THE ROLE OF LARGE ARTERIES IN CONTROLLING BLOOD FLOW TO THE HAND DURING SEVERE LOCAL COOLING

by

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ABSTRACT

Cold vasodilatation describes the increase in blood flow that follows initial vasoconstriction when an extremity is exposed to an environment colder than 12°C. It appears to be due mainly to cold paralysis of local resistance vessels. The reaction is very variable between individuals who are generally chilled; this study was designed to show whether constriction of large arteries of the forearm, protected by fat from local cooling, is responsible for this, enabling such people to maintain low flow and heat loss during cold stress.

Twelve subjects were exposed for 120 minutes to warm (38°C), control (24°C) or cold (12°C) moving air. During the last half hour the non-dominant hand was cooled in ice water. Arterial diameter and blood velocity in the brachial and radial arteries were measured by ultrasound, and in 6 experiments pressure in both arteries was measured by indwelling cannulae.

The arterial diameters constricted significantly in the cold, but only by 27% compared to warm and 17% compared to control (radial), and by 19% compared to warm and 11% compared to control (brachial). Calculated pressure drop (mean ± S.E.) between brachial and radial arteries fell from 3.78 ± 0.23 mm Hg in the warm to 2.02 ± 0.15 mm Hg in the cold. During hand immersion in ice water with increased flow, this pressure difference rose in each of 5 cold subjects but never to more than 4.81 mm Hg. Indwelling arterial cannulae never showed a difference greater than 7.7 mm Hg between brachial and radial arteries in any subject at any time. The general conclusion is that forearm arteries exerted little control over hand blood flow in these circumstances, and that the ability of some people to maintain low blood flow in very cold extremities is due to the ability of downstream vessels to maintain constriction near 0°C.

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STATEMENT OF CANDIDATES ROLE IN CONJOINT PROJECT

The original idea for the project was presented to the Medical Research Council by Professor W. R. Keatinge in a grant application. The experiments were on human subjects and it was therefore ethically necessary to have a medical doctor present at all times. The experiments were planned by the candidate with agreement from the supervisor and medical doctor. The experiments involved too many simultaneous activities for one person to carry out on their own and there were normally three to four people involved in each experiment, these being the candidate and medical doctor at all times and two others. The candidate carried out all the measurements and procedures involved in the project at some stage with the exception of invasive procedures such as the introduction of intra arterial cannulae which were undertaken by a suitably qualified clinician in accordance with the ethical requirements. All collation of experimental data, statistical analysis and production of results was carried out by the candidate.

INTRODUCTION

Introduction

Accidents at sea often result in people entering the water. If the water temperature is below about 12°C and no other immediate danger exists the chances of survival are remote unless rescue arrives very quickly (Molnar, 1946). People with large amounts of subcutaneous fat theoretically have sufficient thermal insulation to be able to maintain their body temperature during immersion even in very cold water (Cannon & Keatinge, 1960). In practice such individuals, when immersed, do temporarily stabilise their core temperature but after a short time their body temperature drops at the same time as large amounts of heat are lost from their extremities. This heat loss is due to cold induced vasodilatation overcoming the normal reflex cold vasoconstrictive response of the blood vessels of the extremities. Cold induced vasodilatation occurs when the temperature of the peripheries drops below about 12°C and is thought to be due to cold paralysis of the smooth muscle of the resistance arteries of the extremities (Keatinge, 1958). It has been observed that the degree of heat loss from the peripheries that different individuals experience varies widely and that some individuals with large amounts of subcutaneous fat and low levels of peripheral heat loss have been shown to be able to survive cold water immersion that would normally prove fatal (Keatinge, 1986). This study is to investigate whether the large arteries of the forearm, which tend to be well insulated in fat people, are able to constrict sufficiently to restrict the increased blood flow seen during cold induced vasodilatation so preventing excessive heat loss leading to a lowering in core temperature.

Control of Thermoregulation

Man maintains the temperature of essential organs at about 37°C, this control of body

core temperature being regulated by the hypothalamus. The temperature control system functions as a negative feedback loop maintaining brain temperature at or near a set point. The normal set point is within a few fractions of a degree of 37°C. Once the blood temperature goes above or below that of the set point, one or other groups of temperature sensitive cells of the hypothalamus start discharging. The set point is capable of some alteration. If for example heat receptors in the skin are stimulated the set point is reduced, usually by between 0.1 and 0.3 °C. If the cold receptors are stimulated the set point is raised by a similar amount. There is evidence in the case of the metabolic response to cold that shivering is largely a reflex from skin cold receptors, which is greatly modified by the level of core temperature sensed by the receptors of the hypothalamus. The set point is also raised by pyrogens diffusing into the blood, pyrogens being the agents responsible for fever. Severe dehydration raises the set point as does exercise (Haight & Keatinge 1973). When the blood temperature is above the required set point the hypothalamus activates various heat dissipating mechanisms and when blood temperature is below the set point then various heat conserving and heat producing mechanisms are brought into play.

Conduction, Convection, Radiation and Evaporation

Heat can be transferred by either conduction, convection, radiation or evaporation. Conduction is the simple transfer of heat along a temperature gradient. In still air, air next to the skin warms up to the same temperature as the skin, this slows heat loss by conduction since the temperature gradient is reduced, the layer of air next to the skin is known as the boundary layer. If the environmental temperature is lower than skin temperature warm air in contact with the skin will rise, since it is less dense than the

environmental air, this is then replaced by the cooler surrounding air which in turn is warmed, this is the process of convection. Convection and conduction also occur in water but the heat loss in water is much greater due to the higher thermal capacity and conductivity of water and to different boundary layer flow. Forced convection is the process which occurs when air or water surrounding an object is forced to move relative to the object due to motion of the object relative to its surroundings. This relative motion may be either motion of the object within its environment for example as a swimmer moves through the water or it may be motion of the environment relative to an object such as a person standing in a high wind. Forced convection decreases the boundary layer so lowering its insulative effects and also carries heat directly away, it is therefore, capable of markedly increasing heat loss. An approximate means of allowing for forced convection in air is the so called "wind chill factor" which is related to wind speed and air temperature.

Radiation is the third process by which heat can be lost or gained, this is the transfer of heat by electromagnetic radiation. Radiant heat is emitted from all bodies above absolute zero. The amount of energy a body emits or absorbs is given by Stefan's Law:

$$E = \sigma.T^4$$

E is the emitted or absorbed energy, T is the absolute temperature and σ is Stefan's constant which is dependent on how perfect a black body the object is (white or black human skin is a 97% - 98% perfect black body for the wavelengths of radiation responsible for temperature change (Mitchell *et al.*1967)). Heat transfer by radiation can be important in air but is of little consequence in water.

In terms of heat loss evaporation is also important, it is the only way to lose heat when the environmental air temperature is above body temperature and it is a process that can disperse very large amounts of thermal energy but plays no part when a person is immersed in water.

Core and Peripheral Temperatures

The human body can be divided roughly into different layers, the core and the periphery. The core consists of essential organs which must be maintained near 37°C for optimum function, the two most critical organs being the heart and brain. The periphery consists of the skin, outer layers of muscle, particularly those of the limbs, all of whose temperatures vary considerably. Core temperature varies during normal everyday life. Body core temperature shows a circadian variation of about 1°C, which is not due simple to a change in the level of activity, but is brought about by changes in thermoregulatory processes (Stephenson, 1984). High environmental temperatures and strenuous activity can raise core temperature above 40°C as has been recorded in marathon runners (Pugh *et al.* 1967).

The skin temperature and the temperature of the extremities can fluctuate considerably more and are on average 2-10°C below core temperature, varying greatly with both environmental temperature and physical activity.

Thermal Equilibrium

In hot conditions it is necessary for excess metabolic heat to be lost to the environment and in cold conditions heat losses must not exceed metabolic heat production. In air

increasing metabolic heat production is a very important way of maintaining core temperature, in cold water however, the increased heat losses to the water caused by the increase in metabolic heat production tend to outweigh the amount of metabolic heat produced. Some heat loss occurs from the surface of the pulmonary airways to the relatively cool air that is inhaled but most is lost from the skin surface to the environment. Some body heat loss occurs by conduction to the surface but the majority of the heat lost is carried to the surface by circulating blood. Blood returning to the right atrium of the heart from the surface of the body is usually cooler than arterial blood entering the skin circulation. This is because a combination of conduction, convection, radiation and evaporation has transferred some of the heat from the blood flowing through skin vessels to the environment. The cool venous blood from the skin and upper respiratory tract mixes with hotter venous blood from the metabolizing tissues and enters the right heart at a temperature somewhere between the extremes.

