0.97 - 1.18 ± 0.11 (mmol/l ± SE). There was no significant change noted in the summer or winter programs (Figure 12c).

Table 9. Mean values of cholesterol, HDL cholesterol and triglyceride for Australian males, aged 25-34 years. (Data from the National Heart Foundation Risk Factor Prevalence Study, 1983).

Normal range for males (mmol/l ± SE)	age (years)	
	25-29	30-34
Total cholesterol (mmol/l)	5.1	5.3
HDL cholesterol (mmol/l)	1.28	1.26
Triglyceride (mmol/l)	0.98	1.12

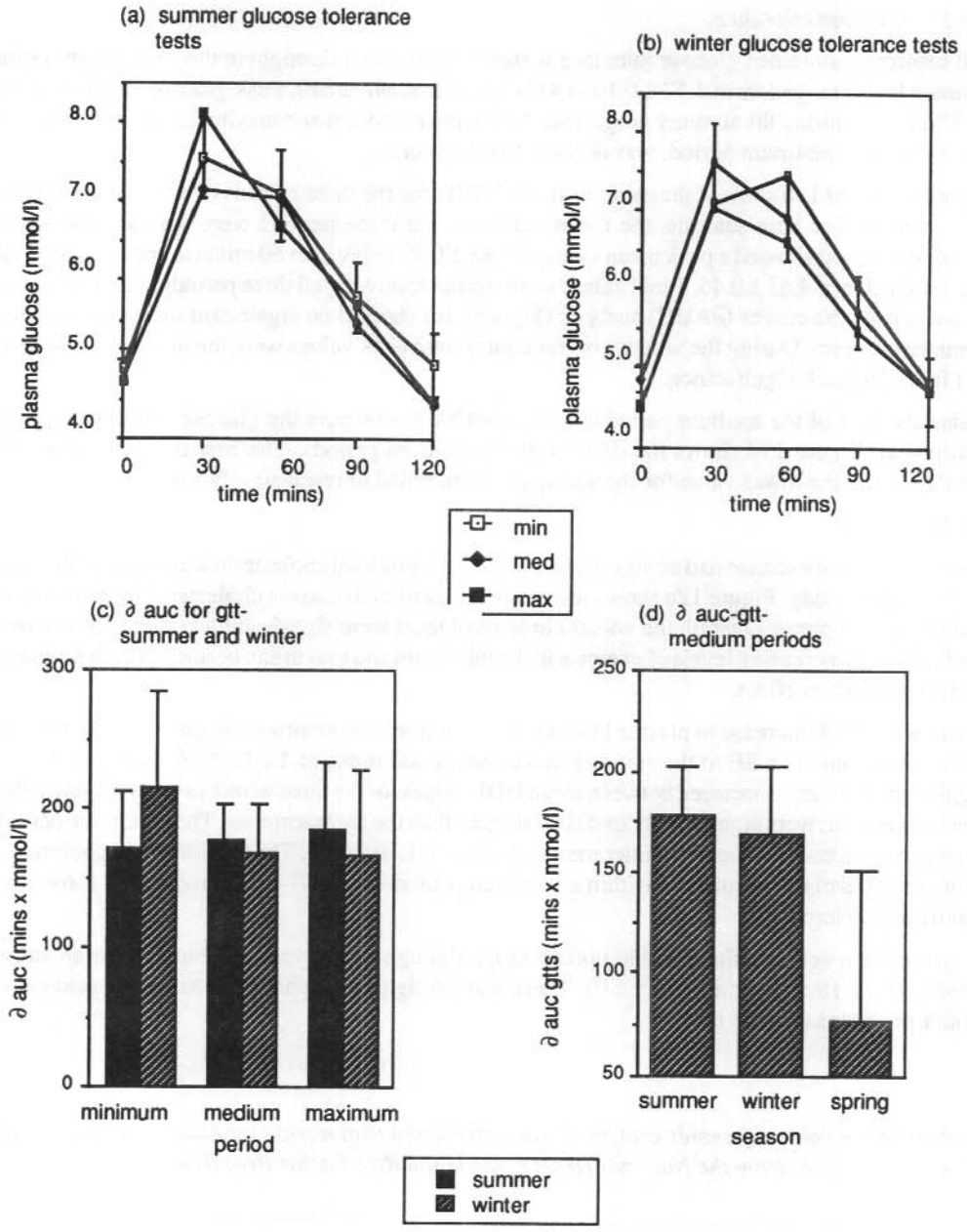


Figure 11. The effects of increasing levels of exercise on glucose tolerance during a) summer b) winter c) the change in area under the plasma concentration x time curve (∂AUC) for summer and winter d) a comparison of the ∂AUC's for summer, winter and spring medium periods.

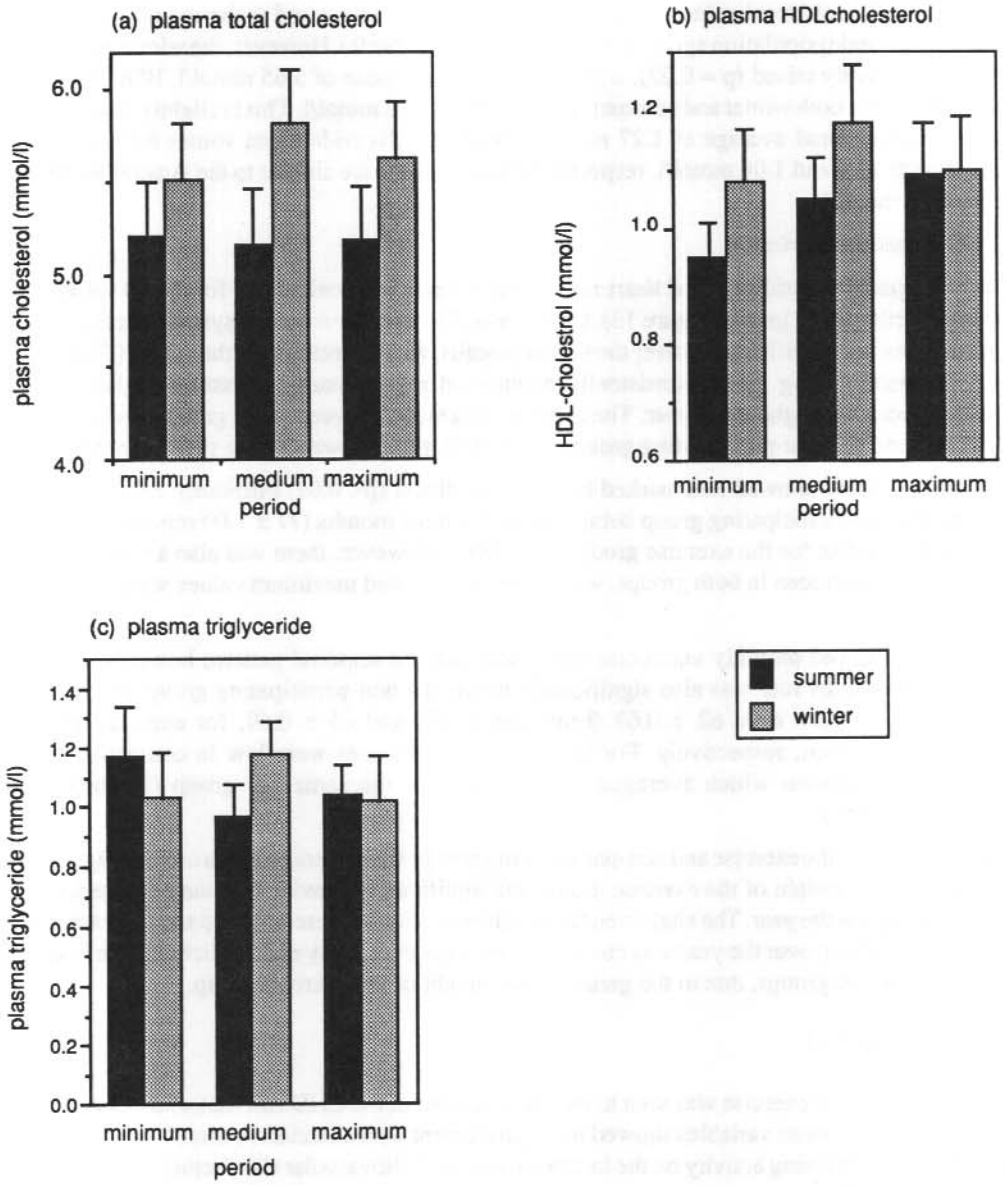


Figure 12. The effects of increasing levels of exercise on a) total cholesterol b) HDL cholesterol and c) triglyceride. A comparison of summer and winter programs are made. Standard error is shown.

Summer total cholesterol values were within normal range, compared to the mainland Australian values in the male population aged 25-34 years for 1983 (Table 9). However, the winter mean values were significantly raised ($p = 0.02$), with a winter overall mean of 5.65 mmol/l. HDL cholesterol mean values for both winter and summer were similar at 1.12 mmol/l. This is slightly lower than the Australian mainland average of 1.27 mmol/l. Plasma triglyceride mean values for summer and winter were 1.06 and 1.08 mmol/l, respectively; these means are similar to the Australian range of 0.98- 1.12 mmol/l.

3.3.10 Seasonal variation

The averages of monthly BP and heart rate measurements were calculated for the 10 subjects and the non-participating group (Figure 13). Casual monthly measurements of systolic pressures show a gradual but not significant fall over the winter months, with an increase in the spring (Figure 13a). The non-participating group consistently maintained mean systolic pressures higher than the exercise group throughout the year. The average difference between study group (126 ± 0.96 mm Hg $\pm$ SE) and the non-participating group (131 ± 0.62 mm Hg) was highly significant ($p = 0.00$).

Diastolic pressure showed less marked but still significant ($p < 0.02$) difference between the two groups, the non-participating group being higher for most months (77 ± 1.00 mm Hg), compared to the yearly mean for the exercise group (75 ± 1.00). However, there was also a non-significant seasonal variation seen in both groups, with a winter nadir and maximum values seen in spring for both groups.

Heart rates showed monthly variations with a less defined seasonal pattern; however, the study group's mean heart rate was also significantly below the non-participating group's ($p = 0.003$). Yearly mean values were 62 ± 0.62 (beats/min $\pm$ SE) and 65 ± 0.69, for exercise and non-participating groups, respectively. For both groups, heart rates were low in comparison to the Australian population which averaged 73 beats/min for the same age group (National Heart Foundation, 1983).

Body weights for the exercise and non-participating groups were averaged each month (Figure 13d). The mean body weight of the exercise group was significantly heavier than the non-participating group throughout the year. The slight trend to weight reduction in exercise group and increase in non-participating group over the year was not significant. However, body mass indices (Table 3) did not differ for the two groups, due to the greater mean height of the exercise group.

3.4 DISCUSSION

Increasing levels of exercise was seen to benefit a number of the CHD risk factors measured in this study. However, some variables showed no improvement with exercise. A useful way to illustrate the effects of increasing activity on the improvement of cardiovascular risk factors is the sigmoidal curve (Figure 14).

It is likely that there is an optimal amount of exercise, beyond which there is no further benefit for reducing that risk factor. It is also likely that the optimal level is different for each risk factor (i.e. it will cause a shift or a flattening in the sigmoidal curve). The following discussion will examine each variable of this study and attempt to determine its optimal level of exercise. The contrast of effects of the summer and winter programs is significant. During the busy Antarctic summer period, all subjects were actively employed outdoors in physical activities. Long work hours were followed by continued activity in the evening, taking advantage of the 24 hour daylight to visit on foot the extensive wildlife colonies.

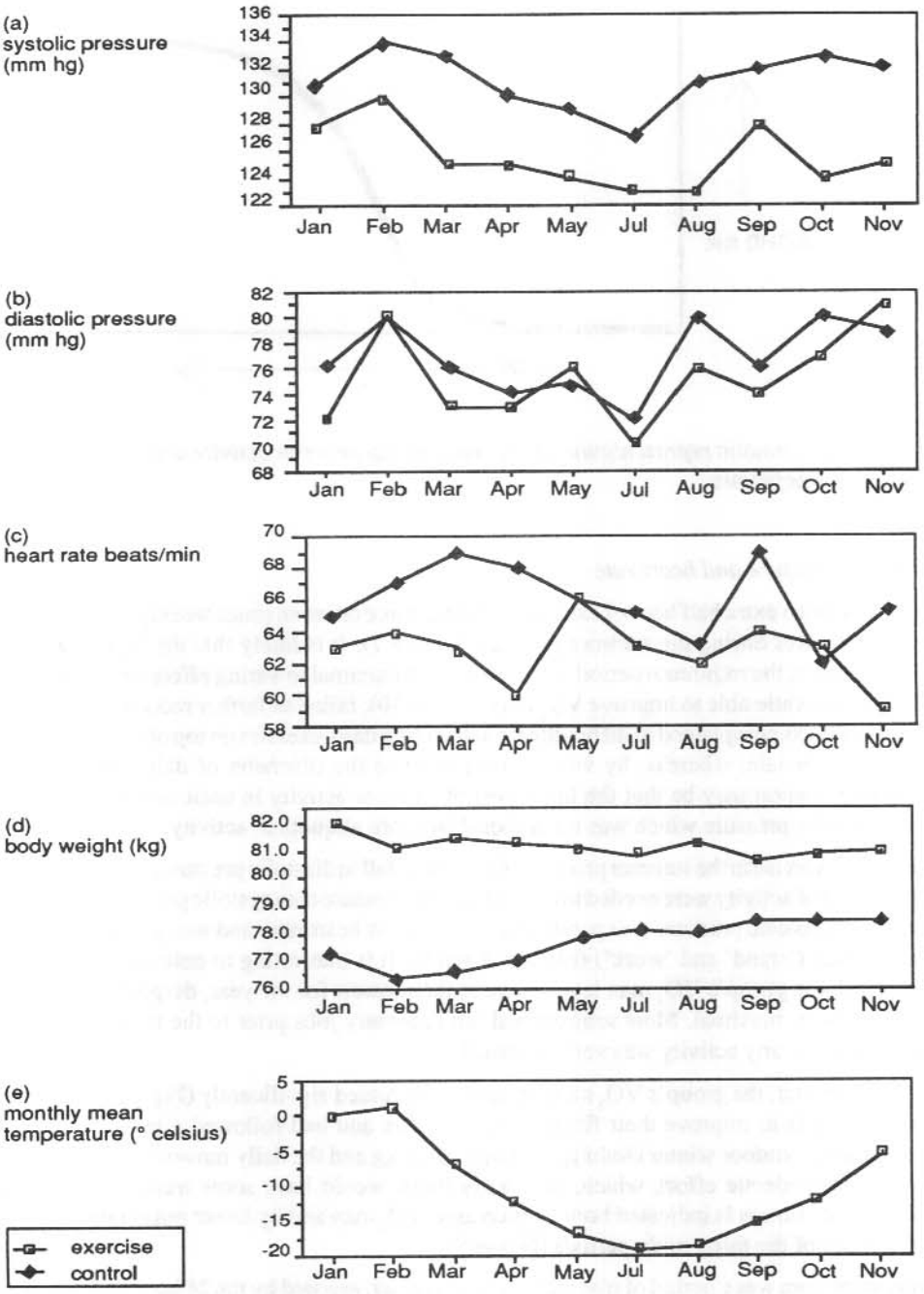


Figure 13. Monthly changes in a) systolic pressure b) diastolic pressure c) heart rate and d) body weight in 'exercise' group - participating in the exercise study and 'control' group - remaining expeditioners e) mean monthly temperature.

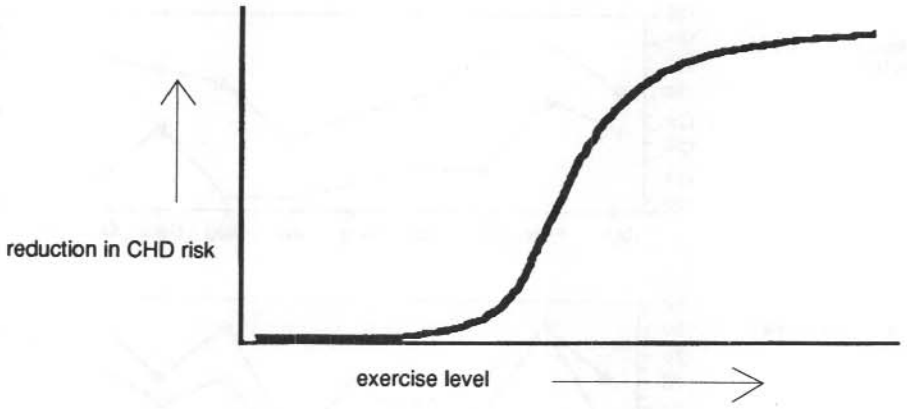


Figure 14. Diagrammatic representation of the relationship between activity and cardiovascular risk factors.

3.4.1 Blood pressure and heart rate

The imposition of an extra half hour of exercise (whether three or seven times weekly) had no effect on systolic pressures during the summer program (Figure 7). It is likely that the high degree of activity even during the minimum period of summer had a maximal lowering effect on systolic BP. Further exercise, while able to improve VO_2 max (Figure 10), failed to further reduce systolic BP. In fact, most subjects complained of difficulties in scheduling daily exercise on top of the demanding summer work schedule; whereas, by winter, most enjoyed the diversion of daily exercise. An alternative explanation may be that the high level of summer activity in unfit subjects led to an increase in systolic pressure which was not affected by more aliquots of activity.

The increase in exercise in the summer program did lead to a fall in diastolic pressure, which suggests that higher levels of activity were needed to effect diastolic pressure than systolic pressure. The level of reduction in diastolic pressure was paralleled by the fall in heart rate, and was greater at higher levels of exertion ('stand' and 'work') (Figures 8 and 9). It is interesting to note that, during the summer period, the group's VO_2 max levels were at their lowest for the year, despite the fact that activity levels were maximal. Most subjects had left sedentary jobs prior to the month's voyage south, during which any activity was very restricted.

In contrast, by winter, the group's VO_2 max values had increased significantly (Figure 10). All ten subjects had sought to improve their fitness since summer and had followed a regular exercise schedule. As well, outdoor winter clothing weighed 10-15 kg and the daily movements around the station required moderate effort, which, on a daily basis, would have some training effect.The improved level of fitness is indicated both by increased VO_2 max and by lower pulse rates at most levels of activity of the three study periods (Figure 9).

The winter minimum was a period of true sedentary behaviour, assisted by the 24 hour darkness and the cessation of most outdoor work and hence physical exertion. This is a common finding in the Antarctic. Norman (1965) reported that time spent outdoors fell from 13% of the day in the summer, to just 5% in the winter months. Despite mean VO_2 max levels being higher during the winter

minimum than the entire summer period, the randomised distribution of the exercise periods help to show that the 3 weeks of inactivity is sufficient to cause the mean VO_2 max value to fall only a small but significant amount, but to markedly elevate systolic and diastolic pressures at all levels of activity (Figures 7 and 8). Winter minimum systolic and diastolic values were the highest of the entire study, and occurred after the period of least activity.

The present study showed that the major determinant of BP was the level of activity in the three weeks prior to testing, rather than VO_2 max. Although it is likely that regular exercisers are the fitter members of society, there may be many exceptions. It is concluded that accurate assessments of activity would be a more suitable indicator of cardiovascular health.

This is supported by evidence from a large Belgian study. De Backer et al. (1981) interviewed 1513 men about their work and leisure time activity and simultaneously measured their fitness levels. They showed that, although both job and leisure time physical activity correlated with physical fitness, both activity scores accounted for only 2% of the variance in physical fitness.

Haskell (1985) has stated that 'physical activity can improve both physical fitness and clinical health status, but the improvement in health may be due to biologic changes different from those responsible for the improvement in fitness.' Observations made in the preceding paragraphs would suggest that activity itself, rather than fitness level, causes a decrease in BP. Fitness, or at least VO_2 max, may therefore be seen as simply another product of increased activity and the mechanism by which increased activity leads to reduced BP is unknown. (If this is so, changes in VO_2 max have a different time course from changes in BP following activity).

The increase in VO_2 max following the winter medium and maximum periods, indicate a rise in activity that was accompanied by significant falls in systolic and diastolic BP. By the maximum period, the winter systolic and diastolic values reached levels similar to those of the entire summer program. These results suggest the following conclusions: firstly, that the individual whose work or leisure activities guarantee moderate, regular physical exertion is unlikely to benefit from further activity, at least in regard to BP levels. Conversely, a truly sedentary individual needs regular daily exercise for brief periods to gain the same benefits. Furthermore, as these changes took place over a three week period, the benefits seem to be as quickly gained as they are lost.

Although there was a gradual increase in VO_2 max levels seen over the year (Figure 10a), these were modified only slightly by the three week periods of varying exercise levels. This suggests that some factors that are affected by training are maintained for long periods, despite the cessation of training (e.g. during minimum periods). On the other hand, the fact that a decrease in VO_2 max is seen after only three weeks shows that some improvements are quickly lost if regular training is not maintained.

Since changes in BP correlated with the small and rapid changes in VO_2 max that occurred with the three week training, it can be deduced that the short-term changes in the cardiovascular system, that cause improved VO_2 max, are possibly the same factors that favourably alter BP levels.

Cullinane et al. (1986) measured VO_2 max, cardiac size, resting BP and heart rate of male distance runners and found no change 10 days after cessation of exercise. However, plasma volume fell 5% within 2 days of no exercise, with an equivalent fall in weight. It would have been interesting to have measured as well the many other factors likely to contribute to the lowering of BP with increasing levels of exercise.

Jennings et al. (1986) have noted that increasing levels of exercise led to a fall in total peripheral resistance and lower heart rate for a given load. Noradrenalin spillover rates were measured and showed that sympathetic neural activity was greatly reduced in subjects who regularly exercised. Similar observations have been made by others (Björntorp 1982). This may help to explain Bodey's (1971) finding that noradrenalin urinary excretion rates fell during the year on a polar station - regular physical exertion, mandatory on polar stations, will guarantee a training effect.

Training leads to an increase in the capillary density in skeletal muscle (Astrand and Rodahl 1977), which, in turn, increases the vascular conductance. Decreased heart rates at a given load will prolong diastolic run-off time; this, combined with the fall in total peripheral resistance may result in the lower diastolic levels seen especially with higher activity levels.

Duncan (1985) studied 56 men with mild hypertension and found reductions in BP following exercise were most pronounced in subjects who were hyperadrenergic. These subjects had mean falls in systolic pressure of 15.5 mm Hg, as compared to the non-participating group who fell an average of 6.3 mm Hg. He concluded that modification of BP by exercise is at least partially mediated by changes in catecholamine levels.