Skin Blood Flow

Skin blood flow is the key critical regulator mechanism for heat loss. The average man has an area of skin of about 1.8 m^2 accounting for about 3% of total body weight, skin has an average thickness of 1.0-1.5 mm. Blood flow to the skin serves two purposes it supplies the metabolic requirements of the skin and transfers heat to the body surface. Cutaneous blood flow in the fingers can vary from as much as 100 ml/min for each 100 g of tissue to as little as 0.1 ml/min for each 100 g of tissue, elsewhere the skin blood flow range is more limited from about 0.4-0.5 ml/min per 100 g of tissue to 30-40 ml/min per 100 g of tissue (Clark and Edholm, 1975). Skin is the body tissue with the highest

temperature variability from core temperature usually being between 2 and 10°C below core temperature in temperate climates in a resting person. Most of the skin has extensive venous plexuses in the dermis and hypodermis. When the arterioles and metarterioles supplying these plexuses are dilated they become engorged with blood and act as radiators of heat. In the hands and feet (especially the apices of the toes and fingers) and in the face (especially the ears, nose and chin) there are number of arteriovenous shunts. The fingertips are particularly rich in arteriovenous shunts, Grant and Bland (1931) found 510 arteriovenous shunts/cm^2 in the human nail bed and 236 in the fingertip. Arteriovenous shunts are coiled vessels with muscular walls that connect small arteries or arterioles to corresponding venous channels allowing the blood to bypass the capillaries. Arteriovenous anastomoses have an interior diameter of about 100 μm when dilated permitting about 10,000 times more blood through them as a comparable length of capillary which has an internal diameter of about 10 μm. The blood flow through the arteriovenous shunts can range from negligible to 80% of the total (Rubinstein & Sessler, 1990). When the shunts are dilated large volumes of warm arterial blood are poured directly into the venous plexuses and heat loss is greatly increased.

Control of skin blood flow

Vasoconstriction of the arterioles, metarterioles and arteriovenous shunts in the skin is mainly under the control of noradrenergic nerves of the sympathetic nervous system (Saumet, 1992). An increase in sympathetic outflow causes vasoconstriction of the skin arterioles, metarterioles and arteriovenous shunts thereby increasing arterial resistance, reducing blood flow and reducing heat loss. The reflex constriction of small blood vessels produced by cooling does not greatly decrease the nutritional blood flow, but the blood

flow in the fingers does significantly decrease, due to the decrease in flow through the arteriovenous anastomoses (Coffman, 1972). When sympathetic activity to these blood vessels ceases the reverse happens, the vessels dilate, and, flow and heat loss are increased. Local cooling of the blood vessels greatly enhances the effect of noradrenaline by increasing the sensitivity of the arteries α_2 adrenoceptors, this has been shown both in the rat (Faber, 1988) and the human finger (Ekenvall *et al.*, 1988). Bandick and Roberts (1991) showed that the femoral artery taken from a hypothermic rabbit would have an increased sensitivity to noradrenaline for several hours more than was the case with an artery taken from a normothermic rabbit. It has been shown that a cholinergic vasodilator mechanism exists in blood vessels of the finger (Coffman & Cohen 1987) and the foot (Lundberg *et al.*, 1989) but this mechanism only affects nutritional blood flow which is only a very small part of the overall blood flow when the arteriovenous shunts are open (Rubinstein & Sessler, 1990). These findings account for the fact that earlier investigators whose measuring techniques were not as sensitive did not observe a change in blood flow during iontophoresis of atropine into the finger (Duff *et al.*, 1953). It is generally accepted that the main control for vasodilatation of the cutaneous finger blood vessels is release of sympathetic tone although active vasodilatation can play a more important role in other skin such as that of the forearm (Pergola, 1993; Saumet, 1992).

There is also evidence of a serotonergic vasoconstrictor mechanism in the fingers which operates during reflex sympathetic vasoconstriction. This mechanism is mediated by S_2 serotonergic receptors activated by 5 hydroxtryptamine (5-HT), it is not known where the 5-HT is released from but may be from adrenergic or serotonergic nerves or platelets (Coffman and Cohen 1988).

Hypothermia

Temperature is critical to an organs performance, if the temperature drops below the optimum the metabolic rate of the cells decreases, and, if it rises much in excess of 37°C the cells will become permanently damaged. The rate at which metabolic processes occur is given by the expression:-

$$Q_{10} = \frac{k_1}{k_2}^{10/(t1-t2)}$$

where Q is the rate of reaction and k_1 and k_2 are rate constants of the reaction at temperatures t_1 and t_2. Generally a drop in temperature of 10°C leads to a two to three fold decrease in metabolic rate of the cooled tissue (Clark and Edholm, 1985). The optimal functioning of certain essential organs such as the heart and brain is critical and if this is compromised by a temperature change the organ can become ineffective. Reports by Alexander (1946) of the notorious Dachau experiments showed that people immersed in water at nearly 0°C died when their rectal temperature fell to between 24.2 and 25.7°C. Since rectal temperature lags behind core temperature under such severe cooling it is probable the temperature of the heart was one to two degrees cooler than this. This evidence for the temperature at which death occurs due to hypothermia is corroborated by documented cases of accidental hypothermia. There have been a number of cases of people recovering from hypothermia after having reached core temperatures of between 23-25°C (Rees 1958; Arneil & Kerr 1963; McNicol & Smith 1964) but few cases of people surviving after having reached lower temperatures. The Dachau experiments showed death from hypothermia to be due to cardiac arrest although respiration continued. This has also been shown in one exceptional case when a woman was cooled to a rectal temperature of 9°C under pentobarbitone anaesthesia in the hope

of treating advanced cancer. The report (Niazi & Lewis, 1958) states her heart rate fell as body temperature fell until at a temperature of 13°C atrial activity ceased. An ectopic focus maintained ventricular activity until at a core temperature of 10.5°C all cardiac contractile activity ceased. This set of events is similar to those reported by Knowlton & Starling (1912) who cooled heart-lung preparations of dogs, they recorded a progressive decline of heart rate followed by cardiac arrest. This slowing of the heart beat is accompanied by a corresponding drop in cardiac output. Generally arrhythmias do not usually occur until core temperature has dropped below 33°C after which atrial fibrillation may develop, below 28°C ventricular fibrillation may occur upon mechanical irritation of the heart as can happen if the patient is handled roughly, below 25°C ventricular fibrillation may develop spontaneously (Keatinge, 1969). Hypothermia causes death due to cardiac arrest in a person who is an otherwise safe environment, but during prolonged accidental immersion in water, cerebral temperature can be the key to survival. Once the cerebral temperature has dropped to about 33°C reasoning becomes impaired which lowers the chance of survival considerably during accidental water immersion. The cause of death in these cases will probably be drowning which is directly attributable to either unconsciousness or irrational behaviour induced by hypothermia. It is therefore important that during accidental cold water immersion core temperature must not drop more than a few degrees otherwise the chance of survival is significantly reduced.

Maintenance of body core temperature during cold water immersion

If man were to live naked he would require an air temperature of about 28-30°C to survive without having to increase heat production and reduce heat loss. This temperature is the so called thermoneutral temperature and it puts man in the class of a tropical

animal. The temperature next to the skin for a comfortably clothed man in a temperate climate is about 34°C, even the populations of very cold environments, such as Eskimos, maintain the air temperature next to the skin at an average of about 33°C (Clark & Edholm 1985). In cold environments man normally maintains his body temperature by trapping warm air around him. By wearing appropriate clothing he effectively produces his own thermoneutral microclimate. When warm air is replaced by stirred water the skin surface temperature becomes virtually identical to water temperature (Keatinge 1959). A person swimming in water loses the warmed boundary layer of water, which has the effect of producing a surface skin temperature very close to that of the water temperature. The body now relies on its physiological mechanisms to maintain its core temperature.

There are two major ways the body attempts to maintain core temperature: first by increasing the insulation around the core by diverting warm blood away from exposed surfaces; secondly by increasing heat production. In cold water by far the most important of these two mechanisms is the ability to divert warm blood away from the surface tissue to deeper vessels, increasing heat production is not very effective for a person immersed in very cold water.

The flow of blood to the skin is reduced by vasoconstriction of the blood vessels supplying the skin this is largely brought about by sympathetic vasoconstrictor nerves releasing noradrenaline. The reduction of heat loss from the hands is greatly enhanced by a counter-current heat exchange process occurring between large arteries and veins of the forearm. Bazett *et al.* (1948) showed that for a man sitting in air at 9°C for an hour and a half the arterial blood temperature drops to about 21.5°C at the wrist; the heat being transferred to blood flowing back along the veins. This exchange is only effective in the

cold when the blood flow is small and when the blood returning back up the arm returns in deep veins alongside the artery and not in the veins on the surface. This process allows the low metabolic needs of the tissues of the extremities to be met without excessive heat loss.

A large part of the heat lost from the trunk is lost by physical conduction from the deep organs to the surface; a process which is beyond physiological control. This was shown by Cannon and Keatinge (1960) by placing subjects in water at different temperatures. At water temperatures of 22 °C rates of heat loss from the hands and feet were almost too small to record (tissue conductance approx. 0.001 cal $cm^{-2} min^{-1}$) while the mean tissue conductance to the chest was as high as 0.018 cal cm^{-2} min^{-1}. When the subjects were vasodilated in warmer water, so that heat was being carried to the surface by cutaneous blood flow, the rates of heat loss from both areas were similar. So in moderately cold water the main heat loss is from the trunk and not the extremities.