To return to Figure 14, it has been observed that while systolic changes were not seen over the summer program, decreases in diastolic pressure accompanied the increase in VO_2 max and fall in heart rate. It is postulated that factors that alter the systolic level are more a function of sympathetic activity (such as stroke volume, dv/dt and heart rate), which reach optimal effectiveness at moderately low levels of exercise. Diastolic pressure is in part a function of the total peripheral resistance, which, in turn, is partly determined by the cross-sectional size of the capillary bed. As Astrand and Rodahl (1977) stated, increasing physical fitness determines the capillary density. Therefore, it is feasible that diastolic pressure can continue to fall while fitness improves (i.e. while capillary density increases).

In other words, once a maximal fall in sympathetic function has been achieved by exercise, further falls in diastolic pressure will only be possible with exercise sufficient to improve fitness; that is, exercise effort and duration will need to be increased according to increases in VO_2 max. This may help to explain why a number of studies have shown changes in systolic and not diastolic pressures, or vice versa (Boyer and Kasch 1970, Bonanno and Lies 1974, Choquette and Ferguson 1973).

Individual VO_2 max levels remained within a relatively small range, (despite an overall increase) over the year. On the other hand, there was a broad range of VO_2 max (Figure 10a) within the group, suggesting that natural endowment is a major determinant of VO_2 max. The highest group mean value for VO_2 max for any period over the year was recorded at 4.12 litres O2/min (± 0.38 SD), following the maximum period in spring. Similar observations have been made by other Australian Antarctic researchers (Dick 1985, Williams 1986) Untrained Australian males of similar age have a mean VO_2 max of 3.22 litres O2/min (range 2.21-4.50), according to Telford et al. (1978). From this can be said both that the Antarctic environment 'selects' those with a higher than normal level of fitness, and that the environment is conducive to significantly increasing that level, with regular moderate exercise.

There was no correlation between an individual's VO_2 max and his BP level. Although it is the author's impression that those subjects with the lower BP recordings belonged to the group that were more regular exercisers, there were a few exceptions and larger numbers would be needed to determine whether fitness or activity is the major determinant of lower BP after training. Of anecdotal interest is one subject, who spent some hours in the gym every day; although he would

routinely use the cycle ergometer for an hour or more, much of this time was spent doing isometric exercises (occasionally lifting more than 50 kg). His resting systolic pressure was one of the highest in the group throughout the year, despite being both the youngest (24 years) and the fittest (VO_2 max 4.58 litres O2/min).

A plateau effect was seen in the winter VO_2 max levels with few subjects able to achieve levels greater than 4.0 litres O2/min (Figure 10). This is not surprising given the brief training period (three weeks) and the duration of each training period (a maximum of 30 minutes daily). Further regular exercise continued to have a training effect, and by spring the group's VO_2 max levels were again improved (Figure 10a).

Inadequate data from the spring period prevented a full comparison of seasonal changes. However, using the medium periods, it is clear that despite the maximal levels of VO_2 max attained in the spring period (Figure 10a) and a high level of activity due to a demanding work program, there were significant increases in systolic and diastolic BP at all levels of activity except 'sleep' (Figure 6).

Unlike the first two programs that progressed without disruption, the spring period was fraught with schedule disruptions, due to frequent field trips involving, at different times, all subjects (see Chapter 1). For this reason, all subjects managed to complete only two of the three exercise periods, and frequently commenced training immediately on return from field trips, or were preparing for departure during an exercise period.

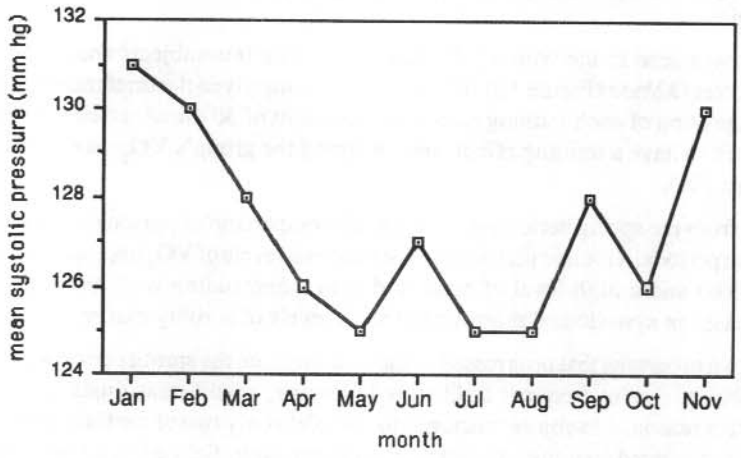
Budd (1965) was one of the first to report elevated BP readings in polar expeditioners preparing for departure on field trips, and attributed it to psychological stress. Factors contributing to the stress include an increase in perceived risk, poor task definition, limited availability of search and rescue and medical support and unknown variables such as weather, ice conditions, vehicle reliability.

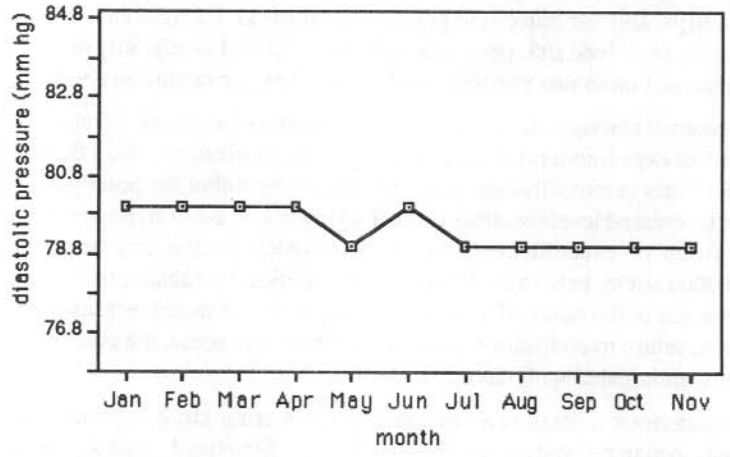
It is commonly accepted among polar researchers that the end of a year of isolation is the period of highest stress for most expeditioners (D. Lugg, personal communication 1985). Bodey (1971) found adrenalin excretion rates in expeditioners were greatest at the end of the polar year. Hicks (1967) similarly observed increased levels of stress in the final months of the year, however, stated that with a well-adjusted group of expeditioners, life at an ANARE station can be singularly free of occupational and other stress. In both his 1963 and 1965 studies, this absence of stress was reflected in the gradual decrease in the basal BP during the year, with a terminal increase to normal values during the spring, as return to civilisation became imminent. For some, the potential hazards of the return voyage were anticipated with anxiety as well.

Williams (1986) undertook a detailed assessment of a wintering group's psychological status on another Australian Antarctic station similar to Davis. Statistical analysis of the results of questionnaires given to the expeditioners showed an almost universal increase in stress levels during the spring period. Similar findings have been reported in other isolated groups, including prisoners and military personnel, where the anticipation of problems in returning to society, looking for work, financial decisions, readjustment to family and friends is a source of considerable stress. This is supported by studies of casual and basal BP and heart rate measurements, routinely taken on all Antarctic stations on a monthly basis. Most years have shown a significant rise in BP and heart rate between winter and spring (see Table 10).

On the basis of the above, it is possible that the BP lowering effect of moderate activity, that was seen in summer and winter programs, was counteracted by the pressor effect of psychological stress during the spring period. Although not directly measured in this study, it is suggested that increased sympathetic function associated with stress contributed to the elevated BP and, perhaps more

Table 10. The monthly mean systolic and diastolic pressure of expeditioners from Mawson station 1977-83 and Davis station 1980-83.





significantly, heart rate (Figure 6). In other words, if the hypotensive effect of exercise relates in part to the reduction of sympathetic neural activity, it seems possible that psychological stress can counteract it by the same pathways.

3.4.2 Glucose tolerance

Population mean fasting glucose levels for Australian males of age 25-35 years is 4.8 mmol/l (National Heart Foundation of Australia 1983), which is similar to findings throughout the present study. However, provided the fasting glucose level is below the recommended upper limit of 6.5 mmol/l, little can be concluded from variations below this limit. This is because the fasting glucose is affected by several factors acting immediately prior to sampling, such as basal metabolic rate, age, body fat content, preceding amount of exercise, duration of fasting period.

However, the glucose tolerance test is a more sensitive test of carbohydrate metabolism. In the present study, glucose tolerance remained well within the normal limit throughout the year. However, following the period of least activity, the winter minimum period, there was a delayed peak and fall in glucose levels, which failed to reach significance (Figure 11b). A number of studies have shown improved glucose tolerance with increased exercise, especially among those subjects with poor glucose tolerance initially, (Björntorp and Krotkiewski 1985). It is postulated that activity levels would need to have been significantly lower than occurred in the present study to produce abnormal glucose tolerance in the normal subjects.

Campbell (1977) did demonstrate significantly decreased glucose tolerance between during winter tests at the British underground station of Halley Bay. Winter climatic conditions at Halley Bay are significantly harsher than those at Davis, and it is possible that this forced the British expeditioners to remain indoors and inactive more frequently.

How exercise effects a sustained increase in glucose tolerance is uncertain. Exercise has an acute insulin-like effect, which lowers plasma glucose, presumably by increasing sugar transport over the muscle cell membrane (Björntorp et al., 1970). It cannot be excluded that such acute effects remain effective in the post-exercise stage, hence reducing the levels of insulin necessary to achieve normal plasma glucose. Lower catecholamine levels may have a role in the glucose- insulin interplay (Duncan et al. 1985).

The Australian incidence of abnormal glucose tolerance is around 2% of the population (National Heart Foundation 1983). The cost of diabetes to society is extensive: mortality excessive by a factor of 2-3; heart disease and stroke excessive by a factor of 2-3; blindness ten times more common than in the general population; gangrene and amputation about twenty times more common than in the general population; second leading cause of fatal kidney disease; other costs to society include costs of medical services, pensions, and loss in productivity and earnings due to both disability and premature death (WHO Expert Committee on Diabetes Mellitus 1980).

From the present study, it is concluded that increases in daily exercise levels in already active, healthy individuals is unlikely to have effect on glucose levels.

3.4.3 Lipids

Increasing levels of activity had no effect on total cholesterol during the summer and winter programs (Figure 12a). However, winter mean values are consistently higher than their summer equivalents. There is no evidence in this study to suggest that exercise has a direct effect on total cholesterol. To refer to the sigmoidal curve (Figure 14), it is not clear from this study whether the level of activity used correlates with the top or bottom of the curve — or not at all.

There is little evidence, from either epidemiologic or prospective investigations, that there is a direct is little evidence, from either epidemiologic or prospective investigations, that there is a direct relationship between exercise and cholesterol concentrations (Goldberg and Elliot 1985). Some studies that have shown lower cholesterol levels in the active have failed to account for body weight and other influences (Cooper et al. 1976, Martin et al. 1977).

Seasonal variation in lipid levels has been reported by several workers (for a review of the literature, see Fager et al. 1982, Kritchevsky 1985). Kritchevsky noted that although there was a trend to higher cholesterol levels during the colder months, there was considerable variation, both intra-individually and between studies. He concluded that psychological factors may be a significant determinant. Due to the lack of stress during the polar winter, psychological factors are unlikely to have contributed to the higher cholesterol levels.

Change in diet is a likely factor. During the summer, the frequent arrival of ships brought to the station fresh supplies, and there was a high proportion of fruit, salads and vegetables in the diet, compared to the winter, when all food was either canned, frozen or dried. In the winter, most expeditioners chose to eat less fibre and complex carbohydrate, finding the meat dishes more palatable. Consequently, large proportions of beef and lamb were eaten twice daily. It is clear the amount of dietary saturated fat and cholesterol was very high in the winter. Daily cholesterol intakes in winter were estimated to be averaging 715 mg per day, with 50-55% of energy intake from fat (refer to Chapter 1 for more detail), that is, a 30% increase in dietary cholesterol and 5-10% increase in saturated fats in the winter diet. Dietary saturated fat and cholesterol (Edington et al. 1987) increases plasma cholesterol. Keys et al. (1965) found that for every 1% of the total energy intake contributed by saturated fatty acids, the plasma cholesterol level is increased by 0.07 mmol/l. The very high intakes in the winter diet would be likely to have the major effect on plasma cholesterol levels, which would only be slightly (if at all) modified by other factors, such as activity, stress reduction and so on.

Hicks' (1965) study in the Antarctic have shown a downward trend over the year in plasma cholesterol, with only a slight rise during winter. Antonis et al. (1963) found no change in total cholesterol, but significantly elevated beta- and decreased alpha-cholesterol levels during the winter at the British station, Halley Bay.

It may be concluded that changes in weight and diet is likely to affect cholesterol levels. As these factors vary between years and stations, it is not surprising no clear pattern has emerged in seasonal variations in cholesterol levels.

HDL cholesterol levels increased concomitantly with fitness and activity over the summer program. This is consistent with earlier findings, showing a positive correlation between activity and HDL cholesterol (Lopez et al. 1974). No significant changes occurred over the winter program, but the increase in mean HDL cholesterol values since the summer period is consistent with the increase in VO_2 max levels seen during the winter program. The three week period of inactivity in winter was not sufficient for HDL cholesterol levels to fall. The higher HDL cholesterol levels of winter paralleled the increased VO_2 max levels and is consistent with the assertion of Nikkilä et al. (1978) that only strenuous exercise such as cross-country skiing or long distance running lead to increased HDL cholesterol and that lesser degrees of exertion are ineffective. One explanation for the increase in HDL in winter may have been the increase in fat intake which was observed in these subjects.

Although the LDL cholesterol levels were not measured, the fact that total cholesterol levels did not alter over summer implies a parallel reduction in LDL cholesterol.

The positive effects of increased HDL cholesterol in winter may be attributed to improved levels of fitness (Figure 12b); nevertheless, any benefits due to raised HDL cholesterol may be cancelled by the concomitant increase in total cholesterol, attributed to dietary changes.

No seasonal trend has been noted in plasma triglyceride levels over the polar year, in spite of marked variations in diet and activity (Figure 12c). This is consistent with polar research done by Antonis et al. (1963).

3.4.4 Seasonal variation

Ambulatory readings of BP showed a trend to higher systolic and diastolic pressures in the winter program when compared with the summer (Figure 7). Spring mean BP values for the medium period (Figure 6) were higher than both summer and winter. The design of this study does not allow comparison of these three programs. While there is great environmental stability within each season, changes over the year in temperature, work and sport activities, population density, daylight hours, diet and clothing confound any comparison.

The small numbers in the study prevented this trend from reaching significance, however the fact that higher winter mean values are present for nearly all periods and levels of activity warrants recognition.

This seasonal pattern is consistent with that generally found in urban populations, who have shown a BP increase over the winter months (Brennan et al. 1982, Hata et al. 1982, Balazs and Walqvist 1985). Kochar et al. (1985) found no seasonal variation in BP of thirty-nine male patients from Milwaukee, however, they concluded the almost universal use of central heating in their region diminished the degree of cold exposure seen in the British and Japanese populations. The British Medical Research Council (1982) studied the BP and heart rate changes of 1000 men and women with mild hypertension over a five year period. A distinct seasonal pattern emerged with BP higher in the winter than the summer. Heart rate showed no consistent seasonal variation. It was concluded that the small weight changes seen were not sufficient to account for the variation, and that biochemistry, including aldosterone and renin activity showed no relationship with temperature, nor did noradrenalin levels or excretion. However, Hata et al. (1982) concluded that the phenonemon is related to increased sympathetic nervous activity in response to the cold.

It is feasible to attribute the increased BP of winter to a cold pressor effect as mean ambient temperatures fell from a summer peak of +5°C to a winter nadir of -18°C. In acute cold exposure, LeBlanc (1973) found BP and pulse rate will steadily increase over a few hours, if human subjects are exposed without clothing protection.

With repeated cold exposure, there is attenuation of the pressor response, associated with modification of the vasoconstrictive reflex (Dill 1964, LeBlanc 1973). However, in these experimental conditions, there is considerable discomfort for the subject due to a marked cooling of surface and core temperatures. Norman (1965) studied expeditioners at the British Station, Halley Bay and noted their sub-clothing temperature remained constant at approximately 32.8 °C, which is only slightly cooler than would be found in subjects living in a temperate climate. Excellent clothing and the dry atmosphere meant that true cold exposure was minimal throughout the year.

Despite the marked changes in temperature, the opportunity for regular, true cold exposure during routine station life was limited, and indeed, discouraged due to risk of cold injury. It is possible that limited exposure to the cold was enough to cause an increased cold pressor effect over winter but was not consistent enough to allow physiological adaptation.

As observed above, BP values within each program fell with increasing levels of activity and fitness (Figures 7 and 8). However, the increase in BP levels observed over the year cannot be explained by the steady increase in fitness levels seen from summer through winter to spring (Figure 10).

Nor can the increasing BP values be attributed to body weight changes, as the exercise group showed no significant changes in weight over the year.

Bodey (1971) also found an increase in basal BP readings over the year, which corresponded to the increased adrenalin excretion. This is in contrast to changes in noradrenalin levels, which rose significantly on arrival in Antarctica, then fell slightly to a level still greater than the pre-departure mean value.

Adrenalin excretion rates did not increase on arrival and therefore, it is likely that some non-climatic factor may have influenced the rise in adrenalin excretion over the year. Previous studies have indicated that adrenalin is the catecholamine most likely to be increased by anxiety (Bodey 1971). Furthermore, anticipation may be more anxiety-provoking then the event itself.

Without catecholamine measurements and formal psychometric testing, it is not possible to determine the true cause for the increase in BP over the year. The stress of isolation and living in a small community may lead to an increase in BP over the year. Alternatively, the cold pressor response may be responsible. In conclusion, seasonal changes in BP may be due to a combination of a number of the factors discussed above.

There is an apparent discrepancy in seasonal variations of the ambulatory BP readings (Figures 7 and 8) and the monthly clinic measurements (Figure 13). Ambulatory BP measurements show an increase over the year, whereas the monthly clinic measurements show a decrease over winter.

The seasonal variations in the clinic systolic and diastolic pressures were statistically examined for significant change. Analysis of variance by SPSS of systolic pressure showed no significant dependence on months for neither the exercise group ($F = 0.791$, $p = 0.625$), nor the non-participating group ($F = 0.278$, $p = 0.985$). Both groups together again showed no significant seasonal change ($F = 0.591$, $p = 0.821$).

Similarly, diastolic pressure changes over months failed to reach significance for both the exercise group ($F = 1.356$, $p = 0.220$), non-participating group ($F = 0.255$, $p = 0.989$) and both groups together ($F = 1.700$, $p = 0.082$).

In the absence of a statistically significant trend there is little need to explain the discrepancy. Nevertheless, it is worth mentioning reasons why the clinic readings were not consistent with the ambulatory readings:

- the casual monthly measurements provide only a superficial view of the expeditioners' BP over the year and it is not appropriate to use the BP changes of only twenty individuals to comment on seasonal trends. Nor is it possible to statistically compare the two sets of BP measurements.

- the timing of the exercise program may help to explain the discrepancy. The exercise program was commenced on arrival in Antarctica in December and completed in January. There was no clinic measurements taken in December and it is possible that these readings would be consistent with the ambulatory BP readings. January's clinic BP values were relatively low and the summer peak does not occur until February/March. Similarly, the winter exercise program was done in May and June. This was before the lowest winter clinic readings in July/August.

- Julius et al. (1974) showed that the 'white coat effect' is greater in clinic BP readings than with ambulatory monitoring. It is possible that the 'white coat effect' on clinic measurements was most pronounced in the summer, when the expeditioners were unfamiliar with the procedure and the author; by winter, routine and familiarity diminished this effect. This effect and others are discussed on pages 26-28, and attest to the superior results obtained by ambulatory BP monitoring.

- clinic measurements were made under conditions markedly different from those of the exercise study itself: all expeditioners were required to attend the clinic on a specific day each month, regardless of recent activity. It is likely that clinic BP measurements were often made shortly after the subject had returned from field trips. This is especially true in summer and spring, when there are many more field excursions. As stated on page 53, elevated BP readings are common before, during and after field trips. By contrast, inclusion criteria for the exercise study were a minimum of three weeks on the station (no field trips). The spring program was disrupted due to subjects being unable to avoid the confounding factor of field work. This is another reason why the data cannot be compared.

- similarly, no attempt was made to control the intake of alcohol on the day prior to clinic measurements, whereas during the exercise study, alcohol intake was maintained at a modest level. Alcohol was more available in the summer and this may have contributed to the higher clinic readings at this time.

- in earlier Antarctic studies, both Bodey (1971) and Lugg (1973) found discrepancies in seasonal trends between basal and casual BP readings during the Antarctic year.

Bodey found the increase in basal systolic and diastolic BP readings in the latter half of the year corresponded to the increased adrenalin excretion. Basal BP might be expected to be strongly influenced by the pressor amine states of the subject, whereas casual BPs are more likely to be affected by the subjects' recent activities, and thus obscure the effects of environmental background or pressor amines.

Nevertheless, in Bodey's study, the casual systolic BP increased during the latter months when adrenalin was increasing. These findings concur with the conclusions of the present study in that increased BP measurements in spring were stress-related (see page 12).

Bodey measured pulse rate, both basal and casual, monthly throughout the year. Basal pulse rate rose during the latter half of the year, concomitant with the increase in basal diastolic BP and adrenalin concentration. Casual pulse rate fell just short of significant regression on time, and were probably affected by recent activities. Once again, there is little or no correlation with a number of other Antarctic studies (Hicks 1967, Godwin 1983).

It is difficult to separate effects of the physical and psychosocial environment on human physiological responses unless detailed and intrusive measurements are made of variables such as ambient temperature, individual surface and core temperatures, psychometric testing, wind chill factor, clothing efficiency, major station events or disruptions to routine, individual and group responses to such events. It is known all these factors will affect BP and pulse rate. As each year and each station's population varies, it can be expected that there is a wide variation in the seasonal changes of BP and pulse rate.

In conclusion, it is possible that a number of factors prevail to cause the apparent discrepancy, but without a statistically significant difference and a study designed to compare the two measurements, it is not possible to conclusively determine the reasons for the difference.

Given the rigorous control of experimental design and inclusion criteria, and the universal trend to higher winter BP values for all periods and all levels of activity, it is likely that the ambulatory BP measurements are true and the seasonal trends (non-significant) of the clinic measurements are dependent on such confounding factors as lack of familiarity in the summer and high stress levels in the following spring.

3.4.5 Selection bias

The pronounced difference in the BP and heart rate between the two groups (study subjects and non-participating expeditioners) is an excellent example of the selection bias involved in clinical studies (Figure 13). Systolic, diastolic pressures and heart rates were all significantly lower in the exercise group, despite the fact that mean weight was higher by 5 kg and mean body mass index being similar (Table 3). The exercise study ran in three parts, each about ten weeks long. During each part, it is recalled that all subjects went through three levels of activity in random order, including a period of minimal activity.

Between the programs, subjects were allowed to do any level of activity, which varied between subjects and throughout the different seasons. The impact of the study does not reflect on the casual BP and heart rate readings shown. The exercise group appeared to be physically more active and drank less alcohol and were non-smokers (half the non-participators smoked cigarettes), however, since no direct measurements were made, all conclusions remain speculative. Nevertheless, these observations suggest that, despite heavier weights and the varied levels of activity throughout the year, the self-selected group used in the study had characteristics that produced beneficial cardiovascular effects, with the lowering of BP. The fact that there was no correlation of VO_2 max with age is further evidence of selection. All members of the expedition needed to show a reasonable level of health and fitness prior to selection, regardless of age; interest in outdoor physical activity is seen as an asset during the selection process. It is postulated that the benefits of regular exercise might be even more apparent in a more sedentary population than was used in the present study.

3.5 CONCLUSION

The present study found that the use of 24 hour ambulatory BP monitor provided a reliable and practical method of cardiovascular assessment during normal daily activities and sleep. The recording of posture and activity during each measurement allowed for a more meaningful analysis of BP and heart rate responses during a 24 hour period.

BP studies are usually limited by the inability to monitor every factor that may act to alter homeostasis. The benefit of a randomly balanced Latin Square Design is that the subject acts as the control. Provided each individual is consistent in lifestyle, diet and habits, there is a good opportunity to study the effects of one variable. And a polar station is ideal for providing a stable environment for such research.

Increased levels of exercise were found to reduce BP and heart rate in subjects living a sedentary lifestyle. The BP-lowering effects were less marked in the same subjects when they were more active. It is concluded that there is a low threshold of benefit from exercise, which may be optimally achieved with as little as three bouts of moderate exercise a week.

The effects of exercise on BP was rapid in both onset and reversibility, in comparison to its effects on VO_2 max levels. In the present study, BP levels correlated well with activity levels but less with

absolute levels of VO_2 max. For example, following three weeks of inactivity in winter, subjects were still more fit relative to summer, but BP had increased considerably.

Despite the high levels of VO_2 max and activity, the increased mean BP in the spring program suggested that physiological and psychological stress may counteract the benefits of exercise on cardiovascular function. This conclusion is supported by the seasonal variation in monthly BP measurements irrespective of activity level, which showed increases during the periods of greatest psychological stress.

HDL cholesterol increased in parallel with VO_2 max values; however, the detrimental effects of a high fat, high cholesterol diet negated the overall benefit of exercise on lipid profile, as seen by the negligible changes in total: HDL cholesterol ratio, despite large changes in activity level.

The fact that no changes were seen in glucose tolerance or triglyceride may suggest that very little activity is required to manifest a maximal benefit in healthy young men.

Oberman (1985) listed many other effects by which exercise may provide cardioprotection:

- weight loss, especially fat
- decreased insulin secretion
- increased glucose tolerance / utilisation
- increased insulin receptor sensitivity
- increased HDL and decreased LDL cholesterol
- decreased triglyceride
- decreased catecholamine release
- decreased platelet aggregation
- increased cardiac output and fitness.

It can be stated that if exercise provides adequate modification of CHD risk factors in any individual, it should be seen as the preferred treatment for essential hypertension.

Harrison (1985) stated that 'effective primary prevention involves intervention throughout the population. Relatively small shifts in the mean and distribution of risk characteristics (and multiple combined risks) have the potential for producing very significant public health effects. These may be estimated in the order of a 4% decrease in disease for a 2% reduction in serum cholesterol levels, a 12% decrease in events associated with a 2% decrease in mean BP and perhaps a 25% decrease in disease from a multifactor combined risk decrease in the order of 3 or 4%. This is the primary prevention phenonemon: a very small benefit, distributed across large numbers of people, may have profound public health effects.'

4. ACUTE AND CHRONIC EFFECTS ON BLOOD PRESSURE AND HEART RATE OF ALCOHOL

A positive correlation between alcohol and BP has been shown by several epidemiological studies. Arkwright et al. (1982) found a progressive increase in systolic pressure with increasing alcohol consumption, and found the prevalence of hypertension in moderate and heavy drinkers to be four times that of teetotallers; Klatsky et al. (1977) studied BP in relation to known drinking habits of nearly 84 000 men and women and found significantly higher BPs in those who drank 3 or more drinks a day - independent of age, sex, race, smoking, coffee, former 'heavy' drinking, educational attainment and adiposity; similar observations were made by MacMahon et al. (1984).

These findings are supported by clinical studies, that have demonstrated raised BP following a period of drinking alcohol for several days or weeks. Howes and Reid (1985) gave normotensive subjects 80 g ethanol/day for four days and found increases in BP and heart rate and reductions in vascular responsiveness to noradrenaline; Puddey et al. (1985) studied forty-four hypertensive men in a randomised, controlled, cross-over trial of the effects of alcohol on BP. Mean systolic and diastolic pressure was significantly lower in the last two weeks of low-alcohol intake than during the normal alcohol period. The BPs in alcoholics undergoing detoxification are highest during withdrawal (with zero blood alcohol) and normalises on recovery (Saunders et al. 1981).

However, little is known about the major effect during and immediately after drinking alcohol. Ireland et al.(1984) found a small and transient rise in BP seen immediately after drinking alcohol and lasting less than an hour. Howes and Reid (1985) noted as well a transient rise in BP followed by a fall, that was sustained for several hours. One consistent finding following the acute administration of alcohol is a concomitant rise in heart rate.

There is a need for a better understanding of the acute effects of alcohol on the BP level. Several investigators have suggested that excessive alcohol consumption predisposes humans to stroke and sudden death. Gill et al. (1986) conducted a retrospective study of 230 patients with stroke and found a four-fold increased risk in heavy drinkers than in nondrinkers. Hillbom and Kaste (1981) examined seventy-five patients with aneurysmal subarachnoid haemorrhage and found that 25% of cases were preceded within 24 hours by a bout of alcohol drinking.

Several studies have found that increased resting BP is associated with regular alcohol use. However, most studies have been done 12-24 hours after cessation of drinking. The duration of the hypertensive effect is unknown. Some studies have shown only a weak association between alcohol consumption and BP; it is possible that a clearer relationship would be shown if the period of abstinence was known. There is some evidence that alcohol-induced hypertension is reversible, especially in its early stages. D'Alonzo and Pell (1968) studied 922 'problem drinkers' and found that recovered problem drinkers had a lower prevalence of hypertension than those whose drinking problem was current. Puddey et al. (1987) demonstrated a rapid normalisation in BP following a period of alcohol abstinence.

A number of studies have shown a reduction in BP with dietary fish oil, containing eicosapentaenoic acid or EPA (Singer et al. 1983; Lorenz et al. 1983), however, there is conflicting evidence: Scherhag et al. (1982) found significant increases in BP of all rats given EPA supplements. This was accompanied by a marked suppression of vasodilator prostacyclin by vascular tissue. The present study sought to determine what effects the co-administration of alcohol and fish oil would have on BP levels of healthy, normotensive volunteers.

Furthermore, most studies of BP have examined solely the resting state. It is important to know the variations in BP and heart rate during normal daily activities, outside the unusual and often stressful environment of the clinic.

The present study examined the acute changes in BP and heart rate for the 24 hours following the administration of large doses of ethanol, and compared them to the effects on BP and heart rate over 24 hours, after regular alcohol use had been ceased for 2 days.

4.1 METHOD

4.1.1 Acute effects of alcohol

Five volunteers took part in a study of the effects over a 24 hour period of acute intoxication. Three of the subjects (2 male, 1 female) were regular light drinkers, with an average ethanol intake of 0-30 g (0-3 standard drinks) daily; the other 2 (male) subjects were heavy drinkers, consuming approximately 60-80 g ethanol (6-8 drinks) per day. No subject smoked nor used medication. The subjects were in good health; their mean age was 35 years, mean weight 80 kg, mean body fat 22% (Durnin and Womersley 1974) (Table11).

During the week prior to the study, the subjects consumed no more than their usual daily amount of alcohol, described above. The study commenced 48 hours prior to an anticipated session of heavy drinking. The subject abstained altogether from alcohol for 24 hours, after which an ambulatory BP monitor was strapped to the right arm of the subject at 1800 h.

The BP monitor was programmed to record BP and heart rate hourly during a normal working day. After this first 24 hour period, the data were stored and the monitor was then re-programmed to record the heart rate and BP every 20 minutes during the binge period to allow for disturbed readings and errors, then half hourly during the sleep period and hourly the following day, when it was finally removed at 1800 h that evening. This gave a total of 48 hours of readings: the first 24 hours being the control (no alcohol), the second recording the period of intoxication and recovery. During the period of intoxication, the author recorded the subject's activities and alcohol intake.

The subject commenced the 'binge' period at 1800 h, ate a normal evening meal and retired to bed by midnight. The mean quantity of ethanol consumed in the intervening six hours was approximately 190 g (range 140-290 g). All rose within an hour of the usual time and carried out normal work activities.

Table 11. Details of subjects' sex, age, body weight, % body fat, BP and heart rate.

CODE (sex)	AGE (yrs)	WEIGHT (kgs)	% FAT	SYSTOLIC PRESSURE	DIASTOLIC PRESSURE	HEART RATE
A(F)	28	61	18	95	55	60
B(M)	28	97	24	140	80	66
C(M)	40	77	16	130	80	74
D(M)	43	93	34	130	85	76
E(M)	38	71	19	130	70	68
MEAN	35	80	22	125	74	69

The study was carried out towards the end of a year spent on an isolated Antarctic station. All the subjects were familiar with the BP monitor, having worn it repeatedly on previous studies. Both the control and binge evenings were spent consecutively in the familiar and comfortable environment of a communal living room. The subjects then slept in their usual accommodation. During the day, each subject pursued their routine work schedules, and meals were provided at regular times by the same chef. The experimental conditions allowed for close control, while the subjects were free to participate in their usual social and work routines. The use of automatic BP monitor eliminated observer bias.

4.1.2 Regular use of alcohol and its effects

Ten subjects were studied over a 24 hour period following a two week period of regular alcohol use. The study was commenced four months after arrival on the Antarctic continent, to ensure environmental adaptation. The subjects were all Caucasian male; their mean age was 34.6 yrs (range 24-49), mean height 179.1 cm (171-186), mean weight 79.4 kg (71-106), mean body fat 20.2% (13.6-26.5). Only one subject smoked. No medication was used (Table 12).

Despite a daily mean temperature of -12.4°C at Davis, indoor living conditions are comfortable, with most buildings centrally heated. Actual time spent outdoors varies with occupation, inclination and, of course, weather, but average daily time spent in outdoor activities is four to five hours (Lugg, 1977). (For details of the physical environment, see Chapter 1.)

With a wintering party of twenty, and very close living conditions, it is possible to be familiar with the daily routines, diet and drinking habits of each individual. It was partly due to this that strict adherence to the program was observed in all subjects.

4.2 STUDY DESIGN

The ten subjects underwent three different periods for two weeks each, successively. A randomised balanced method was used. The order in which the periods were done was determined by a 3 x 3 Latin square. The periods were: 'low alcohol', 'alcohol' and 'alcohol plus oil'. Those on 'low alcohol'

Table 12. Details of subjects' age, height, body weight and percent fat.

PATIENT NO.	AGE (yrs)	HEIGHT (cm)	TOTAL WEIGHT (kg)	PERCENT FAT (%)
1	28	186.0	106.0	26.5
2	43	184.0	78.0	17.9
3	49	183.0	83.0	21.2
4	27	178.0	74.0	13.6
5	36	171.0	79.0	19.5
6	26	180.0	76.0	22.0
7	2	176.0	79.0	19.6
8	35	181.0	79.0	19.2
9	37	177.0	71.0	22.8
10	35	182.0	77.0	19.8
MEAN	34	179.8	80.2	20.2

were given a maximum daily ration of 5 cans of low alcohol beer (Swan Special Light [Perth, Western Australia]; alcohol content 0.9% vol/vol). The daily ethanol intake was approximately 13 g or, on average, 0.16 g/kg/day.

For the 'alcohol' period, pure ethanol (CSR, Australia) was supplied at a rate of 1 g/kg body weight/ day, to a maximum of 100 mls ethanol/day. The alcohol was then diluted in fruit juice or soft drink and consumed over several hours, to avoid intoxication.

The third treatment period, 'alcohol plus oil', commenced with similar alcohol allowances to the 'alcohol' period, (1 g/kg/day). In addition, they were given fifteen gelatin capsules daily, each containing 1 g dietary fish oil, Maxepa, [Scherer, Melbourne, Victoria (see Appendix II for composition)]. The daily dose of eicosapentaenoic and docosahexaenoic acids were 2.7 g and 1.9 g, respectively. Additional daily calories due to fish oil amounted to only 615 kilojoules (kJ) (150 calories). The odourless, tasteless capsules were well tolerated. Some subjects, on the other hand, had difficulty consuming the relatively large amounts of alcohol every day.

The author was present at all meals to issue the ethanol, and was able to ensure all subjects received a similar and consistent diet provided by the same chef. The daily increase in energy intake due to ethanol averaged 828 kJ. However, additional energy due to non-alcoholic beverages taken during the 'low alcohol' period were not calculated, and weights remained constant throughout the study.

At the end of two weeks of a given treatment period, the subject abstained from alcohol for 36 hours prior to testing. The 24 hour ambulatory BP monitor was programmed to record systolic, diastolic and mean BP and heart rate every 30 minutes during the day, and hourly from midnight to 0600. On completion of the 24 hour period, the monitor was returned and the data transferred from the Epsom HX-20 computer via a ROM Baselink to a Macintosh 512K computer for analysis.

4.3 RESULTS

4.3.1 Acute effects of alcohol

All five subjects completed the two day test period. The data has been examined both in a relation to time and to activity level. Only sedentary or sleep readings were used in the time scale. This was in order to remove the confounding effect of higher levels of activity on the BP and heart rates.

The 24 hour periods first were divided into three sections: 'evening', 'sleep' and 'day'. The 'evening' period began at 1800 h, when the monitor was first applied, and lasted until the subject went to bed. 'sleep' consisted of the sleep period, and 'day' measured the time from waking until the following evening. To synchronise the readings of all five subjects, time was corrected to zero at the start of sleep and also at wakening. A mean value was calculated for each subject for the three sections, 'evening', 'sleep' and 'day'. Figure 15 shows the total mean values for all subjects for the control and test periods.

Systolic pressures were lower during the binge period (127 mm Hg ± 5 SD), compared to the control mean value of 132 ± 5. Systolic pressure fell further with sleep after alcohol (106 ± 4). This was significantly lower than the mean sleep systolic pressure for the control period (111 ± 10). The following day showed an increase in systolic pressure (130 ± 7) relative to the control period (125 ± 6), but, overall, this did not reach significance.

Mean diastolic pressures during the 'evening' period were similar during the binge and control period (81 ± 4 and 82 ± 6, respectively) (Figure 15). Although diastolic pressures dropped

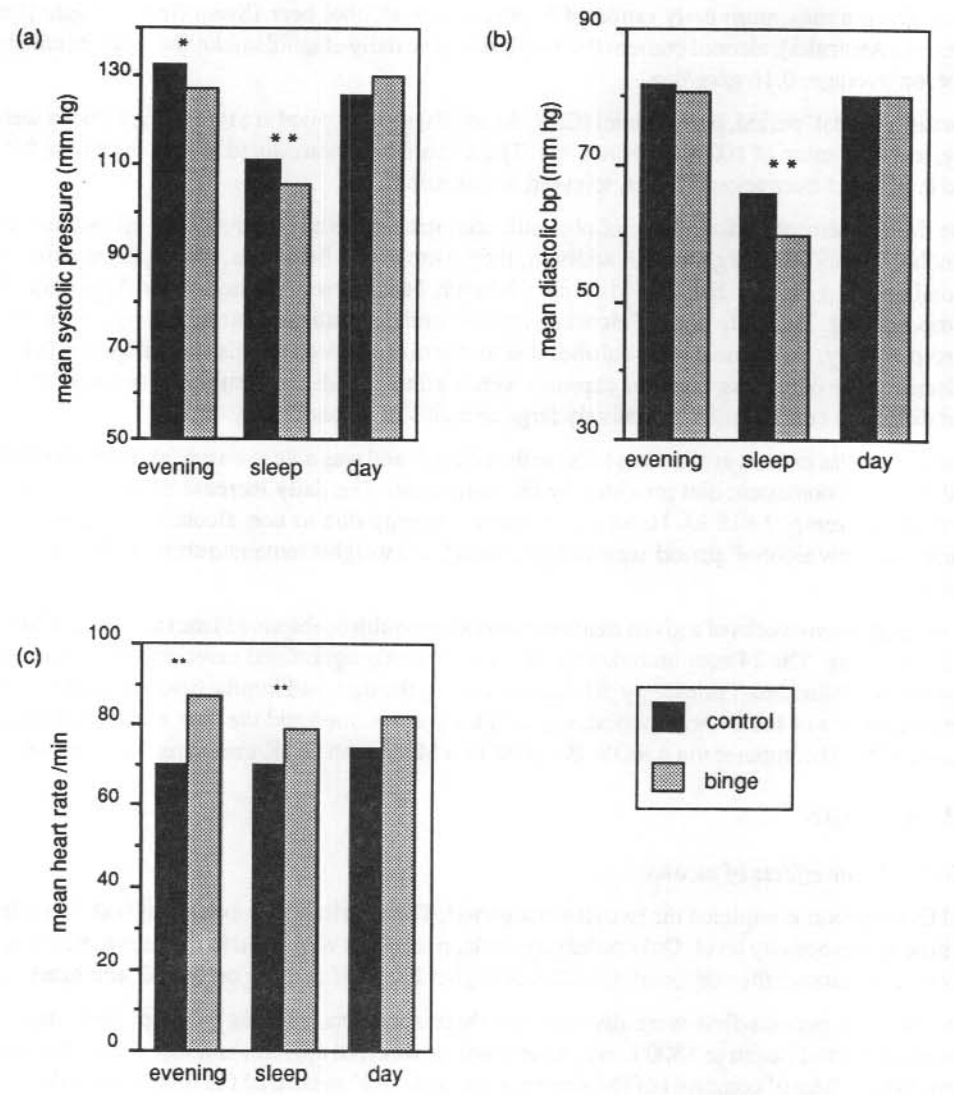


*Figure 15. Changes in a) systolic pressure b) diastolic pressure and c) heart rate over the periods, 'evening', 'sleep' and 'day' (explained in the text). Binge and control periods are compared. Significance is denoted * $p < 0.05$ and ** $p < 0.01$.*

significantly during sleep for both test periods, there was more marked fall in sleep following the binge drinking. Mean diastolic pressure during sleep after drinking was 60 ± 3, as compared to 66 ± 5 during the control sleep period. The following day, mean diastolic pressures rose in both the test and control periods. Comparing the mean diastolic values during the following day, no difference was found between the alcohol or control periods (80 ± 1 and 80 ± 3, respectively).

Heart rates were significantly raised during both the drinking (Figure 15c), (87/min ± 4 S.D.), and the 'sleep' period following (78 ± 4). Control heart rate values were 68 ± 1 and 71 ± 5, respectively. Following the binge period, the heart rates remained raised the following day (mean value 80 ± 1), although this did not reach a significantly higher value than the control (75 ± 5).

4.3.2 Diurnal trends

To examine the changes in heart rates and BPs over the 24 hour period in more detail, the hourly values during the three sections ('evening', 'sleep' and 'day') for all five subjects were averaged. These mean values were then plotted against a time scale, which was corrected to zero at the commencement of drinking, the onset of sleep and wakening the following day. Figure 16 shows the changes in systolic, diastolic BPs and heart rates for the control and binge periods. Figure 17 shows the changes for each individual during the drinking ('evening') period and Figure 18 shows the maximum and final values for each individual during the following 'day' period.

During the first 2 hours of drinking (Figure 16), there was a transient but significant ($p = 0.014$) rise in systolic pressure from an average initial value of 126 mm Hg ±18 S.D. to a peak of 139 ±17.4. Following this, all subjects showed marked fluctuations in systolic pressure; however, after the initial rise, there was a gradual decline ($p = 0.008$) as the continued drinking took effect, and the mean value during the drinking (127 ± 5) was significantly lower than the control (132 ± 5). Despite this, the final systolic value at the end of the drinking time (125±10) was similar to the initial value before drinking started (Figure 17).

With the onset of sleep, there was a precipitous drop in systolic pressure, that was sustained, despite fluctuations, for the entire sleep period (Figure 16). Average sleep values for systolic pressure were 106 ± 4.1. The control sleep period showed a more gradual and less marked decline in systolic pressure to a mean of 111 ± 10. On waking after the binge period, systolic pressure showed a marked increase, which climbed during the day to a mean maximum of 139 ± 21. Only four of the five subjects recorded 24 hours of readings following intoxication; their average systolic pressure had returned to a normal value of 124 ± 15 by the end of the study (24 hours after the commencement, and approximately 18 hours after cessation of drinking). This value was similar to the mean systolic pressure during the 'day' period for the control (125 ± 6) (Figure 18).

Although effects on diastolic pressure varied between individuals during the period of drinking (Figure 16), and there were marked fluctuations, diastolic pressure overall decreased significantly during the evening from an initial mean value of 87 ± 5 to a final value of 79 ± 3 at the end of the binge. Figure 17 shows the initial and final diastolic values of the subjects. The control period showed a reverse trend with a steady rise during the evening, so that there was no significant difference between the total mean values for 'evening' (binge 81 ± 4; control 80 ± 1).