The heat loss from the trunk is largely determined by the amount of subcutaneous fat (Cannon and Keatinge 1960). When a group of subjects was immersed in water at 15 °C for 30 minutes their fall in rectal temperature was found to be roughly proportional to the inverse of the thickness of their subcutaneous fat measured by skinfold callipers (Keatinge 1960). This relationship is as expected for a layer of inert insulation ignoring internal heat production. The effect fat can have on maintaining body heat is illustrated by the series of experiments carried out by Cannon and Keatinge (1960); in these experiments the two fattest men could stabilize their core temperature when immersed in water at 12 and 10 °C whereas the two thinnest could only stabilize at 28 and 22 °C.

A temperature known as the critical temperature was originally defined as the environmental temperature at which maximum tissue insulation is reached and metabolic rate starts to increase (Scholander *et al.*, 1950). It has since been shown that the environmental temperature at which maximum tissue insulation is achieved varies depending on the amount of subcutaneous fat the individual possesses (Cannon and Keatinge 1960; Rennie, 1988). What does not vary in people of different fatness is the environmental temperature which causes an increase in metabolic rate, in still air this temperature is between 26°C and 29°C and in water it is about 33°C. The critical temperature should therefore be redefined as the temperature at which metabolic rate starts to increase (Cannon and Keatinge, 1960). The evidence suggests that it is purely coincidental that subcutaneous fat is a good thermal insulator its major role being a food store. If the deposition of fat were an adaptive protection against cold it would seem likely that those with large amounts of subcutaneous fat would have a lower critical temperature than those with less fat which as just discussed is not the case. In addition if fat was laid down as a protection against cold it would also be likely that those exposed to frequent cold stress would have a tendency to have more subcutaneous fat than those who have less cold exposure this does not seem to be the case either (Rennie, 1988).

Man can sustain an increase in heat production in the cold of about three times resting level (Swift 1932) but this increase is insignificant compared to the rate of heat loss in cold water. When a person is at rest muscle can account for 80% of thermal insulation especially in those with very little subcutaneous fat (Rennie, 1988). In adult man increased muscle tone and shivering are the means of increasing heat production in the cold; there has been some speculation as to whether man is capable of non-shivering

thermogenesis from so called 'brown fat' but although this may be important in newborn infants it is of no real significance in adult man (Astrup 1988). When immersed in cold water, the increase in muscle tone and shivering that produces a raised metabolic rate is counter productive, in that both processes cause muscle blood flow to be increased bringing warm blood closer to the surface, decreasing the thickness of the effective insulating layer of the body, and thereby increasing heat loss. For the same reason active swimming in cold water, as opposed to remaining as still as possible, is detrimental to maintaining core temperature (Cannon and Keatinge, 1960) but to an even greater degree because swimming produces powerful forced convection, whereas the movements of shivering are such that they produce little forced convection. Despite the lowering in the body insulation shivering means a man can maintain body temperature in water a few degrees colder than would otherwise be possible. Increasing subcutaneous fat seems to be the only way individuals can significantly improve their ability to remain in cold water.

Cold Vasodilatation

In water below about 12°C cold vasodilatation occurs in the peripheral blood vessels, this phenomenon is highly detrimental to the maintenance of a normal deep body temperature. Lewis (1930) showed that a finger immersed in water at between 0-12°C first gave the expected vasoconstrictor response with concomitant slowing of blood flow, but then after a time the blood flow increased to levels even greater than the resting level. This cold vasodilatation was only observed in the cooled finger and not in other fingers on the same or contralateral hand. There is usually a delay of about 5 minutes before the onset of cold vasodilatation and this cold vasodilatation alternated with waves of severe

vasoconstriction, this phenomena was initially known as the "hunting reaction". Lewis demonstrated that this phenomena was more marked in the extremities than it was in the more proximal parts of the body. He thought this was due to the greater surface area to mass ratio of the extremities but the magnitude and speed of the dilatation would suggest that the arteriovenous anastomoses are probably the first vessels to dilate (Grant 1930) and these are most numerous in the skin of the extremities (Grant & Bland 1931). The change in blood flow in the hand and forearm rose from less than 2 ml 100 ml^{-1} min^{-1} in water at 14-18°C with comfortably warm subjects to between 4.3 and 4.7 ml 100 ml^{-1} min^{-1} respectively in subjects with their arm and forearm cooled to between 2 and 5°C (Spealman 1945; Clark *et al.* 1958). It was initially thought that cold vasodilatation would not develop to any great extent if there was general body cooling since Spealman (1945) and Greenfield & Shepherd (1950) showed that cold vasodilatation was reduced by general body cooling. However, it was shown by Cannon & Keatinge (1960) that cold vasodilatation was not suppressed by even rapid total body cooling. Cannon & Keatinge's experiments showed that one of the two fattest men, when submersed in water at 5°C, did maintain his rectal temperature for about 40 minutes during which time the heat flow from all parts of the body surface gradually dropped. After 40 minutes the heat flow from the finger, which had had the lowest heat flow of any part of the body, started to rise in waves and the core temperature started to drop. This indicates that if a fat man were subjected to such a cold water immersion, he would be unable to maintain core temperature although he should theoretically have enough insulation available to stabilise his core temperature. The water temperature necessary to induce cold vasodilatation seems to be about 10-12°C; above this temperature men with sufficient fat are able to stabilize their core temperatures. Since cold vasodilatation occurs in circumstances when

there is likely to be intense vasoconstrictor activity it seems unlikely that an active mechanism causes cold vasodilatation. Lewis (1930) initially suggested that cold vasodilatation was caused by axon reflexes since he could not demonstrate the cold vasodilatation in fingers whose nervous supply had been cut and degenerated. Greenfield *et al.* (1951) did manage to demonstrate cold vasodilatation in such fingers by using more sensitive recording methods and they also showed that if the finger was warmed before being cooled the intensity of cold vasodilatation was much the same as in a normally innervated finger possibly due to increased sensitivity of the noradrenergic receptors in the smooth muscle of the blood vessels.

After the discovery that axon reflexes played only a questionable role in causing cold vasodilatation attempts were made to see whether a hormonal mechanism was responsible for cold induced vasodilatation. Duff *et al.* (1953) found that iontophoresis of atropine into the finger made no difference to cold vasodilatation so acetylcholine plays no part in the mechanism; it was later shown that acetylcholine did play a minor part in controlling blood in the finger but not to any significant extent (Coffman and Cohen, 1987). Iontophoresis of histamine into the finger also had no effect on the fingers response to cold (Duff *et al*, 1953). The theory then was that some unidentified substance was responsible for the vasodilatation. The theory of a vasodilator substance was attractive since it could explain the series of events during cold immersion of a finger; the initial delay in onset of cold vasodilatation could be due to the slow accumulation of the vasodilator substance and then washing away of the substance could explain the subsequent vasoconstriction. The first evidence that a process of cold paralysis of the vasoconstrictor mechanism might be responsible was provide by Hertzman & Roth

(1942). They showed that distant stimuli that usually caused reflex vasoconstriction in the finger no longer elicited this effect if cold vasodilatation was just starting in the finger. This was attributed, by them, to cold paralysis of the nerves responsible for vasoconstriction. This theory seems improbable since it had been shown that nerve fibres in the splenic nerve of cats and the hypogastric nerve of cows, which are similar to those responsible for vasoconstriction in the human finger, are not easily blocked and can still conduct at 0°C (Lundberg 1948).

Early work done directly on relaxed blood vessels showed little that could explain cold vasodilatation. Roskam (1920) and Aschoff (1943) showed that cooling arteries *in vitro* caused very little dilatation. The little dilatation that was shown was immediate and completely reversible on warming and probably due to the thermoelastic properties of elastin in the artery wall (Neurath & Bailey 1954) and even then the effect was so small as to have a virtually insignificant effect on flow. Experiments on strips cut from mammalian arteries (Keatinge 1958; 1964) showed that severe cooling greatly reduced their response to vasoconstrictor agents, below 10-12°C no response was given by any of the strips. This suggests that cold vasodilatation was perhaps due to some form of cold paralysis of the blood vessels. It was shown that blood vessels will contract if directly electrically stimulated even at temperatures as low as 5°C so it is not the actomyosin of the arteries losing their ability to contract (Keatinge, 1969). The nerve endings can still release noradrenaline so the dilatation must be due to an interruption between the release of noradrenaline and its effect on the muscle cells. Cold vasodilatation has since been demonstrated *in vitro* in isolated rat tail artery suspended in physiological saline solution. In these experiments the adrenergic nerve endings were stimulated and the artery gave

the characteristic "hunting response". It was shown that this periodic interruption of the vasodilator response after the tail was warmed by returning blood flow was dependent on the integrity of the adrenergic neuroeffector junction (Gardner 1986). The dilatation seems therefore to be due mainly to a breakdown in communication between the smooth muscle cells and the sympathetic nerve endings resulting in release of vasoconstrictor tone, and its periodic interruption was due to rewarming by the resulting high blood flow leading to a temporary return of vasoconstrictor response.

Consequences of Cold Induced Vasodilatation

When a person with large amounts of subcutaneous fat is subjected to an immersion in cold water they should be able to maintain their core temperature for some considerable time. In practice, over a period of about an hour, their core temperature drops towards a steady level that appears to be approaching a plateau. After this initial hour core temperature then starts to drop again even more rapidly than previously. This stabilisation then subsequent drop can be correlated with the heat losses from the fingers. The finger heat loss gradually decreases until it is almost too small to be detectable and then it suddenly increases in waves as cold vasodilatation sets in. The onset of these waves of cold vasodilatation correspond with the decrease in core temperature (Cannon and Keatinge 1960). Cold vasodilatation although detrimental to survival in cold water may to some extent be protective against frostbite in cold air.

Exceptional Cases of Cold Tolerance

There have been a few recorded cases of exceptional survival in cold water. In 1984 a 23 year old Icelandic fisherman survived for five to six hours in water at 5-6°C the air

temperature was -2°C. The man was dressed in a shirt, sweater and jeans, he remained clear headed throughout. He should, from previous observation of such occurrences, have been dead within an hour or two (Molnar, 1946). 17 months after the accident the subject was immersed to the neck in water controlled at between 5.3 - 5.4°C with an air temperature of 21°C clothed as during the accident with him moving his arms and legs to mimic the swim and with water being driven backwards past him at 500 mm/s. The immersion ended after 83 minutes due to pain in his feet. Rectal and aural temperatures fell by 1.15 and 0.85°C respectively but appeared to be stabilising towards the end of the experiment (Keatinge 1986). Heat flow measurements showed that he displayed very little cold vasodilatation. Another notable case is of a long distance swimmer LC who regularly undertakes long swims in very cold water. In 1990 she swam for 3 hours and 18 minutes across the Beagle Channel in water at 8.3-9.0°C, in which time her rectal temperature only fell to 34.7°C from a starting temperature of 36.8°C, this exposure would prove fatal to most (Keatinge, 1990;). Molnar (1946) cites the case of a "corpulent" man who was reported to have swum for between nine to fourteen hours in the sea at 30 °F, Molnar in his paper doubts the veracity of the report but in view of other cases it may be possible.

Postulated Theory for Exceptional Survival in Cold Water

All the individuals mentioned with unusual ability to survive cold water immersion had thick layers of subcutaneous fat, the Icelandic fisherman had a body mass index of 33.6; the long distance swimmer had a body mass index of 32.7 and the survivor reported by Molnar (1946) was described as "corpulent". When the experiment on the Icelandic fisherman is compared against results on some of the subjects used by Cannon and

subjects had thicker subcutaneous fat and yet when immersed in water at 5°C their rectal temperature fell to a greater degree in less time than that seen with the Icelandic fisherman; another important point is that the Icelandic fisherman showed no increase in heat flow from his fingers whereas the other subjects did at about the same time as their rectal temperature started to fall. It appears therefore that some people have a means of suppressing the heat loss caused by cold vasodilatation.

The purpose of this study is to establish if constriction of the large arteries of the forearm are responsible for allowing these individuals to survive prolonged immersion in very cold water. It is postulated that this anomalous survival is due to a constriction of the forearm arteries reducing the blood flow to the cold vasodilated extremities sufficiently to reduce heat loss to a level that does not compromise core temperature. The forearm arteries of a fat individual tend to be protected by subcutaneous fat whereas even in an obese person their hands tend to have very little subcutaneous fat (Edwards, 1950; 1951). It is possible that given these factors the forearm arteries will remain warm enough to maintain constriction and reduce blood flow despite the paralysis of the arterioles of the hand.

Large artery control of blood flow

The control of blood flow is assumed to be largely dependent on the arterioles just proximal to the capillary beds and the majority of the arterial tree is assumed to be at the same pressure as that in the aorta. The assumption is that very little or no control on blood flow is exerted by the larger arteries due to their very much larger radius and hence lower resistance to flow compared to the arterioles. There is however evidence that suggests there may be resistance to flow produced in the large forearm arteries

particularly of a cold stressed person. It has long been observed that the peripheral pulses such as that of the radial artery get weaker and may even disappear in severely cold stressed individuals suggesting a change in flow and pressure may have occurred at this point (Keatinge, 1957;1969). It has also been demonstrated by cannulating the radial and brachial artery that a pressure gradient although small exists at rest in some subjects between these two sites of measurement, it was further demonstrated that if the subject's face was immersed in water vasoconstriction resulted and this pressure gradient increased (Heistad *et al.* 1968). Recently Perret *et al.* (1989) noted a decrease in the radial artery diameter from 2.82 ± 0.12 to 2.60 ± 0.09 mm ($p<.01$) as subjects performed the cold pressor test. Changes in brachial artery diameter have also been recorded following the cold pressor test (Anderson and Mark, 1989). These changes in diameter could be attributed to the decrease in blood velocity which is known to cause vasoconstriction (Melkumyants *et al.*, 1987) but Anderson and Mark (1989) showed that even in an artery where blood flow is occluded a further constriction will occur in the brachial artery when a subject performs the cold pressor test. These changes in diameter will change the resistance of the artery suggesting the forearm arteries may be able to influence blood flow. Additionally during cold induced vasodilatation the vessels that are considered to be the main resistance vessels, that is the small distal arterioles of the fingers, are dilated, whereas, the large relatively better insulated arteries of the forearm remain constricted, so even if the large arteries play no role during normal cold stress they may play a part during the unique circumstances that occur during cold induced vasodilatation; this is especially true if the cross sectional area of the cold dilated arterioles is considered against that of the constricted forearm arteries (Nichols *et al.*, 1990).

Aims and objectives of investigation

Most people when immersed in water near 0°C quickly lose large amounts of heat resulting in a rapidly dropping core temperature leading to hypothermia and death. People with large amounts of subcutaneous fat lose less heat through the well insulated trunk and limbs but after a delay start to lose large amounts of heat from their uninsulated extremities due to cold induced vasodilatation of the local blood vessels. A few individuals with large amounts of subcutaneous fat seem to be able to stabilise their core temperature even after prolonged immersion in ice cold water, there appears to be no large heat loss from the extremities and no subsequent drop in core temperature. This study aims to investigate if the comparatively large well insulated arteries of the forearm, which have been shown to be able to constrict, constrict sufficiently to control blood flow to the extremities during dilatation of the distal resistance arteries. The primary objective was to assess this during exposure of the hand to ice water while the subjects were generally chilled, when variations in intensity of cold induced vasodilatation between individuals are most marked and of most practical importance. The broader objective was to assess this for subjects in warm, near thermoneutral, and cold environments both with and without cooling of the hand in ice water.

METHODS

Volunteers

The subjects were all young, fit males. They consisted mainly of preclinical medical students, friends and members of the physiology department. The subjects wore their underwear and a standard t-shirt and shorts.

Ethics and Safety

All subjects were given a medical examination before being allowed to participate in the study. The medical included a record of past medical history, any current problems and any medication being taken. Subjects were only allowed to take part if they were found to be fit, well and free of any medication, particular care was taken to exclude those with any history of cold disorders such as Raynaud's Syndrome. Permission to carry out these experiments was granted by The North East Thames Ethical Committee. The committee required certain procedures to be carried out by a clinician who regularly undertook such procedures. During the course of all experiments a medical officer was in attendance. Experiments were discontinued if either the subject or medical officer requested. All subjects gave informed written consent, in the presence of an independent witness.

All mains powered electrical equipment was connected through 30 mA earth leakage trips and all electrical equipment used with the subject was either electrically isolated or battery powered. Resuscitation equipment including an emergency drug box and defibrillator were kept ready in the laboratory throughout.

Electrocardiogram

Throughout the study subjects were connected to an electrocardiogram monitor (Siemens

Sirecust 341). Leads were connected across the chest with disposable stick on electrodes (Red Dot, 3M), to reduce interference caused by skeletal muscular movement during shivering electrodes were attached to the skin directly overlying bone.

Anthropometric Measurements

The height, weight and subcutaneous fat thickness of each subject was measured.

Surface Area

The surface area of each subject was calculated in m^2 using the formula of DuBois and DuBois (1915):

$$\text{Surface Area} = 0.007184 \times W^{0.425} \times H^{0.726}$$

where W is weight in kilograms and H is height in centimetres.

Subcutaneous Fat Thickness

Fat thicknesses were measured using an ultrasonic flaw detector (USMB2, Wells Kraütkramer Ltd.).

This has been shown to give a more accurate measurement of fat thickness than skin fold calipers due to the compressibility of fat (Bullen, 1965).