With the onset of sleep, both the control and the binge period showed a sudden drop in diastolic pressure (Figure 16). However, the binge diastolic values remained low (60 ± 3) throughout the night. On wakening, there was a sudden increase to a mean diastolic value of 83 ±10. This was in contrast to the control pattern, which showed a gradual rise during sleep in the early hours of the morning, until wakening when little further change was noted in diastolic pressure for the rest of the

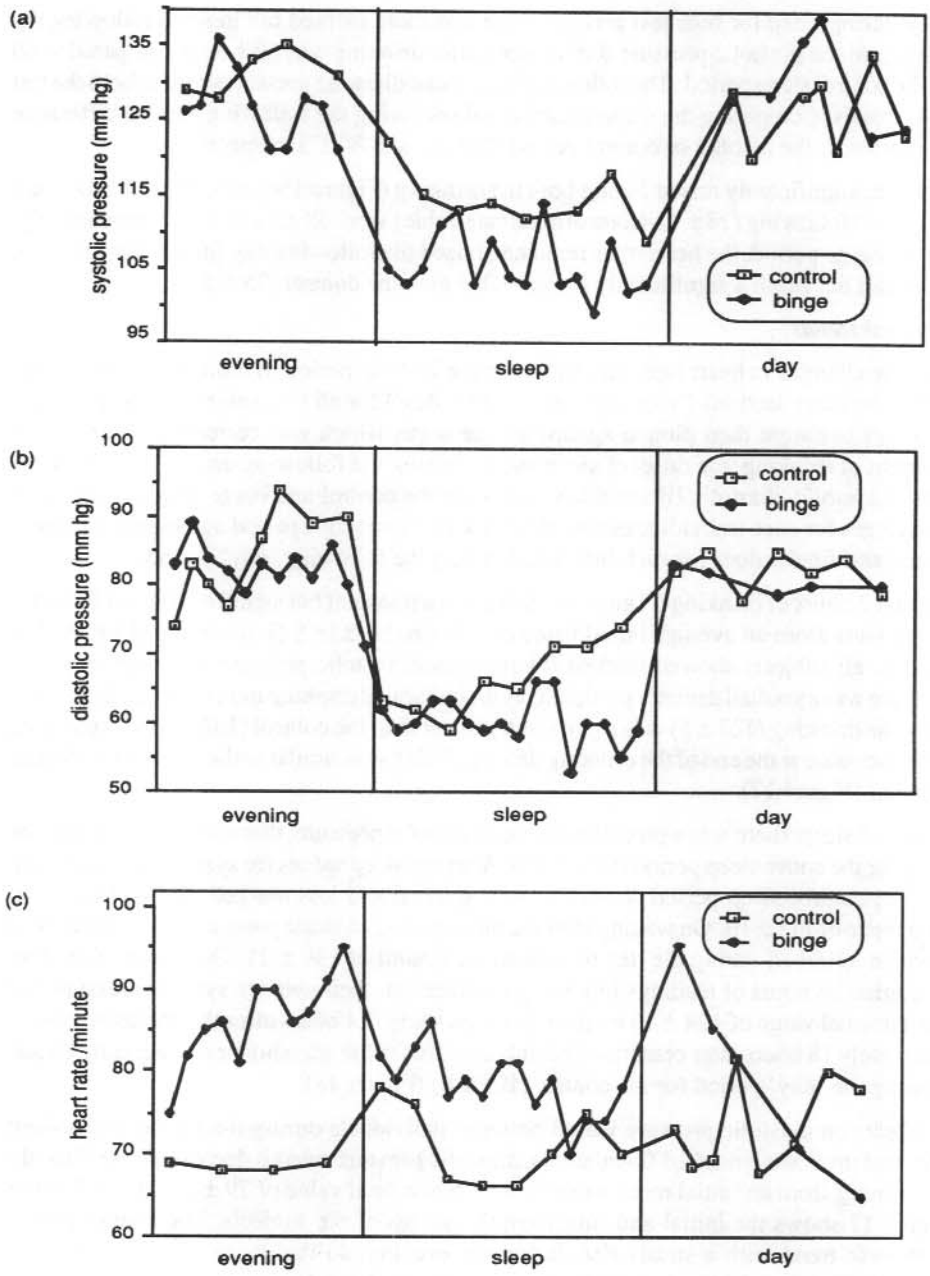


Figure 16. Diurnal variations in a) systolic pressure b) diastolic pressure and c) heart rate during control and binge periods.

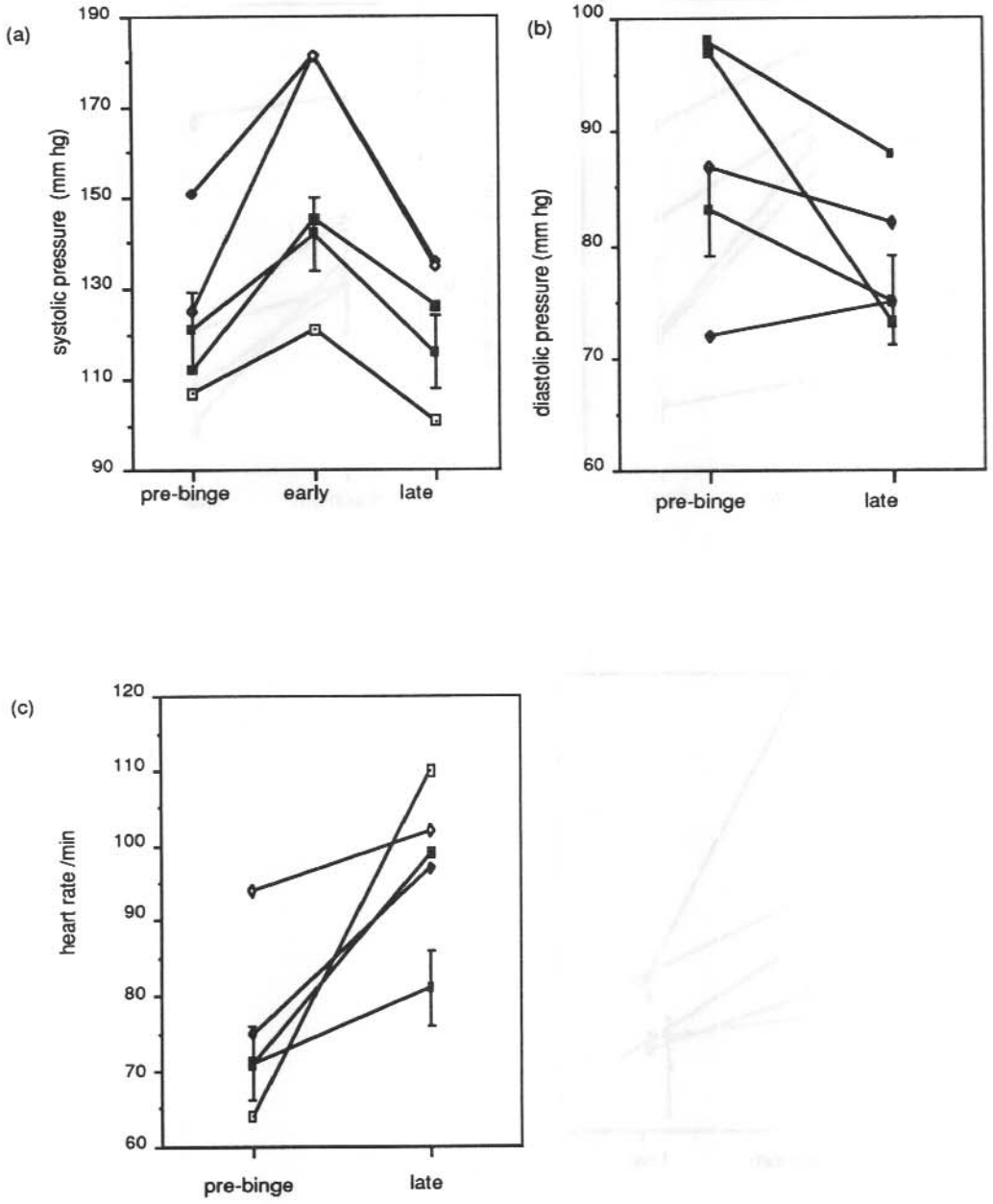


Figure 17. Changes in a) systolic pressure b) diastolic pressure and c) heart rate during acute intoxication. 'Pre-Binge' represents the mean measurements of individual subjects prior to drinking; 'early' refers to the mean values of the first hour of drinking; 'late' refers to the last hour of drinking. Error bars refer to SEM.

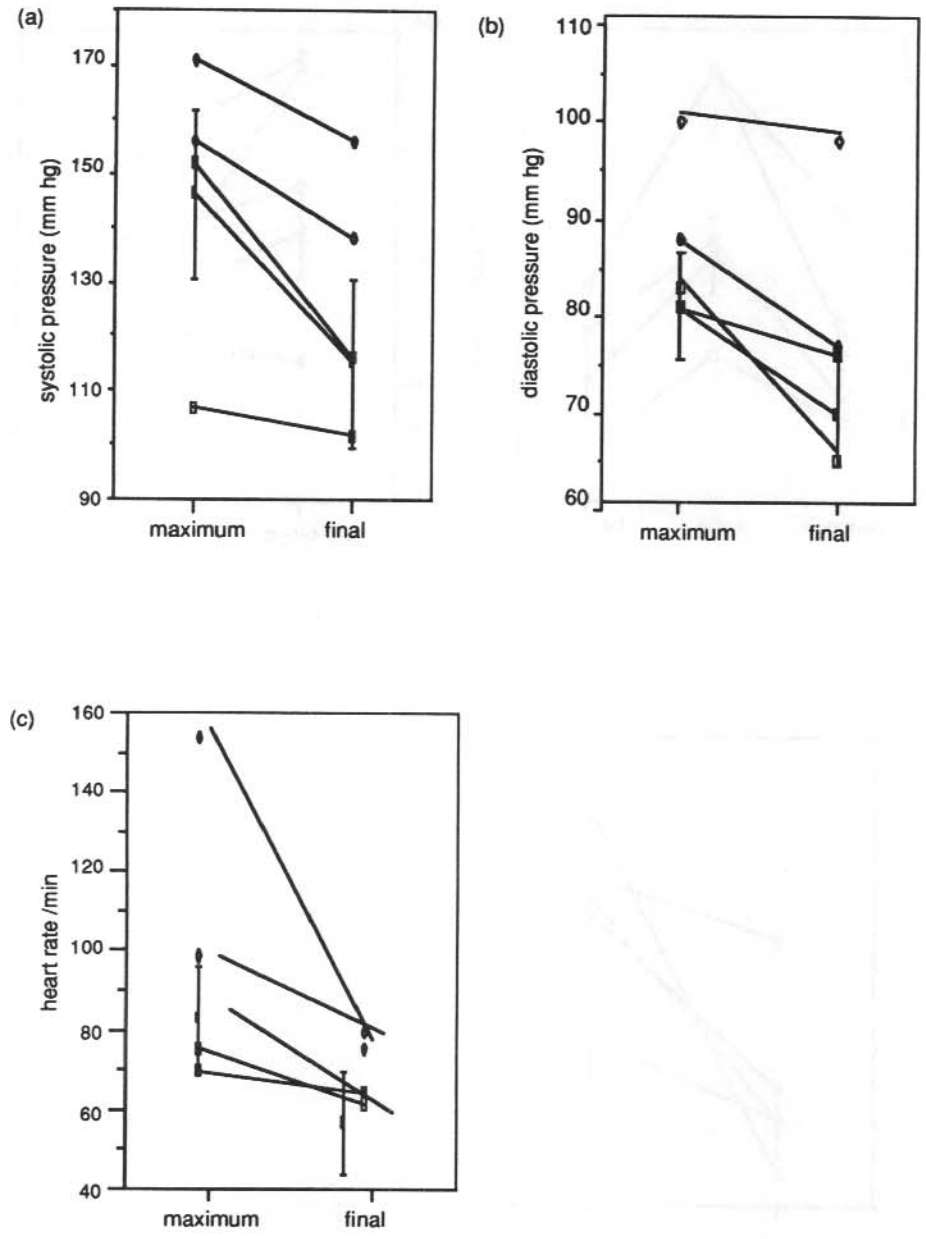


Figure 18. Changes in a) systolic pressure b) diastolic pressure and c) heart rate during alcohol withdrawal. 'maximum' refers to the peak value recorded during the day period; 'final' refers to the mean values of the last hour of recording, ie. 24 hours after the commencement of drinking. SE bars are indicated.

day. For the binge 'day' period, the maximum diastolic value was found on wakening, and there significant fall during the day, so by evening the mean diastolic value was returned to 77 ± 6, which was similar to the control 'day' value of 80 ± 1. Figure 17 shows the individual diastolic values over the 'day' period. The decrease from a maximum mean value of 87 ± 4 to a final diastolic value of 77 ± 6 was significant at p = 0.028.

Mean heart rate (Figure 16) markedly increased during the drinking period from an initial value of 75 beats/min ±13SD, to a maximum value of 95 ± 6. Individual values are given in Figure 17, which shows the marked rise (p = 0.03). This contrasted strongly with the control period, during which heart rates were maintained at an average level of 68 ± 0.5 (Figure 16). Following the binge, sleep heart rates were reduced but remained at a higher level (79 ± 4) than the sleep control period (71 ± 5). Heart rates peaked early the following day at 95 ± 36 and returned to normal wake values (68 ± 10), 24 hours after the onset of drinking. Figure 18 shows the fall in individuals' heart rates over the 'day' period approached significance (p = 0.091).

4.3.3 Blood pressure, heart and activity

The effects of higher levels of activity on BP and heart rate following alcohol was examined (Figure 19). In order to avoid the confounding effects that acute intoxication might have on performance of higher levels of activity, only readings from the last 3 hours of sleep and the following day, when overt signs of intoxication were absent, were used. The readings of all subjects at each level of activity were grouped and the means taken. As seen in Figure 15, there was no significant difference between the control and the binge groups in the sedentary position. However, following the binge period, there was an attenuated response in both systolic and diastolic pressure to increased levels of activity, when compared to control, which reached significance in activity level 'work'. Unfortunately, during the recovery 'day' period following alcohol, there were not sufficient readings at higher levels of activity to show the results for heart rate at 'work' level. Heart rates were significantly increased at all other levels of activity during alcohol withdrawal.

4.4 REGULAR USE OF ALCOHOL AND ITS EFFECTS

Of the 14 subjects who commenced the study, 10 were able to complete it: the 3 oldest volunteers (ages 43, 50 and 51 years) all withdrew due to intolerance of alcohol in such doses. The fourth subject was non-compliant and was rejected from the study. The experimental conditions allowed for close control, while the subjects were free to participate in their usual social and work routines. The use of automatic BP monitor eliminated observer bias.

Table 13 shows the 24 hour mean values of systolic, diastolic pressures and heart rates of all subjects, during the 3 treatments. No significant difference was found by analysis of variance.

The data was divided by level of activity and each subject's mean for four levels of activity ('sleep', 'sit', 'stand', 'work') as described in Chapter 2. Analysis of variance between the 'low alcohol', 'alcohol' and 'alcohol plus oil' periods for each level of activity was performed. (Figure 20).

A marked increase in all variables (systolic, diastolic BP and heart rate) occurred between measurements taken during sleep and while sitting. With further increases in activity (to standing, and working), there was a linear increase of heart rate and systolicpressure in response to activity. However, heart rate and systolic pressure showed no significant difference between control and alcohol at any level of activity. In all measurements, the least difference between control and test periods was seen during sleep.

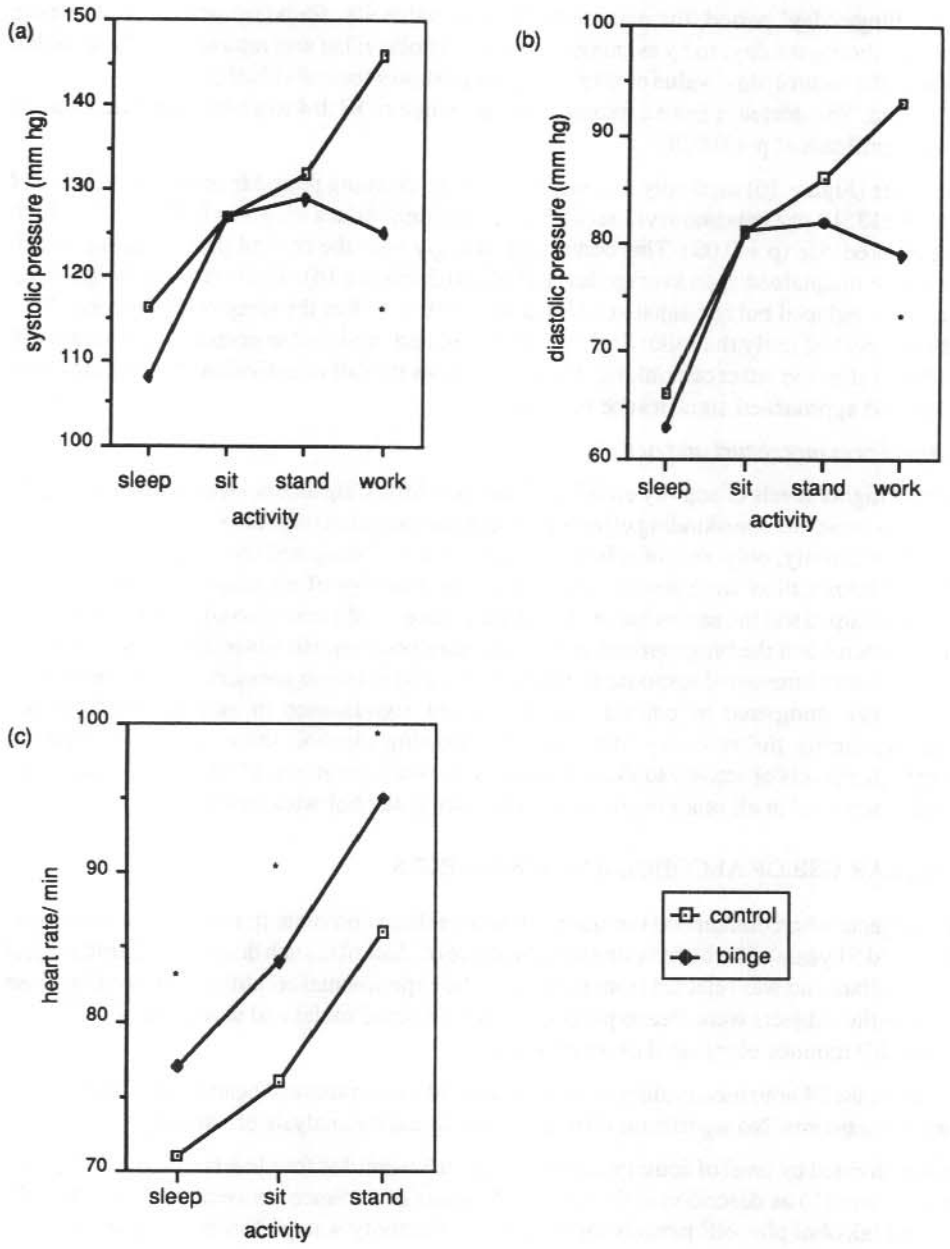


*Figure 19. The effect of activity on a) systolic pressure b) diastolic pressure and c) heart rate, during binge and control periods. Significant differences ($p < 0.05$) between 'control' and 'binge' periods are denoted by *.*

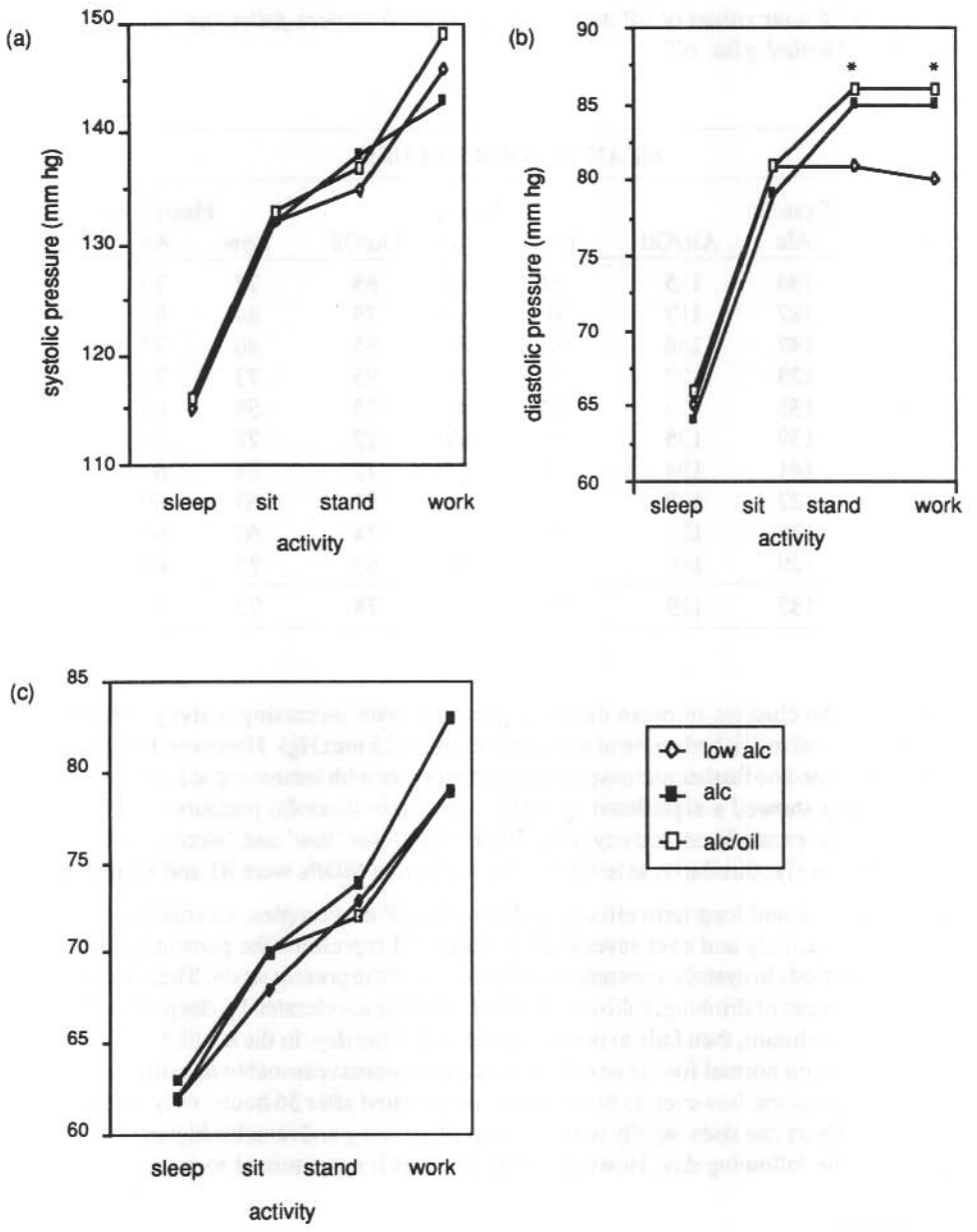


*Figure 20. The effects of increasing levels of activity on a) systolic pressure b) diastolic pressure and c) heart rate. The test periods 'alc' and 'alc/oil' are compared to control 'nil' period. * denotes significance -p< 0.05.*

Table 13. Mean 24 hour values of BP and heart rate of each subject, following periods 'Nil', 'Alcohol' and 'Alcohol plus oil'.

MEAN 24 HOUR VALUES									
Subject		Systolic			Diastolic			Heart Rate	
Code	Low	Alc	Alc/Oil	Low	Alc	Alc/Oil	Low	Alc	Alc/Oil
1	128	134	115	71	80	85	72	70	78
2	116	127	117	79	83	79	84	92	86
3	134	147	146	85	88	85	80	77	77
4	130	123	127	74	74	75	73	74	84
5	129	135	126	74	82	73	58	65	60
6	140	139	135	81	69	72	77	77	69
7	144	141	134	78	77	72	74	69	72
8	128	127	130	77	76	81	63	60	67
9	130	126	121	78	77	74	60	64	60
10	131	129	140	79	76	85	75	62	74
MEAN	131	133	129	78	78	78	72	71	73

Figure 20 shows the changes in mean diastolic pressures with increasing activity. There was a marked change on waking in both control and alcohol (mean 15 mm Hg). However, the subjects on 'low alcohol' exhibited no further increase in diastolic pressure with increasing activity. In contrast, the 'alcohol' group showed a significant ($p<0.05$) increase in diastolic pressures in response to greater activity. For example, at activity level 5/6, the MDP for 'low' and 'alcohol' were 81 and 84 mm Hg, respectively. Similarly, at level 7/8, the respective MDPs were 81 and 84 mm Hg.

In summary, the acute and long term effects of alcohol on BP are complex. Examining the effects of alcohol use both acutely and over several days, Figure 21 represents the percentage difference from the control periods in systolic pressure over the period of the present study. There is a transient rise in BP with the onset of drinking, followed by a fall, which is accelerated by sleep. The following day BP rises to a maximum, then falls to normal by the end of the day. In the healthy normotensive, systolic BP will remain normal for the next 48 hours, and it seems reasonable to assume no further effects. Diastolic pressure, however, is found to remain elevated after 36 hours, only during higher levels of activity. Heart rate rises rapidly with the onset of drinking and remains higher than normal; during sleep and the following day. However, after 36 hours it has returned to normal.

4.5 DISCUSSION

Acute alcohol intoxication is associated with marked haemodynamic changes in sleep and wakefulness over a 24 hour period. The major findings were a significant drop in systolic and diastolic pressure that was unmasked by sleep following alcohol intoxication. There was a concomitant increase in heart rate during the drinking and sleep periods. Recovery was characterised by a peak in systolic and diastolic pressure and heart rate during the following day, and eventual return to normal 'pre-binge' values by evening.

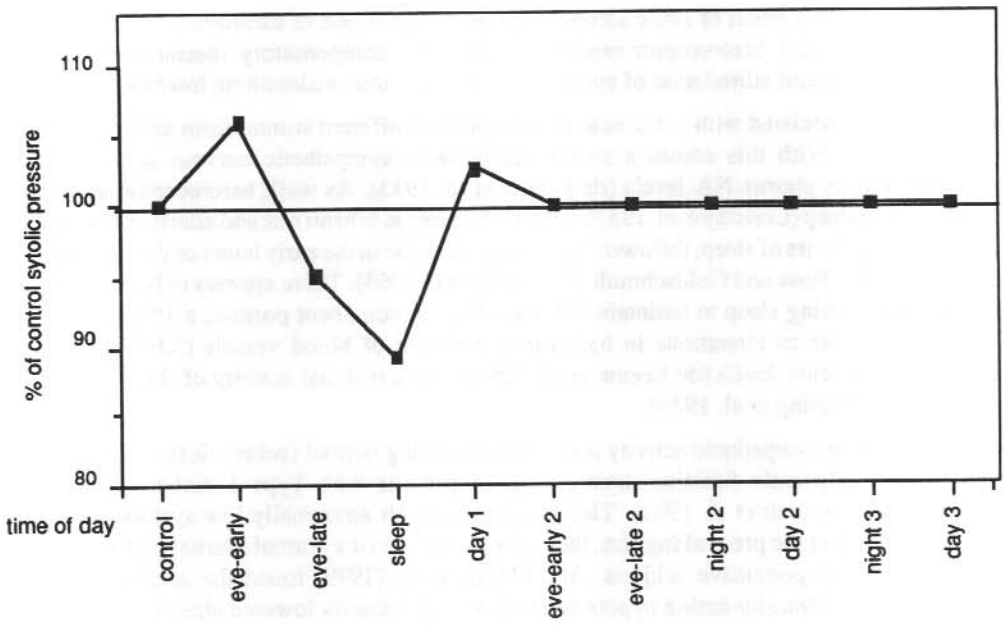


Figure 21. Changes in the mean systolic pressure following acute intoxication, calculated by the percentage difference between mean systolic pressure and control values over a 3 day period.

The initial rise in BP shortly after the commencement of drinking is consistent with the findings of earlier work: the rise in BP precedes the increase in plasma Noradrenaline (NA) (Ireland et al. 1984) and blood alcohol (Howes and Reid 1985), and may be attributed to a reflex pressor response to gastrointestinal irritation by alcohol.

The major acute effect of alcohol administration was, however, a decrease in BP. This occurred in healthy, young subjects, despite disinhibition of the emotional state and consequent increased social interaction, which normally has a pressor effect.

Radionuclide angiocardiography has been used to demonstrate decreases in ventricular contractility following moderate doses of alcohol (Kelbaek et al. 1985). The consequent decrease in BP is countered, in part, by reflex stimulation of the autonomic system via baroreceptors, shown in the consistently found increased heart rates, and possibly by the concomitant increased levels of NA (Howes and Reid 1985, Ireland et al. 1984). Furthermore, as alcohol has no direct effect on peripheral vascular tone, the cutaneous vasodilatation following moderate alcohol consumption is probably due to some central vasomotor depression (Gilman et al. 1975).

It is possible that the increase in heart rate is mediated by catecholamines released by ethanol itself or one of alcohol's metabolites, acetaldehyde, from the myocardium (Eade 1959). James and Bear (1967) showed that acetaldehyde given intravenously to dogs caused an increase in heart rate, whereas ethanol did not. Asmussen et al. (1948) showed that the infusion of acetaldehyde in humans is followed by an increase in heart rate and oxygen consumption.

Therefore, the overall effect of acute alcohol administration is one of cardiovascular depression, leading to a decreased baroreceptor response with reflex compensatory mechanisms such as increased heart rate and stimulation of sympathetic activity, thus maintaining low/normal BP.

Normal sleep is associated with a decrease in perception of afferent stimuli from external sources (Kleitman 1963). With this comes a sudden decrease in sympathetic nervous activity and a concomitant fall in plasma NA levels (de Leeuw et al. 1985). As well, baroreceptor sensitivity increases during sleep (Conway et al. 1983). There is a decrease in heart rate and arterial BP, reaching a nadir in the first hours of sleep, followed by a steady increase in the early hours of the morning (de Leeuw et al. 1985, Boas and Goldschmidt 1932, Kleitman 1963). There appears to be a number of factors working during sleep to maintain BP, including: a recumbent posture; a 15% increase in plasma volume, due to alterations in hydrostatic pressure of blood vessels (Kleitman 1963); increased plasma renin levels (de Leeuw et al. 1985); and a residual activity of the sympathetic nervous system (Maling et al. 1979).

Evidence that some sympathetic activity is maintained during normal (sober) sleep is provided by studies of haemodynamic function during sleep in patients with Type 1 diabetic autonomic neuropathy (Guilleminalt et al. 1985). These patients exhibit abnormally low systolic pressures during sleep, without the pre-waking rise, that is characteristic of a normal diurnal pattern in both normotensive and hypertensive subjects. And Maling et al. (1979) found the administration of clonidine, a potent centrally-acting hypotensive agent, significantly lowered sleep BP.

Boas and Schmidt (1932) showed a positive correlation in normal sleep between heart rate and diastolic pressure. The longer run-off time allows a further fall in diastolic pressure. The present study showed that, after acute intoxication, sleep was accompanied by a lower than normal BP, despite a continued raised heart rate. A possible explanation for this lies in the fact that healthy subjects are able to maintain BP while awake, despite alcohol's direct depressant effects on the heart, vasoactive centres in the brain and total peripheral vascular resistance. This is possibly due to high afferent input from animated activity and aroused emotional state due to alcohol, which provokes a sympathetic outflow. But sleep depresses further any reflex activation of vasomotor centres, and this combined with alcohol's direct effects leads to a marked fall in arterial BP.

The effects of physical activity on BP and heart rate on the day following acute alcohol intoxication was examined. The attenuated response to exercise (Figure 19) of systolic and diastolic pressure supports the findings of Howes and Reid (1986), who suggested the attenuated response to exercise may reflect impaired sympathetic responses or a non-specific reduction in cardiovascular reactivity. They also showed a decreased response to infused NA following regular alcohol consumption.

Another possible explanation for the attenuated response to exercise lies in the enervated state of the subjects, during withdrawal. The degree of alcohol toxicity and withdrawal was not measured, however, all subjects reported withdrawal symptoms and it is likely the subjects maintained lower levels of activity for any given task, which took longer to complete and required less exertion and therefore less sympathetic pressor response.

Hillblom and Kaste (1982) have shown an association between acute alcohol intoxication and subarachnoid haemorrhages, even in occasional drinkers, that was independent of a history of arterial hypertension. Gill et al. (1986) found a relationship between alcohol consumption and incidence of stroke, which was not increased by the presence of hypertension. While long-standing hypertension is a well known risk factor for cerebrovascular disease, the present study suggests that wide swings in BP following intoxication may precipitate a cerebrovascular event. Thus, alcohol should be recognised as an important and independent risk factor for cerebrovascular accidents.

Although the well-known Framingham study (Kannel and Sorlie 1975) showed only a small association between alcohol and BP, it is generally accepted the regular use of alcohol is independently associated with increased BP (Arkwright et al. 1982, Klatsky 1985). Whether this is due to a direct effect, a withdrawal response or even spurious association with other confounding factors is still unclear.

There is evidence that a reduction in alcohol intake leads to a decrease in BP (Saunders et al. 1981, Potter and Beevers 1984), although it is not known how this reversibility is related to the duration both of drinking and of high BP, nor what period of abstinence is necessary to achieve this effect.

In this study, 24 hour BP measurements were commenced 36 hours after completing a 2 week period of moderate drinking. The fact that there was no sustained increase in systolic BP by this stage, suggests a rapid reversibility in healthy, usually normotensive subjects. (Figure 20).

However, a significant increase in diastolic BP during moderate physical activity was still evident at 36 hours (Figure 20). This may throw some light on the mechanism whereby alcohol raises BP. A further observation that regular alcohol use caused no changes, after 36 hours, in sleep and resting diastolic BP, but showed a significant rise in mean diastolic BP with standing and moderate activity suggests that alcohol may exert its effects via the sympathetic nervous system. There is laboratory evidence to support this: Anton (1965) have shown marked increases in urinary excretion of adrenaline and noradrenaline after laboratory animals were given orally moderate doses of ethanol. Ogata et al. (1971) showed a dose-related increase in excretion of adrenaline and noradrenaline, when alcoholics were given ethanol. Further work is necessary to verify this finding. Arkwright et al. (1982) failed to show increased catecholamines in a group of thirty drinkers who had raised BP, however, estimates of adrenaline and noradrenaline need to take into account both the production and clearance rate, which includes both catabolism and renal clearance.

It is worth noting that following the 'low alcohol' period, diastolic BP did not increase with increments in activity (Figure 20), which is consistent with a normal physiological response.

Few studies of the effect of alcohol on BP have controlled for level of daily activity, although recent evidence shows regular exercise to be negatively correlated with BP (Eichner 1983). The ten subjects underwent frequent physical exertion in their daily activities as science and maintenance staff on an Antarctic station (Lugg 1977). It is conceivable that this level of activity could counteract any tendency for moderate ethanol consumption to increase systolic BP in normotensives.

A comparison of Figures 19 and 20 shows a reversed trend in the response of diastolic pressure to activity. Following the period of acute intoxication, there was an attenuated response to exertion, however, after 2 weeks of regular alcohol consumption, there was seen an increased pressor response to exertion. It is possible that different mechanisms are induced in the acute and chronic situations that have varying effects on the haemodynamic functions. Further work needs to be done to investigate this complex area.

In conclusion, alcohol has a triphasic effect on BP, which is returned to a normal level within 24-36 hours. Previous studies have frequently found raised BP in association with regular alcohol use. This may be due to the likelihood of alcohol consumed on the night prior to testing. Careful inquiry after drinking habits and repeated BP measurements over several days of abstinence from alcohol may be warranted when assessing the new hypertensive patient. The wide swings in BP following acute intoxications may be an important risk factor in cerebrovascular accidents.

5. THE EFFECTS OF ETHANOL AND FISH OIL ON PLASMA LIPIDS AND GLUCOSE

5.1 INTRODUCTION

The observation that Greenland Eskimos have the highest recorded intakes of fat (Bang and Dyerberg 1972) in the world yet have a low incidence of coronary heart disease (CHD) (Kromann and Green 1980) has considerably shaken the dietary fat hypothesis, that a high intake of animal fat is a primary cause of coronary heart disease. The risk of CHD among the Eskimos was in accordance with their low serum lipid levels, which were attributed to the type of fat in their traditional fish diet. Kromhout et al. (1985) found a 50% lower mortality rate from cardiovascular disease among Dutch men who consumed at least 30 g of fish per day, compared to those who ate no fish.

Harris and Connor (1980) were first to prove that dietary fish oils, rich in omega-3 fatty acids (especially eicosapentaenoic acid or EPA), are potent agents in the reduction of plasma triglycerides and very low density lipoproteins (VLDL). Several studies have since confirmed their findings (Bronsgeest-Schoute et al. 1981, Nestel et al. 1984, Phillipson et al. 1985).

Simons et al. (1985) showed that fish oils reduced plasma cholesterol in hypercholesterolaemic subjects, using olive oil as control, but this has not been confirmed in studies of normal subjects. However, Harris et al. (1983) found that fish (salmon) oil and polyunsaturated (vegetable) oil were equally effective in lowering cholesterol. Woodcock et al. (1984) made similar observations in patients with peripheral vascular disease; however, 40% of those on fish oil improved clinically, with fall in blood viscosity. Fehily et al. (1983) found no cholesterol-lowering effect on a fish diet, however, the amount of polyunsaturated fats in the diets of the control subjects was not measured and this may be significant.

Since Bang and Dyerberg's (1972) first investigations of the beneficial effects of fish oil, there have been many studies, which suggest alternate mechanisms by which EPA reduces CHD risk. Norris et al. (1986) found EPA supplements significantly reduced supine systolic BP in patients with mild essential hypertension, and suggested this may be due to an effect on platelet prostaglandion metabolism. Similar findings were made in subjects with normal BP (Mortensen et al. 1983, Lorenz et al. 1983, Singer et al. 1983), but other reports show increased BP with fish oil supplementation (Scherhag et al. 1982).

Inhibition of platelet aggregation may be another significant effect of EPA (Dyerberg et al. 1978, Schimke et al. 1984, Sanders 1985), but there is as yet no unanimity of opinion regarding these effects of EPA (Hornstra 1975). Bleeding time is prolonged in healthy subjects taking EPA (Sanders et al. 1981, Herold and Kinsella 1986, Hornstra and Hemker 1979). Hornstra and Hemker (1979) provided evidence that there is a mutual interaction between the injured vessel wall, the platelets and the blood coagulating system, which may suggest that EPA was generally antithrombotic, compared to saturated fats. Other postulates include anti-inflammatory effects by inhibiting the 5-lipoxygenase pathway in neutropohils and monocytes and inhibiting the leukotriene B_4 functions of neutrophils (Lee et al. 1985).

The effects of alcohol consumption on CHD risk is controversial. Some long-term population surveys suggest an association (Blackwelder et al. 1980, Kozararevic et al. 1980, Donahue et al. 1986), but the coincidence of other risk factors, such as obesity and smoking make causality difficult

to prove. Multivariate analysis of the association between problem drinking and 15 year mortality rates showed heavy drinkers have a significantly higher mortality rate from all causes, but the increase CHD mortality rate was not significant (Dyer et al. 1977).

A number of studies have suggested that moderate consumption of alcohol might be protective against CHD (for review of the literature, see Rohan 1984, Eichner 1985). The alcohol-CHD relationship may be U-shaped, so that the risk of CHD associated with moderate levels of alcohol consumption is lower than that for abstainers and heavy drinkers.

Apart from the adverse effects on BP discussed in Chapter 4, there is extensive research into its effects on lipid profile, liver function, steroid metabolism, thrombogenesis and cardiotoxicity. The present study is concerned with the effects of regular moderate alcohol consumption on the plasma lipid and glucose levels.

The consumption of moderate amounts of alcohol leads to increased plasma triglyceride (TG) (Maserei et al. 1986), although its effects on plasma cholesterol are less clear (Herold and Kinsella 1986). Alcohol increases HDL cholesterol. A recent study by Taskinen et al. (1987) showed that moderate drinking led to increased HDL_3 subfraction, whereas chronic alcoholics had increased HDL_2, and a smaller increase in HDL_3 subfractions. Whether the increased HDL_3 subfraction seen in moderate drinkers contributes to their reduced risk of CHD or whether some other mechanism is at work remains uncertain. (Eichner 1985, Wahlqvist 1985).

Any assessment of the therapeutic effects of dietary fish oil must consider the possible adverse effects in areas only indirectly related to lipoproteins. Theoretical concerns derive from the major metabolic effects that alterations in lipid metabolism may have on related biochemical pathways via, for example, the glucose fatty acid cycle (Randle et al. 1965). Clinically, the phenonemon of insulin resistance in the obese subject may be a manifestation of the far-reaching effects of disturbed lipid metabolism. Any attempt to alter lipid metabolism necessitates a full appraisal of effects on other metabolic pathways.

Since it is known that alcohol increases triglyceride, whereas fish oil decreases it, the present study sought to determine whether the co-administration of both substances would show no change in triglyceride; as well, this study examined the effect of dietary fish oil on plasma total cholesterol, HDL cholesterol and glucose and insulin levels 36 hours after a two week period of moderate ethanol consumption. The results were compared with those following periods of alcohol alone and abstinence from both oil and most alcohol.

5.2 METHODS

The present study was done concurrently with the study of regular alcohol use and BP, using the same ten subjects. (Refer to Chapter 4 for method). At the end of two weeks of a given treatment phase, the subject abstained from alcohol for 36 hours prior to testing. After the evening meal, the subject fasted for 12-13 hours. On waking, the subject would walk from the common sleeping quarters into the adjoining surgery building.

After a 15 minute rest, venous blood was taken for fasting lipids (collected in EDTA) and for glucose and insulin (collected in sodium oxalate/potassium chloride). After mixing, the samples were immediately centrifuged and the plasma collected. The supernatant of 1 ml of the EDTA plasma was collected for HDL cholesterol determination after the manganese chloride/heparin precipitation

method (Burnstein et al. 1970), which was commenced within 15 minutes of sampling; all plasma was frozen at -18°C for later analysis.

On completion of the study, all samples were analysed simultaneously. The methods used to measure the plasma glucose and lipids are described in Chapter 2. Insulin concentrations were measured on return to Australia by radioimmune assay, using immunoreactive insulin. Concentrations in plasma were measured using commercially available antiserum, second antibody and human insulin standard, purchased from Burroughs Wellcome. The range of the assay was 5-200 mU/litre; interassay coefficient of variation was 5% at 50 mU/litre.

5.3 RESULTS

Of the 14 subjects who commenced the study, 10 were able to complete it: the 3 oldest volunteers (ages 43, 50 and 51 years) all withdrew due to intolerance of alcohol in such doses. A fourth subject was non-compliant and was rejected from the study. The experiment was not blinded for the author nor the subjects. However, the blood samples were coded and, therefore, the measurements were performed 'blind'.

5.3.1 Lipids

The mean plasma TG during the 'Alcohol' period was 1.09 mmol/l ±0.17 S.D, slightly higher than the mean Australian population value is 0.98-1.12 mmol/l, for similar aged males (Australian National Heart Foundation 1983). This fell 23% to 0.84 ±0.18 with the addition of fish oil; this level was closely similar to the level following the 'low alcohol' period (0.86 ±0.07) (Figure 22).

A significant increase (13%) in total cholesterol following increased alcohol intake (Figure 23). The addition of fish oil made no difference. Total cholesterol levels were 4.60 ±0.30 for 'low alcohol', 5.17 ±0.28 for 'alcohol' and 5.28 ±0.28 for 'alcohol plus oil' periods.

HDL cholesterol levels also increased with the increased alcohol intake and increased by a further 25% with the addition of the fish oil (Figure 24). Fasting plasma HDL cholesterol levels were: 1.21 ±0.11, 1.42 ±0.11 and 1.61 ±0.16, for 'low alcohol', 'alcohol' and 'alcohol plus oil' periods, respectively.

LDL cholesterol showed no significant changes throughout the study. The values were: 3.22 ±0.29, 3.54 ±0.32 and 3.50 ±0.26, for 'low alcohol', 'alcohol' and 'alcohol plus oil' periods, respectively (Figure 25).

The HDL:LDL cholesterol ratios increased from 37% 'low alcohol', to 40% 'alcohol' and 46% 'alcohol plus oil' periods.

5.3.2 Blood glucose

The mean 'low alcohol' period fasting glucose level was 5.18 mmol/l ±0.10 S.D. Australian normal value 4.0-6.0 mmol/l (Biochemistry Department, Alfred Hospital, Melbourne 1986). There was no significant difference during the 'alcohol' period (5.23 ±0.19). However, there was a small but significant (8%) increase to a mean value of 5.60 ±0.14, following the 'alcohol plus fish oil' period (Figure 26).

5.3.3 Plasma insulin

Plasma insulin levels were measured and showed a response similar to the glucose (Figure 27). Fasting mean insulin values were 7.0 mU/l ±0.3S.D, 7.4 ±1.11 and 8.3 ±0.82, for 'low alcohol', 'alcohol' and 'alcohol plus oil' periods, respectively.

5.4 DISCUSSION

The failure of the three oldest subjects to tolerate moderate doses of alcohol is consistent with the common finding of increased sensitivity to alcohol with age. This issue has been recently reviewed, and it remains unclear whether the phenonemon is due to psychosocial, metabolic or physiological changes (Cassel and Walsh 1984).