Fat thicknesses were measured at four sites:

1. the middle of the anterior aspect of the right upper arm
2. the anterolateral point of the middle third of the right side of the trunk (20mm to the side of the midline)
3. the middle of the lower third of the right side of the trunk (50mm below the

umbilicus)

4. the middle of the anterior of the right thigh

The ultrasound unit consisted of a hand held probe and a cathode ray display. The device was calibrated using perspex blocks of known acoustic impedance and thickness. Fat thickness was measured by first applying silicone grease to the skin to provide an acoustic coupling between the skin and the probe and then gently placing the probe on the skin. The probe generated ultrasound pulses that were transmitted into the tissue; some of the ultrasound is reflected at interfaces between tissues of different acoustic impedance such as between muscle and fat. The reflected sound was picked up by the probe and the time delay since transmission, which depends on the depth of the tissue is displayed on the unit. The measurement for the fat thickness reading was the first peak, the distance on the screen being representative of the distance between the skin surface and the first fascia (muscle membrane). The following formulae were used to calculate mean fat thickness in millimetres:

Mean fat thickness = 1.308 + 0.181 x S for men

Mean fat thickness = 1.933 + 0.168 x S for women

where S is the sum of the fat thicknesses at the four sites (Hayward and Keatinge, 1981). The fat thicknesses were checked using skinfold calipers (Harpenden, British Indicators Limited) using the method of Edward *et al.* (1955). Skinfold thicknesses were about twice that of the ultrasound measurements.

Skin temperature and heat flow measurements

Skin temperature and heat flow were measured at five sites on the body and six sites on

the non-dominant hand. The heat flow sensor and thermocouple at each site were mounted as close together as possible without interfering with each other. The sites of measurement on the body were mid forehead, left peri umbilical region of the trunk, mid anterior aspect of the left thigh, dorsum of the left foot and mid anterior aspect of the left forearm. Heat flow and skin temperature were also measured on the pulp of the terminal phalanx of each finger and on the mid-dorsal region of the non-dominant hand, on the fingers this meant putting the heat flow sensor on the pulp of the finger and the thermocouple over the tip of the finger due to the limited size of the finger. Single wire T type copper-constantan thermocouples were used to measure skin temperature. These consisted of copper constantan wire (BioT, T.C. Ltd.) soldered at one end to form a junction. The junction produces a voltage due to the contact between two different metals and the voltage produced depends on the temperature of the junction. The heat flow sensors (Thermonetics) consist of a thin layer of insulation mounted between a series of thermocouples on both sides, the thermocouples are connected in series to each other but with their voltages opposing. The sensor therefore does not produce a voltage unless the thermocouples on either side of it are on average at different temperatures which will give rise to a resultant voltage where the polarity is determined by which side is warmer. If the temperature on one side of the sensor is greater than that on the other side a temperature gradient must exist and a heat flux must be present. The magnitude and direction of the voltage is therefore determined by the magnitude and direction of the heat flux. The heat flux sensors were calibrated according to the method of Gin *et al.* (1980) which allows for the insulation provided by the sensor. The heat flow is given in Watts/m^2 by the formula:

$$\text{Heat flow} = \frac{1}{(1/KE - I_D/\Delta T)}$$

where K is the calibration factor of the sensor in Watts/m^2.μV, E is the voltage measured by the sensor in μV, I_D is the insulation of the sensor in m^2/W and ΔT is the difference in temperature between the core temperature and the environmental temperature.

The heat flow sensors and thermocouples were attached to the skin with adhesive tape (Blenderm, 3M) taking care not to cover the active area of the sensor. A thin layer of thermally conductive grease (Eccotherm TC4) was applied between each sensor and the skin in order to give a good thermal connection. The heat flow sensors and thermocouples both give a voltage output proportional to the parameter they are measuring these were amplified and recorded automatically by two Grant 12 bit "Squirrel" data loggers. The thermocouples were calibrated against National Physics Laboratory Thermometers over the temperature range 0°C to 40°C. The body heat flow sensor and thermocouple measurements were all recorded once a minute and the air temperature, water temperature, all the digit temperatures and the temperature of the dorsal side of the hand and all the hand heat flows were recorded ever 15 seconds.

Arterial Measurements using Doppler Ultrasound

Using ultrasound techniques it is possible to make non-invasive measurements of the internal diameter of an artery and the blood velocity within the artery (Wells, 1990).

Measurement of Arterial Diameter using Ultrasound

When ultrasound is transmitted into body tissues some of it is reflected as the sound

passes from a tissue of one acoustic impedance to tissue of a different acoustic impedance such as between muscle and blood. If the time taken for this reflection to return is measured it is possible to calculate the distance to this interface since the speed of sound, in what is mainly water, is known (about 1500 m/sec). If the time taken for all the reflections to return to the probe is measured then it is possible to calculate the position of a number of different interfaces, if coincident with the position of the first transmitted beam of ultrasound another is transmitted but at a slightly different angle and again the reflected sound is recorded and then another and so on it is possible to reconstruct a real time moving image of the tissue. The image refresh rate is limited by the depth of the investigation and the speed of sound in the tissue. This image can then be used to make measurements of tissue size making it possible to measure the internal diameter of an artery. For medical imaging purposes ultrasound of between 1 and 10MHz is used. The frequency used depends on the application there is a compromise to be made between resolution and depth of field. The higher the frequency used the greater the attenuation but the better the resolution. In this case the depth of field required is only very shallow (less than 3cm) since the structures of interest are very near the surface, this allows the use of a high frequency (10MHz), with a theoretical resolution of 0.15mm.

Measurement of Blood Velocity by Doppler Ultrasound

Blood velocity can be measured by recording the Doppler shifted frequencies of the sound reflected off the blood cells. Erythrocytes are about the same order of size as the wavelength of ultrasound this makes them highly effective scatterers of impinging ultrasound. The ultrasound reflected off a moving blood cell has its apparent frequency changed relative to a stationary receiver, the change in frequency is proportional to the

speed of the cell this change in frequency is known as the Doppler shift. By measuring the Doppler shifted frequencies reflected from the blood cells in an artery it is possible to calculate the velocity of the cells, the measured velocities of the blood cells are averaged and measured over an integer number of cardiac cycles this gives the mean velocity of the blood known as the Time Average Velocity (TAV). The velocity of an object reflecting ultrasound is given by :-

$$f_D = \frac{2vf}{c}$$

where f_D = Doppler shifted frequency
v = velocity of object
f = frequency of source
c = velocity of sound

This is true only for an object moving directly away from or towards the receiver. In most physiological ultrasound measuring procedures the blood is usually moving at an angle to the probe whereupon the above equation becomes:-

$$f_D = \frac{2v(\cos\alpha)f}{c}$$

where α = the angle between the ultrasound beam and the direction of movement of the blood.

The part of the artery that is sampled for Doppler shifted signals, the sample volume, is selected by temporally gating the received signal. This process selects signals returning from a certain depth in the tissue by only processing the signals that are received during a particular period after each pulse of ultrasound is transmitted. The reflected frequencies are recorded and then a Fast Fourier Transform is performed to calculate the time averaged velocity.

... in a tube is given by multiplying the cross sectional area of the tube by the velocity of fluid in the tube. The cross sectional area of an artery can be calculated from the measured diameter assuming a circular arterial cross section. Arteries do tend to have a circular cross section (Milnor, 1989) due to the relatively high pressure of the blood within the artery compared to the surrounding tissue pressure. Since the cross sectional area of an artery and the velocity of blood in an artery can be measured using the ultrasound techniques described the arterial volume flow can be calculated in mls/min from the following formula:

$$\text{Volume Flow} = \pi \times (\text{diameter}/4) \times \text{time average velocity}$$

where diameter is in centimetres and time average velocity is in centimetres/min. The time average velocity is averaged both spatially across the velocity profile in the artery and temporally during the period of the cardiac cycle.

Calculation of Arterial Resistance from Ultrasound Measurements

The Poiseuille relationship gives the volume flow in a tube in mls/s :-

$$Q = \frac{\pi r^4 \Delta P}{8 \eta L}$$

where r is the radius of a section of a tube of length L both measured in centimetres, ΔP is the pressure difference measured in that length of tube in units of [a]dyn/cm^2 and η is the viscosity in [b]poise.

This equation describes a rigid tube of radius r with a pressure drop of ΔP produced along a length L by the viscous drag of the steady Newtonian flow of a liquid of viscosity

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[a] 1 dyn $=10^{-5}$ Newtons

[b] 1poise = 1dyn.sec/cm^2 or (10^{-5} Newtons.sec/cm^2)

η. The Poiseuille relationship describes frictional losses between the different fluid laminar and is based on steady laminar Newtonian flow in rigid tubes however this is not necessarily a good description of arterial flow. Arterial flow is not steady but pulsatile due to the intermittent nature of the heart's pumping action; the forearm arteries are not rigid tubes but are distensible tapered vessels. Each time the left ventricle contracts and ejects its contents into the aorta the artery stretches and as the pressure rises a wave of distension sweeps down the arterial tree. These factors may invalidate use of the Poiseuille relationship in calculating forearm artery haemodynamics. Blood does in fact behave almost identically to a Newtonian fluid in healthy vessels down to a diameter of 0.5 mm and the flow is laminar except in the ascending aorta and main pulmonary artery just beyond the valves (Milnor, 1989). Blood flow in the arterial circulation is not steady but pulsatile it can however be considered in terms of the mean flow if the artery is considered to be a rigid tube (Womersley, 1955). Arteries are not generally considered to be rigid tubes but distensible tapering vessels, Ling *et al.* (1972) produced mathematical models to account for the distensible tapered nature of blood vessels. There models suggest the Poiseuille relationship substantially underestimates the resistance in the blood vessel they were considering. In another paper by Belardinelli and Cavalcanti (1991) another model is described again taking the tapered distensible nature of blood vessels into consideration which suggests the resistance offered by an artery is very much affected by these factors; when comparing the flow calculated using their theoretical equations to actual results obtained by Ling *et al.* (1973) measured on the descending aorta of three dogs a much better correlation is obtained than that obtained by other models including the Poiseuille. The discrepancy between the Poiseuille and more complex models is due to the distensible tapered nature of the descending aorta which the