The question of alcohol's effects on plasma lipids remains complex. It is evident from many animal and perfusion studies that both ethanol and fish oil have manifold effects on lipid metabolism. The quantity and duration of exposure to both alcohol and fish oil can alter the effects. Therefore, it is not surprising that varying results have been found in clinical trials. One usually consistent finding, however, is the TG lowering effect of EPA.

The present study found that fish oil completely reversed the increase in plasma TG induced by alcohol. Compared to alcohol alone, there was a 23% fall in plasma TG when fish oil was coadministered with alcohol (Figure 22). These findings are plausible when the effects of ethanol and fish oil on hepatic lipid metabolism are compared: ethanol increases, inter alia, hepatic VLDL production and free fatty acid esterification to TG (Nestel and Hirsch 1965); EPA decreases hepatic VLDL production and is likely to increase fatty acid oxidation (Wong et al. 1984).

The decrease in TG shown in Figure 22 was significant. However, because the alcohol-induced increase in these (healthy) subjects was still in the lower range of normal for their age group (0.98 -1.12 mmol/l), the absolute fall in TG (and, presumably, VLDL) was small.

Lieber (1973) reviewed the literature and stated that hyperlipaemia follows the fatty accumulation induced in the liver by ethanol. There is decreased fat oxidation and increased hepatic lipogenesis. Nestel and Hirsch (1965) found, in particular, an increase in plasma TG under the influence of ethanol. One clinical study (Ginsberg et al. 1974) found a significant rise in triglycerides following ethanol ingestion in hypertriglyceridaemic people, but not in normal subjects. However, measurements were made after only seven days, whereas the Swedish group (Belfrage et al. 1977) showed an increase in triglycerides after two weeks in healthy subjects taking moderate alcohol, as was found in the present study.

With daily administration of fish oil, Simons et al. (1985) showed plasma TG fell 41% and 58% in types IV and V hyperlipidaemic patients (respectively). Nestel et al. (1984) showed marked TG falls in both normal and hyperlipidaemic subjects following fish oil. There are many studies to support the potent triglyceride-lowering effect of fish oil (Bronsgeest-Schoute et al. 1981, Fehily et al. 1983, Herold and Kinsella 1986).

Although well tolerated in the present study, the daily dosage of 15 capsules used in the present study is likely to lead to compliance problems in all but the most motivated patient. Sanders and Roshani (1983) showed that 10 g (capsules) daily, but not lower doses, had a significant triglyceride-lowering effect in normal subjects. Saynor et al. (1984) lowered triglycerides in hyperlipidaemic patients using 5 g/day. The potent and almost universal lipid-lowering effects of EPA in these patients make it an attractive therapeutic option.

Throughout the study, plasma total cholesterol remained within the 'normal' range for the Australian male population, aged 25-34 years, which is 5.15-5.33 mmol/litre (National Heart Foundation 1983).

Figure 22. Plasma Triglyceride

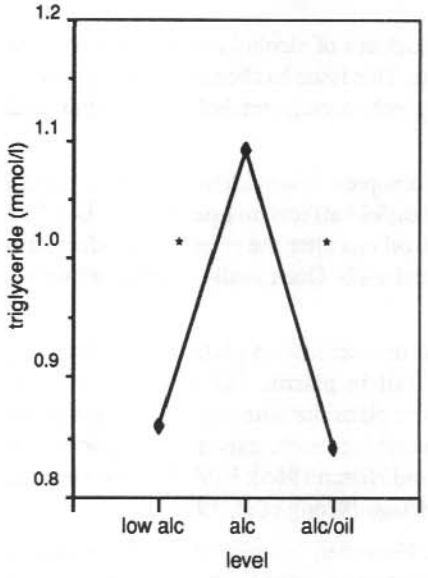
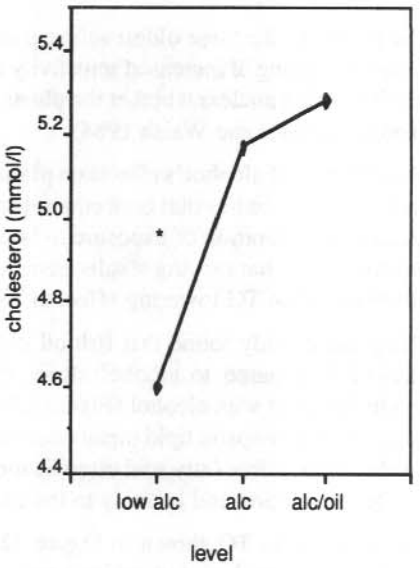


Figure 23. Total cholesterol levels



Fgure 24. HDL cholesterol

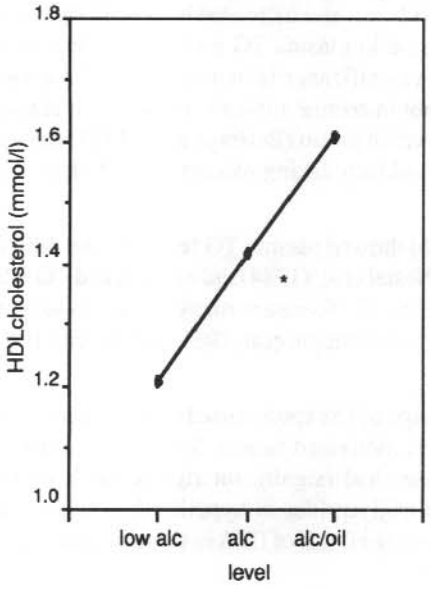
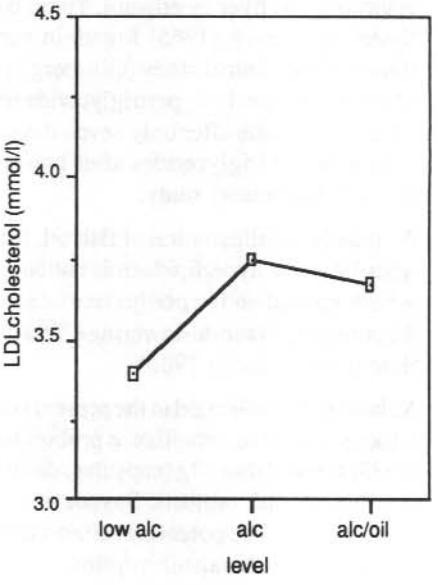


Figure 25. LDL cholesterol



*Figures 22—25. Changes in mean fasting plasma levels of: triglyceride, total cholesterol, HDL-cholesterol and LDL-cholesterol following 2 week's treatment of 'low alcohol', 'alcohol', and 'alcohol plus oil' (see text for details). Significance ($p < 0.05$) is denoted by *.*

Figure 26. Fasting glucose.

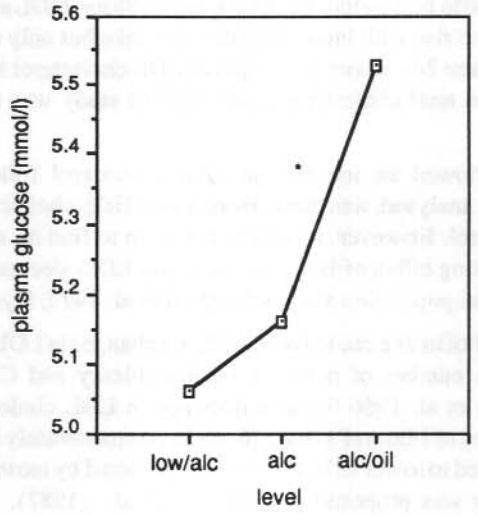
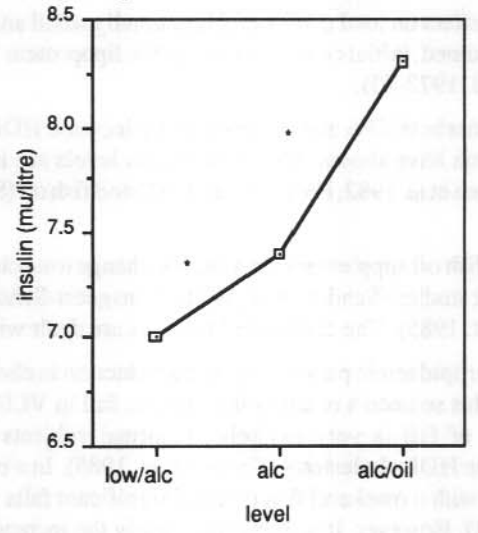


Figure 27. Plasma insulin.



*Figures 26 and 27. Changes in mean fasting plasma levels of glucose and insulin following 2 week's treatment of 'low alcohol', 'alcohol', and 'alcohol plus oil' (see text for details). Significance is denoted by * ($p<0.05$).*

Alcohol produced a small but significant rise in cholesterol (Figure 23). The net movement of total cholesterol can be explained in part by the changes in the fractions, HDL and LDL. HDL cholesterol levels in this study tended to rise with increased ethanol intake but only reached significance with the addition of fish oil (Figure 24), whereas changes in LDL cholesterol levels were not significant (Figure 25). The change in total cholesterol in the present study was small, and unlikely to be clinically significant.

Ginsberg et al. (1974) showed an increase in total cholesterol following moderate alcohol consumption, which, when analysed, was due to increases in HDL cholesterol, as seen in the present study, and VLDL cholesterol. However, it is more common to find no significant change in total cholesterol due to a cancelling effect of HDL- increase and LDL- decrease (Taskinen et al. 1987). This is supported by several population studies (Castelli et al. 1977, Dyer et al. 1977).

The fact that moderate alcohol intake caused no significant changes in LDL cholesterol in the present study is consistent with a number of previous studies (Fleury and Couzigou 1984, Berg and Johansson 1973). Masarei et al. 1986 found a decrease in LDL cholesterol following alcohol, however, the longer duration of Masarei's study (6 weeks) on moderately large quantities of ethanol (450 mls/week) may have led to lower LDL levels being depleted by inhibited conversion of VLDL to LDL. This mechanism was proposed by Taskinen et al. (1987), who showed lower LDL cholesterol levels in alcoholic men, but not in non-alcoholic men drinking moderately (32-90 g/day), a finding which would support the present study (1 g ethanol/kg/day). Population studies are consistent with this view, with a weak but consistent negative correlation between alcohol consumption and LDL cholesterol levels.

In summary, alcohol's net effect on total cholesterol is generally small and appears to be dependent on the dose of alcohol consumed, initial concentrations of the lipoprotein variables and the duration of treatment (Belfrage et al. 1972-73).

The present study showed that both EPA and ethanol acted to increase HDL levels. This is consistent with previous studies, which have shown HDL cholesterol levels are increased by both ethanol (Castelli et al. 1977, Taskinen et al. 1982, Haskell et al. 1985) and fish oil (Saynor et al. 1984, Simons et al. 1985).

The present study showed fish oil supplementation did not change total cholesterol levels, a finding which is supported by most studies (Sanders et al. 1981, Bronsgeest-Schoute et al. 1981, Saynor et al. 1984, von Schacky et al. 1985). The cholesterol fractons are dealt with separately below.

One study of Type IIb hyperlipidaemic patients showed a reduction in cholesterol following fish oil administration, however, this seemed a result of the massive fall in VLDL cholesterol (Phillipson et al. 1985). This degree of fall is very unlikely in normal subjects and would probably be counteracted by increases in HDL cholesterol (Simons et al. 1985). In a cross-over study, a full-fat cheese diet was compared with a mackerel fish diet and significant falls in cholesterol were noted (von Lossonczy et al. 1978). However, it is likely that simply the increase in the polyunsaturated/ saturated fat ratio itself was enough to produce the fall in cholesterol, rather than the specific qualities of the n-3 and n-6 polyunsaturated fatty acids in the fish (Harris et al. 1983).

The preparation of fish oil used in the present study provided 67.5 g of cholesterol daily and it is conceivable that this counteracted the potential fall in plasma cholesterol. However, Bang et al. (1976) found the daily cholesterol intake of the predominantly carnivorous Greenland Eskimos to

be about 245 mg/1000 calories. Still, their plasma cholesterol was low, averaging 5.58 ±0.75 mmol/l±SD, compared to the Danes with 6.28 ±0.19. This is consistent with the findings of Harris et al. (1983), who reported a fall in plasma cholesterol following an increase in polyunsaturated fats, despite a continued daily cholesterol intake of 500 mg.

The present study found no alteration in LDL cholesterol levels with EPA. Simons et al. (1985) found an increase LDL cholesterol in hyperlipidaemic patients, whereas Harris et al. (1983) showed a reduction in LDL. Harris et al. (1984) suggested fish oil acted primarily by inhibiting VLDL synthesis rather than increased conversion to LDL cholesterol. Therefore, the effect of fish oil on LDL is only indirectly linked to VLDL levels, which might explain the varying results.

In conclusion, the major effects of marine fish oils on human lipid metabolism is as follows: a marked fall in plasma TG levels, and, presumably, VLDL cholesterol; a rise in HDL cholesterol; a fall in LDL cholesterol in some subjects. The various changes of these lipid components determine the net movement in total plasma cholesterol.

It is concluded that these lipid changes are likely to be beneficial in regard to CHD risk, and might be considered as a useful adjunct to dietary manipulation in the presence of hyperlipoproteinaemia, especially in those patients with elevated TG levels.

5.4.1 Blood glucose and insulin

The present study found plasma glucose was increased following a fish oil diet. The increase was small, and remained within normal limits for fasting glucose levels (<6.00 mmol/l). The concomitant increase in insulin levels with the fish oil suggests a relative hepatic insulin resistance (Figure 26).

Wong et al. (1984) found an increased glucose output, in the presence of increased fatty acid oxidation to acetyl-CoA in rat livers following a fish oil diet, and attributed it indirectly to alterations in lipid metabolism. Illman et al. (1986) supported these findings with their work on diabetic rats: they found fasting blood glucose to be raised following two weeks on a fish oil diet. Further work by Topping et al. (1987) again found glucose to be increased in normal rats on a fish oil diet (when compared with a safflower oil diet). The glucose remained elevated for a prolonged time after insulin administration, suggesting a degree of insulin resistance. The finding of elevated ketone bodies following a fish oil diet in rats (Nestel and Topping 1986) supports the hypothesis that fish oil's positive effect on fatty acid oxidation may be directly responsible for decreased glucose tolerance with fish oil supplementation. Ketone bodies were not measured in the present study.

Under normal conditions, increased fatty acid oxidation in the fasting state is associated with low plasma glucose. In the fasting state, increased levels of fatty acid metabolites, including acetyl-CoA, must be available for energy (Martin et al. 1983). Randle and Garland (1965) first described the disturbance to the glucose fatty acid cycle in maturity onset diabetes, with persistently high concentrations of glucose despite an increased rate of fatty acid oxidation to acetyl-CoA, a situation which would suggest decreased insulin sensitivity. They concluded that increased rates of release and oxidation of fatty acids may make an important contribution to impaired glucose tolerance in patients with insulin resistance. There is an apparent parallel in the subjects taking fish oil in the present study.

It is concluded that diets with high levels of the n-3 polyunsaturated fatty acids may exacerbate some of the metabolic disturbances of diabetes. There is very little in the literature regarding the effects of fish oil on human fasting glucose levels, therefore, the significance of this finding needs further

examination. Furthermore, it would be interesting to examine the effects of EPA without the presence of ethanol.

5.5 CONCLUSION

This study found marine fish oil can reverse the hypertriglyceridaemic effects of alcohol. Fish oil had no effect on the raised total cholesterol levels following alcohol consumption. This may be due to the cancelling effects of HDL cholesterol increase and LDL cholesterol decrease, in some subjects, caused by fish oil. The benefit of fish oil in the reduction of cardiovascular risk factors must be balanced against the potentially lowered glucose tolerance.

Fish oil may be an important dietary supplement in the management of alcoholic fatty liver. It has been suggested that an excess of triacylglycerol is deposited in the liver, when the lipoprotein mechanism to remove, it is inadequate to cope with the surplus of free fatty acid (FFA). This FFA excess is the result of ethanol's blockade of FFA oxidation. As EPA increases FFA oxidation, it may decrease the available FFA and prevent fatty deposition.

CHAPTER 6 - SYNTHESIS AND CONCLUSION

"Non est vivere, sed valere vita est."
"Life is not living, but living in health."

Martial, 43 AD.

Discussion of the findings of the present study has been included in each chapter. Here, these conclusions will be considered in relation to each other and interpreted within the present understanding of effects and significance of cardiovascular risk factors.

Australia's cardiovascular death rate compares unfavourably with many countries. The World Health Organization ranks twenty-seven countries according to their death rates from cardiovascular disease. In 1980, there were 14 countries with a lower death rate amongst men than Australia and 13 countries with a lower death rate amongst women (Uemera and Pisa 1985). For CHD, death rates in Australia were eighth highest for men and seventh highest for women.

Since the mid-1960s Australia, like the United States, has experienced a spectacular decline in mortality form CHD (Leeder and MacMahon 1985). The rate for stroke has been falling steadily since the early 1950s. Despite this, the level remains unacceptably high and cardiovascular disease continues to be a major health problem. The fall in CHD mortality has been attributed, in part, to a decline in the three major risk factors (Better Health Commission 1986).

As mentioned in Chapter 1, the three primary factors associated with CHD are high BP, high blood cholesterol and cigarette smoking. They occur frequently in the Australian community at levels which contribute to the disease.

As a medical officer on an Australian Antarctic station, the author had a prime opportunity to observe the presence of CHD risk factors in apparently healthy expeditioners living in a closed community for the period of a year. The present study examined BP and cholesterol levels, as well as triglyceride levels and glucose tolerance to determine the effects of varying levels of activity and environmental conditions in the polar context.

It was found for the first time that moderate exercise, three times a week, in already active individuals had no effect on BP, whereas the same individuals, during a later sedentary period, showed a major reduction in BP following exercise three times a week, and daily exertion had minimal further hypotensive effect, assuming other variables such as weight, diet and stress levels were constant. All subjects in the present study were in good health. It is possible that greater levels of exercise are required to produce maximum benefit in those with higher levels of CHD risk.

Reduction in BP correlated with level of activity rather than level of fitness, and this has major implications for the type and duration of exercise to be recommended for the reduction of CHD risk. This finding supports the study done by Brownell (1982) who reported that relatively modest levels of exercise may reduce cardiovascular risk. Again, the study by Jennings et al. (1984) mentioned in the first chapter is further evidence that maximal improvement in CHD risk occurs before maximal fitness is achieved.

Attempts to reduce a risk factor by one modification may be counteracted by a continuation or increase in adverse conditions. For example, moderate exercise did not alter the total : HDL cholesterol ratio during the winter program, despite a higher level of fitness and associated increase in HDL cholesterol. The lack of improvement was attributed to winter's higher dietary fat intake. This finding supports the

'global' approach to therapeutic intervention, which recommends the slight modification of many aspects of lifestyle, diet and activity levels to achieve an overall benefit in regard to CHD risk factors.

A new model to further understanding of the relationship between activity and CHD risk factors is the sigmoidal curve. It is suggested that there is an identifiable quantum of, for example, activity required to achieve maximal benefit and the addition of further quanta is unproductive. The ideal quantum for each cardiovascular risk factor is likely to be different. It would be necessary to tailor the 'exercise prescription' for each individual depending on the presence and severity of each risk factor and the individual's response to intervention.

As with any medical intervention, whether pharmacological or not, the risks of treatment must be considered. In the habitually inactive individual, physical exercise is associated with 56 times the risk of a cardiovascular event than sedentary activity. When intervention is aimed at preventing the development of disease in a currently healthy (premorbid) individual, there is a special onus to heed the advice 'primum non nocere'.

The effects of the Antarctic environment varied with the seasons and changes in station activities. The beneficial effects of a high level of activity during the summer and spring might be counteracted in part by the raised level of psychological stress during those hectic periods. On the other hand, the relatively quieter winter months allowed a more sedentary lifestyle and potential for increased cardiovascular risk due to increases in BP and lipid levels.

This thesis was the first to make use of ambulatory BP monitoring in the Antarctic. The effects of a number of factors on BP changes were studied over a 24 hour period. The extent of these findings support the view that ambulatory BP monitoring is a useful and informative non-invasive research tool, which can add to our understanding of the aetiology of hypertension and, in turn, its prevention.

The study of regular alcohol intake effectively highlighted the association of regular 'social' drinking (six to eight drinks daily) with prolonged raised diastolic BP and plasma triglyceride. It is concluded that these results underline the important relationship between alcohol consumption and increased CHD risk factors.

Although the hazards of alcoholism are well recognised, occasional binge drinking is less likely to be considered a potentially life-threatening situation. The present study highlighted the wide swings in BP following acute intoxication, which supported the findings of Hillblom and Kaste (1982) regarding the high incidence of intracranial haemorrhage following acute intoxication, independent of previous BP levels. Individuals with compromised circulation may be particularly at risk.

Another important finding of the present study pointed to the rapid reversibility of the cardiovascular and haematologic effects of alcohol. Increased BP was noted during withdrawal stages and was largely absent by 36 hours after drinking. This may be a significant factor in the epidemiological understanding of the effect of alcohol intake on the CHD risk factors of hypertension and hyperlipidaemia. Abstention from alcohol should be considered as part of the management of essential hypertension.

This thesis confirmed eicosapentaenoic acid as a potent agent in the lowering of plasma triglyceride concentrations; furthermore, EPA was found to reverse the increase in triglyceride following regular alcohol use. Beneficial changes were noted in cholesterol fractions, with the increase in HDL cholesterol and decrease of LDL cholesterol in some subjects. Dietary fish oil may have an important role in the management of hyperlipidaemic patients. The decrease in insulin sensitivity seen with the co-administration of fish oil and alcohol needs further investigation. EPA is postulated to cause

the increase of fatty acid oxidation, which may be a useful adjunct to the treatment of such problems as alcoholic fatty liver.

In conclusion, the present study in Antarctica has added to the knowledge and understanding of the modification of coronary risk factors. The emphasis must now be on the means of introducing effective risk reduction to broader sections of society.

ACKNOWLEDGMENTS

Research for this thesis was carried out on the Antarctic Continent with the support of the Australian Antarctic Division. I am grateful for the cooperation of the Australian National Antarctic Research Expeditioners at Davis station in 1986, without whose ongoing support the completion of this thesis would not have been possible.

The inspiration for undertaking this study is largely due to Dr Desmond Lugg, Assistant Director of Polar Medicine, Antarctic Division. His support and interest has been invaluable. Dr Garry Jennings has provided much advice and encouragement during my time at the Baker Medical Research Institute, Alfred Hospital, Melbourne. Professor Paul Korner and Dr Murray Esler have assisted greatly with editorial comment.

Thanks also to Professor John McNeil, who gave advice on statistical analysis, to Dr Abe Wan who provided guidance in biochemical analytical method. The determination of plasma insulin levels by Dr Keryn O'Dea is gratefully acknowledged.

I wish also to thank Mrs Mary Delafield, Mrs Enid Meldrum and Miss Cate Browne for assistance in the literature search; Mr John Homfrey and Miss Judith Roget for the development of an appropriate exercise testing technique; Dr Peter Gormly for valuable editorial comment; Dr Phillip Barter whose knowledge of lipid metabolism was most helpful; Professor Zen Meglo for advice on spectrophotometric techniques; Mr. Bob Reeves for assistance with the production of photographics.

Finally, I wish to thank my father, Dr JH Deakin who read the manuscript, and my fiancé, Chris Haywood, who has provided support and encouragement for the duration of this study.

APPENDIX I. CALCULATON OF VO_2max. (Consolazio et al. 1963)

$VO_2 = V_i \times F_iO_2 - V_e \times F_eO_2$
if you assume $V_i = V_e$, then
$VO_2 = V\ (F_iO_2 - F_eO_2)$ ..... equation 1

Gas concentrations do, however, vary slightly from inspired to expired depending on the ratio of O_2 uptake to CO_2 evolved. The effect of change in volume can be corrected by using N_2 which itself does participate significantly in gas exchange but which is affected by the small change in volume from inspired to expired.

$V_i \times F_iN_2 = V_e \times F_eN_2$

Inspired gas concentrations:
Inspired O_2 20.94%
Inspired CO_2 0.03%
Inspired N_2 79.04% (including Argon, etc.)

$VO_2 = V_i \times F_iO_2 - V_e \times F_eO_2$ ..... equation 2
$V_i \times F_iN_2 = V_e \times F_eN_2$
$V_e = V_i \times F_i N_2 / F_eN_2$

Substitute in equation 2:
$VO_2 = V_i \times F_iO_2 - V_i \times F_iN2 \times FeO_2 / F_eN2$
$F_eN_2 = 1 - F_eO_2 - F_eCO_2$
$VO_2 = V_i \times (F_iO_2 - F_eO_2 \times F_iN_2 / (1 - F_eO_2 - F_eCO_2)$
$= V_i \times (F_iO_2 - 0.7903 \times F_eO_2 / (1 - F_eO_2 - F_eCO_2))$

VO_2 is by convention reported at standard pressure (760 mm Hg) and temperature (0°C).

and as a dry gas, ie. VO_2 STPD*.
VO_2 STPD = $V_{i\ atp}$ $(0.2648 \times F_eO_2 / (1 - F_eO_2 - F_eCO_2))$
V_i is expressed in terms of BTPS, which is normal body temperature and atmospheric pressure, saturated with water.

F_eO_2 will change if CO_2 is absorbed from the expirate before analysis. The percentage change in F_eO_2 will be proportional to the change in volume of the CO_2 absorbed relative to the non-absorbed gas.
i.e. $100/(100 - F_eCO_2) = F_eO_2\ (1) / F_eO_2\ (2)$
where F_eO_2 and F_eCO_2 are expressed as a percentage and
F_eO_2 (1) = F_eO_2 of expired dry gas.
F_eO_2 (2) = F_eO_2 of dry expired gas which has been drawn through a CO_2 absorber first.

* $V_{stpd} = \frac{(V_{observed} \times 273)}{(T+273) \times \frac{Pb}{760}}$

where Vobserved = gas volume
T = ambient temperature/°Celsius
Pb = ambient pressure/mm Hg

APPENDIX II. FISH OIL COMPOSITION

Cholesterol		4.5mg/g
a-Tocopherol		1.0 IU/g
Vitamin D		0
Vitamin A		<100 IU/g
Fatty acids:		
	myristate	8%
	palmitate	19%
	palmitoleate	12%
	stearate	3%
	oleate	18%
	linoleate	4%
	arachidonate	<1%
	eicosapentaenoate	17%
	docosahexaenoate	12%
Kilojoules		41/g

REFERENCES

Alexander, S. (1984). Physiologic and biochemical effects of exercise. *Clinical Biochemistry 17*:126-31.

Anton, A.H. (1965). Ethanol and urinary catecholamines in man. *Clinical Pharmacology Therapeutics 6*:462.

Antonis. A., Bersohn, I. *and* Easty, D.L. (1963). Serum lipid changes in young men in Antarctica. *Journal of Physiology (London) 167*:26-27.

Arkwright, P.D., Beilin, L.J., Rouse, I., Armstrong, B.K. *and* Vandongen, R. (1982). Effects of alcohol use and other aspects of lifestyle on prevalence of hypertension on a working population. *Circulation 66*:60-66.

Arkwright, P.D., Beilin, L.J., Vandongen, R., Rouse, I. *and* Lalor, C. (1982). The pressor effect of moderate alcohol consumption in man: a search for mechanisms. *Circulation 66*:515-519.

Armitage, D.P., Fox, W., Rose, G.A. *and* Tinker, C.M. (1966). The variability of measurements of casual blood pressure, II: survey experience. *Clinical Science (London) 30*:337-344.

Asmussen, E., Hald, J. *and* Larsen V. (1948). The pharmacological action of acetaldehyde on the human organism. *Acta Pharmacologica 4*:311.

Astrand, P-O. *and* Rodahl, K. (1977). *Textbook of work physiology: physiological basis of exercise*. McGraw-Hill Book Co., New York. (second edition)

Australian National Blood Pressure Study. (1980). *National Heart Foundation risk prevalence survey*.

Ayman, D. *and* Goldshine, A.D. (1940). Blood pressure determinations by patients with essential hypertension. I. The difference between clinic and home readings before treatment. *American Journal of Science 200*:465-474.

Bachelard, M. (1982). The health organization of T.A.A.F. *Medicale Tribune 41*:12-21.

Balazs, N.D.H. *and* Walqvist, M.L. (1985). Variability of lipid risk factors in normal men. *Clinical and Biochemical Reviews 6*:94.

Bang, H.O., Dyerberg, J. *and* Hjørne, N. (1976). The composition of food consumed by Greenland Eskimos. *Acta Medica Scandinavica 200*:69-73.

Bang, H.O. *and* Dyerberg, J. (1972). Plasma lipids and lipoproteins in Greenlandic West Coast Eskimos. *Acta Medica Scandinavica 192*:85-94.

Beaglehole, R. (1986). Medical management and the decline in mortality from coronary heart disease. *British Medical Journal 292*:33-35.

Beckman, M., Panfilov, V., Sivertsson, R., et al. (1981). Blood pressure and heart rate recordings at home and at the clinic. *Acta Medica Scandinavica 210*:97-102.

Belfrage, P., Berg, B., Cronholm, T., et al. (1972-73). Prolonged administration of ethanol to young, healthy volunteers: effects on biochemical, morphological and neurophysiological parameters. *Acta Medica Scandinavica 552*:5-44.

Belfrage, P., Berg, B., Hagerstrand, et al. (1977). Iterations of lipid metabolism in healthy volunteers during long-term ethanol intake. *European Journal of Clinical Investigation* 7:127-131.

Berg, B. *and* Johansson, B.G. (1973). Effects on parameters of liver function, plasma lipid concentrations and lipoprotein patterns. *Acta Medica Scandinavica 552*:13.

Björntrop, P. (1982). Hypertension and exercise. *Hypertension 4* (III): III-56-III-9.

Björntrop, P., de Jounge, K., Sjöstrom, L. *and* Sullivan, L. (1970). The effect of physical training on insulin production in obesity. *Metabolism 19*:631-638.

Björntrop, P. *and* Krotiewski, M. (1985). Exercise treatment in diabetes mellitus. *Acta Medica Scandinavica 217*:3-7.

Blackwelder, W.C., Yano, K., Rhoads, G.G., et al. (1980). Alcohol and mortality: the Honolulu Study. *American Journal of Medicine 68*:164-169.

Blair, S.N., Goodyear, N.N., Gibbons, L.W. *and* Cooper, K.H. (1984). Physical fitness and incidence of hypertension in healthy normotensive men and women. *Journal of the American Medical Association 252*:487-490.

Blankenhorn, D.H., Nessim, S.A., Johnson, R.L., Sanmarco, M.E., Azen, S.P. *and* Cashin-Hemphill, L. (1987). Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass graft. *Journal of the American Medical Association 257*:3233-3240.

Boas, E.P. *and* Goldschmidt, E.F. (1932). *The heart rate*. Springfields, Ill., Thomas. 166 pp.

Bodey, A.S. (1971). *Human acclimatization to cold in Antarctica*. A thesis submitted for the degree of Doctor of Medicine , University of Melbourne.

Bonnano, J.A. *and* Lies, J.E. (1974). Effects of physical training on coronary risk factors. *American Journal of Cardiology 33*:760-764.

Boriskin, V.V. (1973). Causes of changes in the state of well-being and individual physiological functions during work at polar stations. In: Matusov, A.L. (Ed.). *Medical Research on Arctic and Antarctic Regions Proceedings Volume 299*. Gidrometeorologicicheskoe Izdatel'stvo, Leningrad, 1971. Israel Program for Scientific Translations, Jerusalem.

Boyer, J.L. *and* Kasch, F.W. (1970). Exercise therapy in hypertensive men. *Journal of the American Medical Association 211*:1668-1671.

Brennan, P.J., Greenberg, G., Miall, W.E. *and* Thompson, S.G. (1982). Seasonal variation in arterial blood pressure. *British Medical Journal 285*:919-923.

Brensike, J.F., Levy, R.I., Kelsey, S.F., et al. (1984). Effects of therapy with cholestyramine on progression of coronary arteriosclerosis: results of the NHLBI type II coronary intervention study. *Circulation 69*:313-324.

Bronsgeest-Schoute, H.C., van Gent, C.M., Luten, J.B. *and* Ruite, A. (1981). The effect of various intakes of omega-3 fatty acids on the blood lipid composition in healthy human subjects. *American Journal of Clinical Nutrition 34*:1752-1757.

Brown, G.E. (1930). Daily and monthly rhythm in the blood pressure of a man with hypertension: a three year study. *Annual International Medicine 3*:1177-1189.

Brownell, K.D. (1982). Obesity: understanding, and treating a serious, prevalent and refractory disorder. *Journal of Consulting and Clinical Psychiatry 50*:820-840.

Budd, G.M. (1965). Effects of cold exposure and exercise in a wet, cold Antarctic climate. *Journal of Applied Physiology 20*:417-422.

Budd, G.M. *and* Warhaft, N. (1970). Urinary excretion of adrenal steroids, catecholamines and electrolytes in man, before and after acclimatization to cold in Antarctica. *Journal of Physiology (London) 210*:799-806.

Budd, G.M. *and* Warhaft, N. (1966). Cardiovascular and metabolic responses to noradrenalin in man, before and after acclimatization to cold in Antarctica. *Journal of Physiology 186*:233-242.

Burnstein, M., Scholnick, H.R. *and* Morfin, R. (1970). Rapid method for isolation of lipoproteins from human serum by precipitation with polyanion. *Journal of Lipid Research 11*:583.

Campbell, I.T. (1977). Glucose tolerance in Antarctica. *British Antarctic Survey Bulletin* (46):29-38.

Carlson, L. *and* Bottiger, A. (1972). Ischaemic heart disease in relation to fasting values of plasma triglyceridesand cholesterol: Stockholm Prospective Study. *Lancet 1*:865.

Cassel, C.K. *and* Walsh, J.R. (Eds). (1984). *Geriatric Medicine: alcohol and drug abuse II*:221.

Castelli, W.P., Doyle, J.T., Gordon, T., et al. (1977). Alcohol and blood lipids: the Co-operative Lipoprotein Phenotyping Study. *Lancet 2*:153-155.

Choquette, G. *and* Ferguson, R.J. (1973). Blood pressure reduction in 'borderline' hypertensives following physical training. *Canadian Medical Association Journal 108*:699.

Connor, W.E. *and* Connor, S.L. (1972). The key role of nutritional factors in the prevention of coronary artery disease. *Preventive Medicine 1*:49.

Consolazio, C.F., Johnson, R.E. *and* Pecora, L.J. (1963). *Physiological measurements of metabolic functions in man*. McGraw-Hill Book Company. Chapter 5.

Conway, J., Boon, N. *and* Vann Jones, J. (1983). Involvement of the baroreceptor reflexes in the changes in blood pressure with sleep and mental arousal. *Hypertension 5*:746-748.

Cook, D.G., Shaper, A.G., Pocock, S.J. *and* Kussick, S.J. (1986). Giving up smoking and the risk of heart attacks. A report from the British Regional Heart Study. *Lancet 2*:1376-1379.

Cooper, K.H., Pollock, M.L. *and* Martin, R.P. (1976). Physical fitness levels vs selected coronary risk factors: a cross-sectional study. *Journal of the American Medical Association 236*:166-169.

Cullinane, E.M., Sady, L., Vadeboncoeur, M., Burke, M. *and* Thompson PD. (1986). Cardiac size and VO2max do not decrease after short-term exercise cessation. *Medical Science in Sports and Exercise 18*:420-424.

D'Alonzo, C.A. *and* Pell, S. (1968). Cardiovascular disease among problem drinkers. *Journal of Occupational Medicine 10*:344.

De Backer, G., Kornitzer, M., Sobolski, J., Dramaix, M., Degré, S., de Marneffe, M. *and* Denolin, H. (1981). Physical activity and physical fitness levels of Belgian males aged 40-55 years. *Cardiology 67*:110-128.

de Leeuw, P.W., van Leeuwen, S.J. *and* Birkenhäger, W.H. (1985). Effect of sleep on blood pressure and its correlates. *Clinical and Experimental Hypertension A7*:179-186.

Dembrowski, T.M. *and* MacDougall, T.M. (1984). Validation of the Vita-Stat automated noninvasive blood pressure recording device. In: Herd, J.A., Gotto, A.M., Kaufman, P.C. *and* Weiss, S.M. (Eds). *Cardiovascular instrumentation: applicability of new technology to bio-behavioural research.* Bethesda, MD, National Institutes of Health. Pp. 55-78.

Dick, A.F. (1985). *Work, health and applied physiology on an expedition in Antarctica.* University of Sydney, Sydney. Master of Public Health, thesis. Pp. 112.

Dill, D.B. (1964). *Handbook of physiology. Section 4: Adaptation to the environment.* Pp. 160-163.

Di Rienzo, M., Grassi, G., Gregorni, L., et al. (1983). Discontinuous blood pressure measurements do not prevent accurate estimation of 24-hour average blood pressure. *Journal of Hypertension 1*(2):299-301.

Donahue, R.P., Abbott, R.D., Reed, D.M. *and* Yano, K. (1986). Alcohol and hemorrhagic stroke: the Honolulu Heart Program. *Journal of the American Medical Assocation 255*:2311-2314.

Drayer, J.I.M., Weber, M.A. *and* Chard, E.R. (1984). Non-invasive automated blood pressure monitoring in ambulatory normotensive men. In: Weber, M.A. *and* Drayer, J.I.M. (Eds). *Ambulatory blood pressure monitoring.* Darmstadt, Steinkopff. Pp. 129-136.

Duffield, R.G.M., Lewis, B., Miller, N.E., Jamieson, C.W., Brunt, J.N.H. *and* Colchester, A.C. (1983). Treatment of hyperlipidaemia retards progression of symptomatic femoral atherosclerosis. A randomised controlled trial. *Lancet 2*:639-642.

Duncan, J.J., Farr, J.E., Upton, S.J., Hagan, R.D., Oglesby, M.E. *and* Blair, S.N. (1985). The effects of aerobic exercise on plasma catecholamines and blood pressure in patients with mild essential hypertension. *Journal of the American Medical Association 254*:2609-2613.

Durnin and Womersley. (1974). *British Journal of Nutrition 32*:77.

Dyer, A.R., Stamler, J., Oglesby, P., et al. (1977). Alcohol consumption, cardiovascular risk factors and mortality in two Chicago epidemiological studies. *Circulation 56*:1067-1074.

Dyerberg, J., Bang, H.O., Moncada, S. *and* Vane, J.R. (1978). Eicosapentaenoic acid and prevention of thrombosis? *Lancet 2*:117-119.

Eade, N.R. (1959). Mechanism of sympathomimetic action of acetaldehydes. *Journal of Pharmacology and Experimental Therapeutics 127*:29.

Edington, J., Geekie, M., Carter, R., et al. (1987). Effect of dietary cholesterol on plasma cholesterol concentration in subjects following reduced fat, high fibre diet. *British Medical Journal 294*:333-336.

Eichner, E.R. (1983). Exercise and heart disease. Epidemiology of the 'exercise hypothesis'. *American Journal of Medicine 75*:1008-1023.

Eichner, E.R. (1985). Alcohol versus exercise coronary protection. *American Journal of Medicine 79*:231-240.

Fager, G., Wiklund, O., Olofsson, S.O. *and* Bondjers, G. (1982). Seasonal variations in serum lipids and apolipoprotein levels evaluated by periodic regression analyses. *Journal of Chronic Diseases 35*:643-648.

Fehily, A.M., Burr, M.L., Phillips, K. *and* Deadman, N.M. (1983). The effect of fatty fish on plasma lipid and lipoprotein concentrations. *American Journal of Clinical Nutrition 38*:349-351.

Fitzgerald, D.J., O'Malley, K. *and* O'Brien, E.T. (1984). Reproducibility of ambulatory blood pressure recordings. In: Weber, M A. *and* Drayer, J.I.M. (Eds). *Ambulatory blood pressure monitoring*. Darmstadt, Steinkopff. Pp. 71-74.

Fletcher, L. (1980). *Annual Medical Report, Mawson Station, Antarctica.* Antarctic Division, Kingston. (unpublished)

Fleury, B. *and* Couzigou, P. (1984). Modifications in plasma HDL cholesterol and apoprotein A-I in healthy subjects after chronic moderate consumption of alcohol. *Bulletin de la Societe France d' Alcool 6*:30.

Friedewald, W.T., Levy, R.I. *and* Frederickson, D.S. (1972). Estimation of the concentration of Low-Density Lipoprotein Cholesterol in plasma, without the use of preparative ultracentrifuge. *Clinical Chemistry 18*:499-502.

Fry, M.M., Spector, A.A., Connor, S.L., et al. (1973). Intensification of hypertriglyceridemia by either alcohol or carbohydrate. *American Journal of Clinical Nutrient 26*:798.

Fuller, J.H., Shipley, M.J. *and* Rose, G., et al. (1980). Coronary heart disease and impaired glucose tolerance. The Whitehall Study. *Lancet 1*:1373.

Gill, J.S., Zezulka, A.V., Shipley, M.J., Gill, S.K. *and* Beevers DG. (1986). Stroke and alcohol consumption. *New England Journal of Medicine 315*:1041-1046.

Gilman, L.S., Goodman, A.G. *and* Gilman, A. (1975). *The pharmacological basis of therapeutics*. MacMillan Publishing Co. Pp. 137.

Ginsberg, H., Olefsky, J., Farquhar, J.W. *and* Reaven, G.M. (1974). Moderate ethanol ingestion and plasma triglyceride levels: a study in normal and hypertriglyceridemic persons. *Annual of International Medicine 80*:143-149.

Godwin, J.A. (1983). *A preliminary investigation into stress in Australian Antarctic expeditioners*. Master of Arts thesis. University of Melbourne. 195 pp.

Goldberg, L. *and* Elliot, D.L. (1985). The effect of physical activity on lipid and lipoprotein levels. *Medical Clinics of North America 69*:41-55.

Gordon, T., Kannel, W.B., Castelli, W.B., et al. (1980). Lipoproteins, cardiovascular disease and death. The Framingham Study. *Archives of International Medicine 141*:1128-1131.

Gotto, A.M., Jr. (1984). Can the progression of atherosclerosis be halted? *Drug therapy*. Pp. 37-39.

Gould, B.A., Mann, S., Davies, A.B., Altman, D.G. *and* Raftery, E.B. (1981). Does placebo lower blood pressure? *Lancet II*:1377-1381.

Grundy, S.M., Mok, H.Y.I., Zech, L., et al. (1979). Transport of very low density lipoprotein triglycerides in varying degrees of obesity and hypertriglyceridemia. *Journal of Clinical Investigation 63*:1274.

Guilleminault, C., Mondini, S. *and* Hayes, B. (1985). Diabetic autonomic dysfunction, blood pressure and sleep. *Annals of Neurology 18*:670-675.

Gunderson, E.K.E. (1968). Mental health problems in Antarctica. *Archives of Environmental Health 17*:558-564.

Gyntelberg, F., Brennan, R., Holloszy, J.O., et al. (1977). Plasma triglyceride lowering by exercise despite increased food intake in patients with type IV hyperlipoproteinemia. *American Journal of Clinical Nutrient 30*:716-720.

Harris, W.S *and* Connor, WE. (1980). The effects of salmon oil upon plasma lipids, lipoproteins and triglyceride clearance. *Transactions of the Association of American Physicians 43*:148-155.

Harris, W.S., Connor, W.E. *and* McMurry, M.P. (1983). The comparative reductions of the plasma lipids and lipoproteins by dietary polyunsaturated fats: salmon oil versus vegetable oils. *Metabolism 32*:179-184.

Harris, W.S., Connor, W.E., Inkeles, S.B. *and* Illingworth, D.R. (1984). Dietary omega-3 fatty acids prevent cartbohydrate-induced hypertriglyceridemia. *Metabolism 33*:1016-1019.

Harrison, D.C. (1985). Chairman's summary. In: Harrison, D.C., Haskell, W.L. *and* Lamdin, E.A. (Eds). *American Journal of Cardiology 55*:27D-28D.

Harshfield, G.A., Pickering, T.G. *and* Laragh, J.H. (1979). A validation study of the Del Mar Avionics ambulatory blood pressure system. *Ambulatory Electrocardiology 1*:7-12.

Haskell, W.L. (1985). Physical activity and health: need to define the required stimulus. *American Journal of Cardiology 55*:4D-9D.

Haskell, W.L., Camargo, C., Williams, P.T., et al. (1984). The effect of cessation and resumption of moderate alcohol intake on serum high density lipoprotein subfractions. A controlled study. *New England Journal of Medicine 310*:805-810.

Haskell, W.L., Taylor, H.L., Wood, P.D., Schrott, H. *and* Heiss, G. (1980). Strenuous physical activity, treadmill exercise test performance and plasma high-density lipoprotein cholesterol. *Circulation* (Suppl IV) *62*:IV-53- IV-61.