Poiseuille relationship does not account for and which the other models are based on. Ling *et al.* (1973) measured the increase in the diameter of a dog descending aorta diameter as the pressure rose from a diastolic pressure of 90 mmHg to a systolic pressure of 135 mmHg as about 17% of the diastolic diameter. In a study done on a group of normotensive humans the increase in diameter of the radial artery during the cardiac cycle was 1.6% of the diastolic diameter (Mooser, 1988) and in a further study the brachial artery diameter was shown to change by only 3% (Simon, 1985). There is further evidence that the distensibility of the peripheral arteries is very small (Milnor, 1989) and will not have a marked effect on the arteries haemodynamics it is therefore justifiable to assume the muscular forearm arteries are rigid tubes for the purposes of calculating arterial impedances. The other possible major source of error using the Poiseuille relationship to make haemodynamic calculations involving forearm arteries is if tapering of the vessels produces energy changes in the blood. As the arteries change their cross sectional area the energy of the blood is changed from potential to kinetic or vice versa depending on whether the arterial cross section is getting larger or smaller this is as described by the Bernoulli relationship. If a blood vessel tapers it will have a smaller cross section at a given point on its length compared to a more proximal point. There is very little difference in the combined cross section of the radial and ulnar arteries measured in various studies compared to the brachial artery (Mooser, 1988; Perret, 1989; Demolis, 1991; Anderson, 1989 and Blair, 1991) and generally any overall change in cross sectional area in these arteries in healthy individuals is very gradual (Milnor, 1989). The evidence therefore suggests the use of the Poiseuille relationship is justified in the forearm arteries (Simon, 1990; Back, 1994).

The expression for arterial resistance by Poiseuille's relationship in units of dyn sec/cm^5

is:

$$\text{Resistance (R)} = \frac{8\eta L}{\pi r^4}$$

where η is the blood viscosity in poise

L is a given length of artery in centimetres

and r is the radius of the artery in centimetres

The unit of resistance is therefore

The calculations of arterial resistance are made in terms of the arterial pressure gradient so are in units of resistance per centimetre of artery length. So the pressure gradient is in units of dyn.sec/cm^5/cm and becomes:-

$$\text{Arterial resistance per cm length} = \frac{8\eta}{\pi r^4}$$

All the factors in this equation are relatively easy to measure except the blood viscosity (η). The viscosity of blood changes depending on the shear rate of the blood and the temperature of the blood (Barbee, 1973; Rand, 1964). Bazett (1948) showed that the brachial and radial blood temperature remains very close to normal body temperature when in a room at 22°C or higher. He also demonstrated after prolonged exposure to cold air the blood temperature in the brachial artery remained very close to core temperature but blood temperature in the radial artery could drop to 21.5°C after 95 minutes exposure to air at 9°C; this would give a rise in radial artery blood viscosity of between 60 and 90% depending on shear rate. No measurements have been done to determine the blood temperature in the digital arteries. The shear rate of the blood which also influences its

viscosity depends on the arterial blood velocity; it is possible to calculate the average shear rate from the average velocity (Levenson, 1987; 1988). The relationship between mean shear rate and mean velocity is derived from the Poiseuille relationship giving:-

$$\text{Mean shear rate } (\gamma) = \frac{16 \text{ X mean blood velocity}}{3 \text{ X diameter}}$$

Using this equation it is possible to calculate shear rates and use the appropriate viscosity from experimental measurements of viscosity made at different shear rates and temperatures (Rand, 1964). With these calculated values it is therefore possible to calculate the resistance of the forearm arteries.

Control of Blood Flow Calculated from Ultrasound Measurements

In order to determine the importance of the forearm arteries in controlling blood flow it is necessary to know their contribution to the resistance along the arterial tree. The contribution to arterial resistance made by any one element of the arterial tree is given by the pressure drop that is produced by that length of arterial tree. From the arterial resistance and the arterial blood flow it is possible to calculate the arterial pressure gradient of the artery. The relationship is derived as follows from the equation for flow in terms of ultrasound measurements and in terms of the equation for flow as described by the Poiseuille relationship:

$$\text{Flow} = \text{Time average velocity} \times \pi.r^2$$

also,

$$\text{Flow} = \frac{\pi . r^4 . (P_1 - P_2)}{8\eta L}$$

therefore:

$$\frac{\pi . r^4 . (P_1 - P_2)}{8\eta L} = \text{Time average velocity} \times \pi . r^2$$

therefore:

$$P_1 - P_2 = \text{Time average velocity} \times \frac{8\eta L}{r^2}$$

This will give a result in dyn cm^{-2}. The equation for the pressure gradient per centimetre of artery length is:

$$\text{Pressure gradient per centimetre length} = \text{Time average velocity} \times \frac{8\eta}{r^2}$$

This formula produces results in units of $dyn.cm^{-2}/cm$. It is generally more common to quote arterial pressures in terms of mmHg and therefore all pressures are quoted in mmHg and in the case of pressure gradients mmHg/cm. To convert from $dyn.cm^{-2}$ to mmHg it is necessary to divide by the conversion factor of 1334.

If the distance between two sites at which pressure gradients have been calculated is known then it is possible to make a crude approximation of the overall pressure drop that occurs along that arterial segment by taking an average of the pressure gradient calculated at the two sites and multiplying it by the distance between the two sites of measurement.

Practical Procedure for Making Ultrasound Measurements

Blood flow measurements were made using a Diasonics DRF-1000 Doppler ultrasound system with a high resolution 10 MHZ "small parts" probe. For these experiments the system was used in both imaging or B-mode and pulsed Doppler mode. Initially the ultrasound was switched to image mode and the ultrasound probe placed gently over the artery of interest which was previously located by palpation. The ultrasound probe was acoustically coupled to the skin using ultrasonic transmission gel (Aquasonic, Parker Laboratories Inc.). The arteries, when viewed with ultrasound, are distinguishable from other structures of similar appearance by their pulsatile movements, once located the orientation of the probe is adjusted so as to give a central longitudinal image of the artery. The ultrasound is now switched to pulsed Doppler mode and a cursor appears on the monitor screen, the cursor consists of a straight line originating from the position of the probe on the surface which shows the angle of the pulsed Doppler beam, part way down this line there are two short lines crossing the Doppler beam angle line and they give the size of the sample volume for Doppler sampled frequencies. The direction of the Doppler beam is adjusted with the control on the probe to select the segment of the artery of interest and the sample volume is adjusted to exactly match the internal diameter of the artery. Angle correct is selected on the ultrasound control unit and another line appears on the cursor in the middle of the two lines delimiting the sample volume, the angle correct line is adjusted to lie parallel with the artery wall. The depth and size of the sample volume adjustments give the Doppler ultrasound control unit the information it requires to temporally gate for only those Doppler shifted frequencies returning from the vessel of interest. The angle correct adjustment gives the necessary information for the unit to correct for the angle at which the returning signals are originating from.

Once the sample volume and angle correction are appropriately adjusted the ultrasound display is changed to give a continuous display of the Doppler shifted frequencies against time. The display is calibrated to show blood velocity on the vertical axis in centimetres per second and time in seconds on the horizontal axis. The Doppler gain control is adjusted so only Doppler shifted frequencies reflected from the arterial blood are displayed with all noise excluded . The system possess a high pass filter often known as "the wall thump filter" which is used to remove low frequency Doppler shifted frequencies originating from tissue movements such as that from the wall of the artery; this filter was left on its lowest setting of 100 Hz throughout. The shift in frequency of ultrasound reflected off red blood cells is within the audible range and is monitored through a speaker, the characteristics of the sound can be useful in distinguishing blood flow from other background noise and in distinguishing arterial from venous flow. Once the monitor screen has several complete cardiac cycles displayed (usually between about four and seven depending on the heart rate) the waveform is frozen. A cursor is used to select as many complete cardiac cycles as is possible on the displayed waveform. The ultrasound system's built in computer performs a Fast Fourier Transform on the selected area of the velocity waveform to calculate the time average velocity (TAV) the result is given in centimetres per second.

The ultrasound is returned to image mode and during diastole the image is frozen. The mode for measuring diameter is selected which brings up a pointer superimposed on the image. The pointer is placed at one side of the outer boundary of the artery lumen and the point is selected then the pointer is placed at the opposite boundary of the artery lumen and the point selected. This gives a measure of the internal diameter of the artery and the

unit automatically calculates values for the cross sectional area, time average velocity and volume blood flow which are displayed and manually recorded. Two further measurements of diameter are made which are recorded. Later all measured diameters are averaged and the flow recalculated. Ultrasound measurements were made on the brachial artery at the antecubital fossa and the radial artery just proximal to the fold of the wrist. Measurements were made at these two sites since they are at the extremes of the forearm arteries and changes recorded in them should make it possible to predict the overall state of the arterial tree. Measurements of diameter and blood velocity were also made in the palmar digital branch of the superficial palmar arch for the middle and index finger. The distance between the brachial and radial site of measurement on each individual was measured and recorded.