Haskell, W.L., Montoye, H.J. *and* Orenstein D. (1985). Physical activity and exercise to achieve health-related physical fitness components. *Public Health Reports 100*:202-212.

Hata, T., Ogihara, T., Maruyama, A., et al. (1982). The seasonal variation of blood pressure in patients with essential hypertension. *Clinical and Experimental Hypertension 3 (A)*:341-354.

Heller, R.F. (1986). The rise and fall of cardiovascular disease. *Medical Journal of Australia 144*:686-688.

Herold, P.M. *and* Kinsella, J.E. (1986). Fish oil consumption and decreased risk of cardiovascular disease: a comparison of findings from animal and human feeding trials. *American Journal of Clinical Nutrition 43*:566-598.

Hicks, K.E. (1965). Changes in the blood-clotting mechanism time, serum cholesterol level, and plasma-prothrombin index in Antarctica. *Lancet 1*:30-32.

Hicks, K.E. (1967). Changes in the blood-clotting mechanism, serum lipids, and basal blood pressure in Antarctica. *Clinical Science 33*:527-538.

Hillbom, M. *and* Kaste, M. (1981). Does alcohol intoxication precipitate aneurysmal subarachnoid haemorrhage? *Journal of Neurology Neurosurgery and Psychiatry 44*:523-526.

Hillbom, M. *and* Kaste, M. (1982). Alcohol intoxication: a risk factor for primary subarachnoid haemorrhage. *Neurology 32*:706-711.

Holloszy, J.O., Skinner, J.S., Toro, G. *and* Cureton, T.K. (1964). Effects of a six month program of endurance exercise on serum lipids of middle-aged men. *American Journal of Cardiology 14*:753-760.

Hornstra, G. (1975). Specific effects of types of dietary fats in arterial thrombosis. In: Vergroesen, A.J. (Ed.), 'The Role of Fats in Human Nutrition.' Academic Press Inc., London. Pp. 244-256.

Hornstra, G. *and* Hemker, H.C. (1979). Clot promoting effect of platelet-vessel wall interaction: influence of dietary fats and relation to arterial thrombus formation in rats. *Haemostasis 8*:211-226.

Howes, L.G. *and* Reid, J.L. (1986). Changes in blood pressure and autonomic reflexes following regular, moderate alcohol consumption. *Journal of Hypertension 4*:421-425.

Howes, L.G. *and* Reid, J.L. (1985). Changes in plasma free 3,4-dihydroxyphenylethylene glycol and noradrenaline levels after acute alcohol administration. *Clinical Science 69*:423-428.

Howes, L.G. *and* Reid, J.L. (1985). Decreased vascular responsiveness to noradrenalin following regular ethanol consumption. *British Journal of Clinical Pharmacology 20*:699-674.

Illman, R.J., Trimble, R.P., Storer, G.B., Topping, D.L. *and* Oliver, J.R. (1986). Time-course of changes in plasma lipids in diabetic rats fed diets high in fish or safflower oils. *Atherosclerosis 59*:313-321.

Ireland, M.A., Vandongen, R., Davidson, L., Beilin, L.J. *and* Rouse, I.L. (1984). Acute effects of moderate alcohol consumption on blood pressure and plasma catecholamines. *Clinical Science 66*:643-648.

James, T.N. *and* Bear, E.S. (1967). Effects of ethanol and acetaldehyde on the heart. *American Heart Journal 74*:243.

Jennings, G., Nelson, L., Esler, M.D., Leonard, P. *and* Korner, P.I. (1984). Effects of changes in physical activity on blood pressure and sympathetic tone. *Journal of Hypertension 2* (Suppl. 3):139-141.

Jennings, G., Nelson, L., Nestel, P., et al. (1986). The effects of changes in physical activity on major cardiovascular risk factors, hemodynamics, sympathetic function, and glucose utilization in man: a controlled study of four levels of activity. *Circulation 73*:30-40.

Julius, S., Ellis, C.N., Pascual, A.V., et al. (1974). Home blood pressure determination. Value in borderline ('labile') hypertension. *Journal of the American Medical Association 229*:663-666.

Kannel, K.B. (1985). Epidemiological assessment of the role of physical activity and fitness in development of cardiovascular disease. *American Heart Journal 109*:876-885.

Kannel, K.B. (1983). High density lipoproteins: epidemiologic profile and risks of coronary artery disease. *American Journal of Cardiology 52*:913.

Kannel, K.B. *and* Sorlie, P. (1979). Some health benefits of physical activity: Framingham study. *International Medicine 139*:857-860.

Kannel, K.B. *and* Sorlie, P. (1975). Hypertension in Framingham. In: Paul, O. (Ed.). *Epidemiology and control of hypertension*. Stratton Intercontinental Medical Book Corp., New York. Pp. 553.

Kaplan, N.M. (1983). Hypertension: prevalence, risks, and effect of therapy. *Annual of International Medicine 98*:705-709.

Keatinge, W.R. (1961). The effect of repeated daily exposure to cold and of improved physical fitness on the metabolic and vascular response to cold air. *Journal of Physiology (London) 157*:209-220.

Kelbaek, H., Gjørup, T., Hartling, O.J., Marving, J., Christensen, N.J. *and* Godfredsen, J. (1987). Left ventricular function during alcohol intoxication and autonomic nervous blockade. *American Journal of Cardiology 59*:685-688.

Keys, A., Anderson, J.T. *and* Grande, F. (1965). Serum cholesterol response to changes in diet. II. The effects of cholesterol in the diet. *Metabolism 14*:59-65.

Klatsky, A.L., Friedman, G.D., Siegelaub, A.B. *and* Gerard, M.J. (1977). Alcohol consumption and blood pressure. *New England Journal of Medicine 296*:1194-1200.

Klatsky, A.L. (1985). Blood pressure and alcohol consumption. In: Bulpitt, C.J. (Ed.). *Handbook of Hypertension 6*:175-190. Epidemiology of Hypertension, Elsevier , Amsterdam.

Kleitman, N. (1963). *Sleep and Wakefulness*. Chicago University Press. (revised edition)

Klimt, C.R., Prout, T.E., Bradley, R.F., et al. (1969). Standardization of the oral glucose tolerance test. Report of the Committee on Statistics of the American Diabetes Association. *Diabetes 18*:299-310.

Kochar, M.S., Ristow, S. *and* Kalbfleisch, J.H. (1985). Effect of seasonal temperature change on blood pressure in a treated hypertensive population. *Journal of Clinical Hypertension 1*:49-52.

Kozararevic, D., McGee, D., Vojvodic, N., et al. (1980). Frequency of alcohol consumption and morbidity and mortality: the Yugoslavia Cardiovascular Disease Study. *Lancet 1*:613-616.

Kritchevsky, D. (1985). Variation in serum cholesterol levels. In: Weininger, J. *and* Briggs, G.M. (Eds). *Nutrition Update N.Y. 2*:91-103. John Wiley.

Kromann, N. *and* Green A. (1980). Epidemiological studies in the Upernavik district, Greenland. Incidence of some chronic diseases. *Acta Medica Scandinavica 208*:401-406.

Kromhout, D., Bosschieter, E.B., De Lezenne *and* Coulander, C. (1985). The inverse relationship between fish consumption and 20-year mortality from coronary heart disease. *New England Journal of Medicine 312*:1205-1209.

LeBlanc, J. (1973). Evaluation of adaptation to the polar environment by autonomic nervous system responses. In: Edholm, O.G. *and* Gunderson, E.K.E. (Eds). *Polar Human Biology*. Pp. 256-64.

Lee, T.H., Hoover, R.L., Williams, J.D., et al. (1985). Effect of dietary enrichment with eicosapentaenoic and docosahexaenoic acids on in vitro neutrophil and monocyte leukotriene generation and neutrophil function. *New England Journal of Medicine 312*:1217-1224.

Leeder, S.R. *and* MacMahon, S.W. (1985). Epidemiological research in cardiovascular disease in Australia: 1984. *Medical Journal of Australia 142*:130-135.

Lieber, C.S. (1973). Effects of ethanol upon lipid metabolism. *Lipids 9*:103-116.

The Lipid Research Clinics Program. (1984). The Lipid Research Clinics Coronary Primary Prevention Trial results: I. Reduction in incidence of coronary heart disease. *Journal of the American Medical Association 251*:351-364.

Lipson, L.C., Bonow, R.O., Schaefer, E.J., et al. (1980). Effects of exercise conditioning on plasma high density lipoproteins and other lipoproteins. *Atherosclerosis 37*:529.

Lopez, S.A., Vial, R., Balart, L., et al. (1974). Effect of exercise and physical fitness on serum lipids and lipoproteins. *Atherosclerosis 20*:1.

Lorenz, R., Spengler, U., Fischer, S., Duhm, J. *and* Weber, P.C. (1983). Platelet function, thromboxane formation and blood pressure control during supplementation of the Western diet with cod liver oil. *Circulation 67*:504-511.

Lugg, D.J. (1973). Antarctic epidemiology - a survey of ANARE stations 1947-72. In: Edholm, O.G. *and* Gunderson, E.K.E. (Eds). *Polar Human Biology*. Heinemann, London. Pp. 93.

Lugg, D.J. (1977). Physiological adaptation and health of an expedition in Antarctica, with comment on behavioural adaptation. *ANARE Scientific Report Number 126*. Pp. 65-69.

Lugg, D.J. (1982). Australian Medical Services in Antarctica. In: Harold, B., Hart-Hansen, J.P. (Eds). *Circumpolar Health 81*. Oulu:Nordic Council for Arctic Medical Research. Pp. 71-73.

MacMahon S. (1987). Alcohol consumption and hypertension. *Hypertension 9*:111-121.

MacMahon, S.W., Blacket, R.B., MacDonald, G.J. *and* Hall, W. (1984). Obesity, alcohol consumption and blood pressure in Australian men and women. The National Heart Foundation of Australia risk factor prevalence study. *Journal of Hypertension 2*:85-91.

Maling, T.J.B., Dollery, C.T. *and* Hamilton, C.A. (1979). Clonidine and sympathetic activity during sleep. *Clinical Science 57*:509-514.

Martin, D.W., Maynes, P.A., Rodwell, V.W. *and* Granner, D.K. (1983). *Harper's Review of Biochemistry*. Lange Medical Publications, Los Altos, California. (twentieth edition).

Martin, R.P., Haskell, W.L. *and* Wood, P.D. (1977). Blood chemistry and lipid profiles of elite distance runners. *Annual New York Acadamy of Science 301*:346.

Maserei, J.R.L., Puddey, I.B., Rouse, I.L., Lynch, W.J., Vandongen, R. *and* Beilin, L.J. (1986). Effects of alcohol consumption on serum lipoprotein-lipid and apolipoprotein concentrations. *Atherosclerosis 60*:79-87.

Miller, N.E., Hammett, F., Saltissi, S., et al. (1981). Relation of angiographically defined coronary artery disease to plasma lipoprotein subfractions and apolipoproteins. *British Medical Journal 282*:1741-1743.

Moritch, M.E., Oill, P. *and* Odell, W.D. (1974). Massive hyperlipemia during estrogen therapy. *Journal of the American Medical Association 227*:173.

Mortensen, J.Z., Schmidt, E.B., Nielsen, A.H. *and* Dyerberg, J. (1983). The effects of N-6 and N-3 polyunsaturated fatty acids on haemostasis, blood lipids and blood pressure. *Thrombosis and Haemostasis 50*:543-546.

Moulds, R.F.W. (Ed.). NHMRC workshop of non-pharmacological methods of lowering blood pressure. *Medical Journal of Australia 2*:S1-S23.

Nakamura, N., Uzawa, H., Maeda, H. *and* Imomoto, T. (1983). Physical fitness: its contribution to serum high density lipoprotein. *Atherosclerosis 48*:173-183.

National Heart Foundation of Australia Risk Factor Prevalence Study. No. 2. (1983).

Nestel, P.J. *and* Hirsch, E.Z. (1965). Mechanism of alcohol-induced hypertriglyceridaemia. *Journal of Laboratory and Clinical Medicine 66*:357-365.

Nestel, P.J., Connor, W.E., Reardon, M.F., Connor, S., Wong, S. *and* Boston, R. (1984). Suppression by diets rich in fish oil of very low density lipoprotein production in man. *Journal of Clinical Investigation 74*:82-89.

Nestel, P.J., Wong, S. *and* Topping, D.L. (1986). Dietary long chain polyenoic fatty acids: 1. Suppression of triglyceride formation in rat liver; 2. Attenuation in man of the effects of dietary cholesterol on lipoprotein cholesterol. In: *Health Effects of polyunsaturated fatty acids in seafoods*. Academic Press. Pp. 211-224.

Nikkilä, E.A. (1978). Metabolic regulation of plasma high density lipoprotein concentrations. *European Journal of Clinical Investigation 8*:111.

Nikkilä, E.A., Taskinen, M., Rehunen, S., et al. (1978). Lipoprotein lipase activity in adipose tissue and skeletal muscles of runners: relation to serum lipoproteins. *Metabolism 27*:1661.

Norman, J.N. (1965). Cold exposure and patterns of activity at a polar station. *British Antarctic Survey Bulletin 3*:1-13.

Norris, G., Jones, C.J.H. *and* Weston, M.J. (1986). Effect of dietary supplementation with fish oil on systolic blood pressure in mild essential hypertension. *British Medical Journal 293*:104-105.

Oberman, A. (1985). Exercise and the primary prevention of cardiovascular disease. *American Journal of Cardiology 55*:10D-20D.

Ogata, M., Mendelson, J.H., Mello, N.K. *and* Majchromicz, E. (1971). Adrenal function and alcoholism. II. Catecholamines. *Psychosomatic Medicine 33*:159.

Perloff, D., Sokolow, M. *and* Cowan, R. (1983). The prognostic value of ambulatory blood pressures. *Journal of the American Medical Association 249*:2792-2798.

Pessina, A.C., Plantini, P., Sperti, G., et al. (1984). Adaptation to non-invasive continuous blood pressure monitoring. In: Weber, M.A., *and* Drayer, J.I.M. (Eds). *Ambulatory blood pressure monitoring*. Darmstadt: Steinkopff. Pp. 57-64.

Phillipson, B.E., Rothrock, D.W., Connor, W.E., Harris, W.S. *and* Illingworth, D.R. (1985). Reduction of plasma lipids, lipoproteins, and apoproteins by dietary fish oils in patients with hypertriglyceridaemia. *New England Journal of Medicine 312*:1210-1216.

Pickering, T.G. (1961). The nature of essential hypertension. London: Churchill, Ltd. Pp 1-151.

Pickering, T.G. *and* Harshfield, G.A. (1982). Ambulatory monitoring in the evaluation of blood pressure in patients with borderline hypertension and the role of the defense reflex. *Clinical and Experimental Hypertension [A] 4* (4 and 5):675-693.

The Pooling Project Research Group. (1978). Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events: final report of the Pooling Project. *Journal of Chronic Diseases 31*:201-306.

Potter, J.F. *and* Beevers, D.G. (1984). Pressor effect of alcohol in hypertension. *Lancet 1*:119-122.

Puddey, I.B., Beilin, L.J., Vandongen, R., Rouse, I.L. *and* Rogers, P. (1987). Evidence for a direct effect of alcohol consumption on blood pressure in normotensive men. A randomized controlled trial. *Hypertension 7*:707-713.

Randle, P.J., Garland, P.B., Newsholme, E.A., et al. (1965). The glucose fatty acid cycle in obesity and maturity onset diabetes mellitus. In: Whipple, H.E. (Ed.). *Adipose tissue metabolism and obesity. Annals of the New York Academy of Sciences 131*(Art. 1):32433.

Rhoads, G.G., Gulbrandsen, C.L. *and* Kagan, A. (1976). Serum lipoproteins and coronary heart disease in a population study of Hawaiian Japanese men. *New England Journal of Medicine 294*:293.

Rohan, T.E. (1984). Alcohol and ischaemic heart disease: a review. *Australian and New Zealand Journal of Medicine 14*:75-80.

Ross, R. (1986). The pathology of atherosclerosis - an update. *New England Journal of Medince 31*:488-500.

Rubin, M.J. *and* Weyant, W.S. (1965). Antarctic meteorology. In: Hatherton, T. (Ed.). *Antarctica*. Methuen, London. Pp. 375.

Sanders, T.A.B. (1985). Influence of fish-oil supplements on man. *Proceedings of the Nutrient Society 44*:391-397.

Sanders, T.A.B *and* Roshanai, F. (1983). The influence of different types of omega- 3 polyunsaturated fatty acids on blood lipids and platelet function in healthy volunteers. *Clinical Science 64*:91-99.

Sanders, T.A.B., Vickers, M. *and* Haines, A.P. (1981). Effect on blood lipids and haemostasis of a supplement of cod-liver oil, rich in eicosapentaenoic and docosahexaenoic acids, in healthy young men. *Clinical Science 61*:317-324.

Saunders, J.B., Beevers, D.G. *and* Paton, A. (1981). Alcohol-induced hypertension. *Lancet 2*:653-656.

Saynor, R., Verel, D. *and* Gillott, T. (1984). The long-term effect of dietary supplementation with fish lipid concentrate on serum lipids, bleeding time, platelets and angina. *Atherosclerosis 50*:3-10.

Schaller, M.D., Nussberger, J., Waeber, B., Porchet, M. *and* Brunner, H.R. (1984). Transdermal clonidine therapy in hypertensive patients: effects on office and ambulatory recorded blood pressures. *Journal of the American Medical Association 253*:233-235.

Scherhag, R., Kramer, H.J. *and* Düsing, R. (1982). Dietary administration of eicosapentaenoic and linoleic acid increases arterial blood pressure and suppresses vascular prostacyclin synthesis in the rat. *Prostaglandins 23*:369-382.

Scow, R.O., Blanchette-Mackie, E.J. *and* Smith, L.C. (1980). Transport of lipid across capillary endothelium. *Federation Proceedings of the Federation Social American Experiments of Biology 39*:2610.

Simons, L.A. *and* Gibson, LA. (1980). *Lipids: a Clinician's guide*. Adis Press.

Simons, L.A., Hickie, J.B. *and* Balasubramaniam, S. (1985). On the effects of dietary n-3 fatty acids (Maxepa) on plasma lipids and lipoproteins in patients with hyperlipidaemia. *Atherosclerosis 54*:75-88.

Singer, P., Jaeger, W., Wirth, M., et al. (1983). Lipid and blood pressure-lowering effect of mackerel diet in man. *Atherosclerosis 49*:99-108.

Snedecor, G.W. *and* Cochran, W.G. (1967). *Statistical Methods*. Iowa State University Press. (sixth edition)

Society of Actuaries and Association of Life Insurance Medical Directors of America. (1979). *Blood Pressure Study*.

Sokolow, M., Werdegar, D., Kain, H.K. *and* Hinman, A.T. (1966). Relationship between level of blood pressure measured casually and by portable recorders and severity of complications in essential hypertension. *Circulation 34*:279-298.

Stary, H.C. (1983). Macrophages in coronary artery and aortic intima in atherosclerotic lesions of children and young adults up to age 29. In: Schettler, F.G., Gotto, A.M., Jr *and* Middelhoff, G., et al. (Eds). *Sixth International Symposium of Atherosclerosis*. Berlin, Atherosclerosis IV. New York, Springer-Verlag. Pp. 462-66.

Stout, R.W. (1981). Blood glucose and atherosclerosis. *Arteriosclerosis 1*:227-234.

Taskinen, M.R., Välimäki, M., Nikkilä, E.A., Kuusi, T., Ehnholm, C. *and* Ylikahri, R. (1982). High density lipoprotein subfractions and postheparin plasma lipases in alcoholic men before and after ethanol withdrawal. *Metabolism 31*:1168-1174.

Taskinen, M.R. *and* Nikkilä, E.A. (1977). Nocturnal hypertriglyceridaemia and hyperinsulinaemia following moderate evening intake of alcohol. *Acta Medica Scandinavica 202*:173-177.

Telford, R.D., Briggs, C.A. *and* Chennels, M.H.D. (1978). Cardiorespiratory fitness of untrained and trained Australian males and females. *Australian Journal of Sports in Medicine*. Pp. 59-66.

Thompson, P., Cullinane, E., Henderson, LO., et al. (1980). Acute effects of prolonged exercise on serum lipids. *Metabolism 29*:662.

Topping, D.L., Trimble, R.P. *and* Storer, G.B. (1987). Failure of insulin to stimulate lipogenesis and triacylglycerol secretion in perfused livers from rats adapted to dietary fish oil. *Biochimica et Biophysica Acta 927*:423-428.

Uemera, K. *and* Pisa, Z. (1985). Recent trends in cardiovascular disease mortality in 27 industrialized countries. *World Health Statistics Quarterly 38*:142-162.

von Lossonczy, T.O., Ruiter, A., Bronsgeest-Schoute, H.C., van Gent, C.M. *and* Hermus, R.J.J. (1978). The effect of a fish diet on serum lipids in healthy human subjects. *American Journal of Clinical Nutrient 31*:1340-1346.

von Schacky, C., Fischer, S. *and* Weber PC. (1985). Long-term effects of dietary marine omega-3 fatty acids upon plasma and cellular lipids, platelet function, and eicosanoid formation in humans. *Journal of Clinical Investigation 76*:1626-1631.

Wahlqvist, M.L. (1985). Is moderate drinking cardioprotective? *Editorial- Current Therapeutics 26*:13-15.

Wan, A. (1985). Personal communication.

Warnick, G.R., Nguyen, T. *and* Albers, A.A. (1985). Comparison of improved precipitation methods for quantification of high density lipoprotein cholesterol. *Clinical Chemistry 31*:217-222.

WHO. (1980). *Expert Committee on Diabetes Mellitus*. Pp. 71-75. (second report)

Williams, D.L. (1986). *Health, hormonal and stress-related studies in isolated Antarctic and sub-Antarctic communities*. MD thesis, University of New South Wales.

Wissler, R.W. *and* Vesselinovitch, D. (1975). Studies of regression of advanced atherosclerosis in experimental animals and man. *Annuals of the New York Academy of Science 275*:363.

Wong, S.H., Nestel, P.J., Trimble, R.P., Storer, G.B., Illman, R.J. *and* Topping, D.L. (1984). The adaptive effects of dietary fish and safflower oil on lipid and lipoprotein metabolism in perfused rat liver. *Biochimica Biophysica Acta 792*:103-109.

Woodcock, B.E., Smith, E., Lambert, W.H., et al. (1984). Beneficial effect of fish oil on blood viscosity in peripheral vascular disease. *British Medical Journal 288*:592-594.