Core temperature measurement

Continuous measurements of core temperature are generally made at one of three sites: in the oesophagus, rectum and aural canal. Rectal temperature tends to be slightly higher than other sites of core temperature measurement and lag slightly behind changes shown at other sites but is otherwise reliable and causes the subject little discomfort (Molnar and Read, 1974). Oesophageal probes are uncomfortable and are affected by the subject swallowing (Livingstone, 1983). The tympanic temperature can be an accurate means of measuring core temperature and is of particular interest because of its proximity to the hypothalamus it is however easily affected by local cooling when used in cool environments (Cooper *et al.,*). The problems with measurements of core temperature using aural probes in the cold can however be alleviated by the use of a zero gradient aural thermometer (Keatinge and Sloane, 1975). This device has a thermistor next to but

not touching the tympanic membrane which is supported in place by cotton wool. To prevent local cooling there is another thermistor and a heating pad over the outer ear held in place by a headphone casing. This outer pad and thermistor is maintained at 0.1°C below the tympanic temperature by an appropriate servo feedback mechanism. Additionally a hood is worn over the assembly with the edges taped down to prevent draughts affecting the tympanic temperature. This device was shown to very closely follow tympanic temperature during rapid changes in body temperature in a cold environment (Keatinge and Sloane, 1975). It was decided to use a zero gradient aural thermometer and a rectal probe because of the combination of accuracy, reliability and comfort in use.

Rectal temperature was measured using a thermistor (Light Laboratories 3GID) inserted 10cm past the anal sphincter.

The aural thermistor was inserted about 10 mm into the outer aural meatus and held in place with cotton wool, the head set with the servo controlled heating pad was then placed over the head. The head set contained the second thermistor which monitored the temperature of the outer ear allowing the heating pad to be controlled as appropriate. The whole assembly was then covered with a hood whose edges were taped down to prevent local draughts. Once in place the device was allowed at least 30 minutes to stabilise. The control unit produced a digital display of the temperature measured by the thermistor in the external auditory meatus.

The aural and rectal probes were both calibrated against National Physics Laboratory calibrated mercury in glass thermometers. Both rectal and aural temperature were

recorded before the start of the experiment and then every 5 minutes throughout.

The Climatic Chamber

The experimental chamber was an insulated room 4.30 m long, 3.28 m wide and 2.16 m high the temperature can be controlled between -5°C and 70°C by means of a heating and refrigeration unit that circulates air around the room with two integral fans. The average wind speed around the subjects was 0.177 ± 0.027 m/s. The heating and refrigeration unit were thermostatically controlled but in addition a thermocouple was mounted close to the subject and minor adjustments were made to the thermostat as necessary.

Blood Pressure Measurement

Blood pressure was measured four different methods:

1. indirectly by auscultation using a sphygmomanometer.
2. indirectly by an oscillometric method (Dinamap)
3. indirectly by volume clamp technique (Finapres)
4. directly by indwelling cannulae

Blood Pressure Measurement by Auscultation

The method of auscultation was used to measure blood pressure in the brachial and radial artery of the non-dominant arm (Kirkendall *et al.*, 1980; Petrie *et al.*, 1986). One cuff was applied around the left upper arm so the area of the antecubital fossa where the brachial artery had previously been located by palpation was left unobstructed; the other cuff was applied around the left forearm as close to the hand as possible whilst leaving the distal end of the radial artery unobstructed. Care was taken that the cuff was of the appropriate size and that the bladder was over the artery it was applied to the arm so as

to be snug but not tight. The sphygmomanometer cuffs were attached to a mercury manometer (Eccosan). Blood pressure was determined by inflating the cuff 10 mm Hg above the pressure required to obliterate the palpated pulse in the appropriate artery, a stethoscope was then placed over the artery and the cuff pressure gradually decreased. When the first Korotkoff sound was identified the pressure was recorded as systolic pressure, the cuff pressure was further lowered until the fifth Korotkoff sound disappeared this pressure was recorded as diastolic pressure. Mean arterial pressure was calculated as the sum of one third of the pulse pressure plus the diastolic pressure.

Measurement of Blood Pressure by Indirect Oscillometric Technique

Blood pressure was also measured indirectly by the use of a Dinamap Adult/Paediatric Vital Signs Monitor (Model 845XT). This is an automated system that consists of a microprocessor controlled inflation and measuring system connected to a cuff which was wrapped snugly around the dominant arm in the same way as for the auscultatory measurements. The system works by an oscillometric technique and it measures and displays systolic, diastolic and mean arterial pressure as well as heart rate. Initially the cuff is automatically inflated to about 170 mmHg which will normally occlude the artery; after this initial inflation the microprocessor will inflate the cuff to a higher level if necessary. After the artery is occluded the cuff will deflate in increments of about mm Hg , at each level the monitor measures the amplitude of the pressure pulsations caused by movement of the arterial wall. At cuff pressures above systolic pressure the blood flow ceases and arterial movement is small and relatively constant, once the cuff pressure drops just below systolic pressure the amplitude of pressure pulsations in the cuff increase significantly, this pressure is recorded as systolic pressure. As the pressure level

in the cuff drops still further the amplitude of the pulsations increases until they reach a maximum after which they start to decrease until they reach a low relatively constant amplitude. The pressure in the cuff at which the pressure pulsations are at maximum amplitude is the point which the system takes as mean arterial pressure, after this the pressure at which the pulsations become constant with decreasing levels of cuff pressure is the point which the system takes to be diastolic pressure. The microprocessor measures the time between consecutive pulsations and uses an average to determine heart rate. The arterial pressure measurements and heart rate are displayed and recorded manually.

Blood Pressure Measurement by Volume Clamp Technique

Blood pressure was measured in the finger by a non-invasive device (Ohmeda Finapres 2300 blood pressure monitor). This device works on the principle of "unloading" of the arterial wall by pressure on the skin surface which allows the intra arterial pulse pressure to be transferred to a sensor on the surface of the skin without any distortion or attenuation that would be caused by a distended arterial wall. This system increases the pressure on the surface of the finger by means of an appropriately sized cuff. Pressure on the surface of the skin is transmitted to the tissue surrounding the artery and thence to the artery wall thereby unloading the arterial wall. When the artery is compressed to the point at which it just begins to collapse transmural pressure is zero; transmural pressure being the difference in pressure between the inside and outside of the artery. At the point of zero transmural pressure the pressure in the artery and in the cuff will be the same with the pressure being transmitted between artery and cuff by the tissue and fluid surrounding the artery in the finger. The cuff pressure is monitored by a fast acting pressure transducer and so long as transmural pressure is zero intra arterial pressure is mirrored by cuff

pressure. In practice this method is not perfect since the tissue and fluids of the finger are not completely incompressible, tissue moves in and out from under the cuff with each pulsation and "cuff end effects" occur whereby arteries are compressed more in the middle under the cuff than at the ends under the cuff. This method has been tried on the forearm, upper arm and fingers. In 1969 a Czech patent was granted to J. Penaz for a new method based on this principle.

Penaz improved on earlier methods by separation of the instrumentation by which unloading of the artery was achieved from that by which unloading of the artery was observed. Penaz used a pneumatic cuff to unload the artery and a light transmission plethysmograph to observe the artery. The light transmission plethysmograph consists of an infra red emitting diode, producing a wavelength of light that is specific for arterial blood. This diode is situated on one side of the tissue and an infra red detecting diode placed on the other side of the tissue. This light plethysmograph responds to changes in blood volume within its field of view and not to blood volume in the whole compartment under the cuff as in earlier systems. Once the venous system is collapsed and capillary flow blocked by cuff pressure only arterial volume changes are monitored by the plethysmograph. Early systems kept the total volume under the cuff constant so the arteries would cycle between open and collapsed against the residual compliancies in the system. In the Penaz system the volume of just the arteries can be held constant by appropriately varying cuff pressure guided by the light plethysmograph whilst the total liquid volume can be allowed to vary freely. By limiting the field of view of the plethysmograph to a small volume near the middle of the cuff the "cuff-end-effects" are effectively reduced.

The Finapres 2300 used for this study is based on the Penaz system (Boehmer, 1987). Initially the system finds the necessary pressure to unloaded the arterial wall. Once this pressure is determined the device adjusts the pressure in the cuff so as to maintain the transmural pressure at zero. The pressure required to keep the artery unloaded at all stages of the cardiac pressure wave is therefore mirrored by the cuff pressure. The cuff pressure is constantly monitored by a fast response transducer which is therefore effectively giving a measure of intra arterial pressure. Errors in the system are caused by shifts away from the plethysmograph of any red blood cells trapped in the microcirculation. The plethysmograph sees these changes as a change in arterial volume and therefore compensates by adjusting the cuff pressure thereby producing an error in the pressure recorded. Another potential source of error is if the artery is not precisely unloaded that is if the transmural pressure is not zero. In normal use this system has two procedures of "locking" the artery at zero transmural pressure. When the system is first activated to make measurements it pumps the cuff up in steps each one of which it holds for a complete cardiac cycle. The pressure required to unload the artery is taken to be the pressure at which the light plethysmograph measures the maximum amplitude excursion for the arterial volume during a cardiac pressure wave. Once this point has been established the system will lock this arterial volume by changing the cuff pressure to counter any change in arterial volume as described previously thereby measuring intra arterial pressure. This mode of operation continues for between 4 and 20 beats depending on the magnitude of the mean pressure change between one beat and the next. If the critical pressure change between beats is detected by the device its programme goes into "lock adjust" which varies the pressure stepwise, as for start up mode, at around the

pressure that was last measured by the machine in order to verify the artery is still fully unloaded. The "lock adjust" procedure is of great importance since the arteries degree of constriction can change fairly rapidly with time. As the degree of constriction of the artery changes the blood volume measured by the plethysmograph changes and the device compensates by a change in pressure of the cuff thereby producing an error in the measured pressure. Many papers have commented on the reliability of the Finapres the majority find it works well in general but several comment on the fact that occasionally there are some aberrant readings with no apparent explanation especially if conditions are not optimal.

The Finapres cuff was applied around the middle phalanx of the middle finger. The Finapres cuff was wrapped around the finger so as to fit snugly and could just slip over the distal interphalangeal joint but would not pass over the proximal interphalangeal joint as recommended by the manufacturers. The cuff was orientated such that the line on the cuff was in line with the mid anterior aspect of the finger. The cuff had this orientation in order to place the infra red light emitting diode opposite the infra red light dependent diode with the arteries of the finger in between. If the cuff is accidentally turned so the arteries are not directly in between the light source and detector the signal becomes weak and can disappear altogether particularly if the bone becomes interposed. The Finapres was allowed to run for between 30 and 60 seconds each time which allowed it to make between 20 and 30 separate measurements of systolic and diastolic pressure. When the device is started it goes through a programme to find the unloaded set point of the artery. When this is found the artery volume is locked and the device starts measuring arterial pressure stopping every few beats to check and if necessary readjust the unloaded

position of the artery. The Finapres automatically made measurements when activated, the display showed both a continuous arterial pressure waveform and a digital readout of the systolic, diastolic and mean arterial pressure automatically measured from this waveform. The Finapres system has both a serial computer output which outputs its measurements of blood pressure and an analogue output which gives a continuous voltage signal proportional to the measured pressure at that instant.

Direct Measurement of Arterial Pressure by Indwelling Cannulae

An attempt was made to make direct measurements of arterial pressure by performing "arterial stabs" at key points, it proved very difficult to obtain pressure measurements this way probably because at the time the punctures were attempted the arteries were at their most constricted.

Direct continuous arterial pressure measurements were made using indwelling arterial cannulae introduced prior to the subject entering the climatic chamber. One was inserted in the brachial artery in the area of the antecubital fossa as close as possible to the major skin fold of the elbow. The second cannula was inserted in the radial artery at the wrist about 1 cm above the major skin fold of the wrist both cannula were pointing downstream. In accordance with the ethical committee requirements this procedure was carried out by a physician who performs the procedure on a regularly basis. The cannula were Abbocath 20 gauge No. G-717 (outer diameter 1.1 mm, internal diameter 0.7 mm and length 32 mm) connected via 150 cm of low compliance tubing to a Viggio-Spectramed DT-XX disposable pressure transducer. The transducer was connected to a bag of heparinized physiological saline that was adjusted to give a slow flush of 3-4 mls

per hour to prevent clogging of the cannula. Care was taken to keep the transducer at the same height as the cannula. After each procedure the pressure transducer was calibrated for its static response against both a mercury manometer and a aneroid manometer; a selection were "pop tested" to test their dynamic response (Milnor, 1989). Mean blood pressure was measured off the recorded trace by integrating the area under the pressure wave for a 30 second interval of the part of the trace for which measurements were required. Care was taken that only a whole number of cardiac cycles was used for each mean and that the same part of the pressure wave was used for both the brachial and radial measurement.

Method for producing cold vasodilatation in the hand

Cold induced vasodilatation was produced in the hand by inserting it through a hole in the side of a plastic box of about 10 litre capacity this box was subsequently filled with water and ice. A seal between the wrist and box was made using a loose fitting surgeon's rubber glove from which the hand had been removed the rubber cuff was taped around the subjects wrist to make a watertight seal. Care was taken that the blood flow through the wrist was not affected by the seal. The water was kept vigorously stirred by blowing air through the mix of water and ice and the temperature of the water usually went below 5°C within 60 seconds of the first addition of water. This method of hand immersion was used so that the hand could be maintained at the level of the heart without making the position unduly uncomfortable for the subject. The temperature of the water and ice mix was constantly monitored and ice was added as necessary.

Recording Systems

Core temperature, indirectly measured blood pressure, and ultrasound measurements were recorded manually. Heat flow and temperatures were electronically recorded onto two loggers which were later transferred via a serial link onto a personal computer additionally an on line print out was produced to guard against loss of data due to logger failure. The loggers and printers were battery powered so as to prevent any mains voltage risk to the subject.

The direct pressure measurements were recorded using a Cambridge Electronic Devices 1401 analogue to digital converter interfaced to a personal computer and an isolated 1902 programmable signal conditioner provided the necessary excitation voltage and amplification required for the pressure transducer. The computer gave an on line display graphical display of pressure as well as recording the data to disk for later analysis the pressure wave was sampled at 100 Hz.

Data analysis

Results are given as means ± standard error of mean except where otherwise stated. For each experiment the results are analysed in two parts; the initial ninety minutes in which the subjects are in air at 38°C, 24°C and 12°C; and the subsequent 30 minutes in which they remained in air at these temperatures, but also immersed one hand in ice water. Statistical comparisons for the first part were made between results at the three temperatures; comparisons between different times in any one experiment were only made between the results before entering the chamber and at the end of the 90 minutes in order to avoid making the corrections necessary for multiple comparisons.

In order to determine if the subsequent 30 minutes hand immersion in ice water produced a change the average value of a given parameter just before hand immersion (90 minutes) was compared to the average value at the end of the hand immersion (120 minutes) and comparisons were made between the three experiments at the end of the 120 minutes. All these comparisons were made using the two tail paired Student's T- test, since the results approximated to a normal distribution. Comparisons were also made between individuals, using Pearson's linear regression analysis. The p value for significance was taken as 0.05.

PROTOCOL

Overall Experimental Outline

All the experiments were carried out at the same time of day to prevent any circadian variation confusing the results. The subjects were all asked to refrain from exercise and the consumption of alcohol for 24 hours before the experiment. The subjects remained supine on a net bed throughout; the net bed consisted of a string hammock stretched over a frame this gave firm comfortable support when supine without providing the insulation of a mattress. The subject was weighed and subcutaneous fat was measured using both skin fold callipers and ultrasound. The subject remained on the bed whilst being instrumented this would take about one hour which gave the subject time to stabilize, the room temperature during this time was controlled at 24.27±0.07°C. The subjects non-dominant arm was positioned in the empty hand immersion tank. The height of the tank and arm were adjusted in order to keep the arm level at heart height. Three consecutive sets of measurements were made on the subject at 10 minute intervals at the end of the period of stabilisation just before entering the experimental chamber. The subject remained supine on the net bed which was then wheeled into the temperature controlled room.

Throughout all the experiments aural and rectal core temperature and heart rate were recorded every five minutes, and, blood pressure measured with the Dinamap were recorded every 15 minutes. Body skin temperature and heat flow was recorded every minute and hand skin temperature and heat flow were recorded every 15 seconds.

Six experiments were carried out on all twelve subjects. The order of the experiments was crossed over in a Latin Square Design, with groups of six subjects in each crossover.

For any one subject the experiments were separated by at least seven days to prevent any acclimatization effects. Six of the subjects then took part in a further experiment.

The key investigations were also done on a long distance swimmer with known ability to maintain core temperature during prolonged cold water immersion.

All the exposures in the climatic chamber had the same general form, a total of two hours exposure to moving air at the desired temperature during the last half hour of which the subject's non-dominant hand was immersed in stirred ice and water. Subjects were allowed to watch television during the experiments to combat boredom.

Experimental Protocol for Indirect Investigation of Forearm Blood Pressure

Three experiments were carried out on each subject at air temperatures of 38°C, 24°C and 12°C during which indirect measurements were made of arterial pressure. Brachial and radial artery pressures were measured by auscultation and finger artery pressure was measured with the Finapres every 10 minutes during the initial 90 minutes of each experiment and then every 5 minutes during the hand immersion phase.

A set of measurements consisted of a Finapres measurement, followed by a radial artery measurement and finally a brachial artery measurement. The measurements were done in this order so that each one was progressively more proximal thereby preventing the effect of the previous measurement from effecting the subsequent measurement. The Finapres was allowed to run for between 30 and 60 seconds each time which allowed it

to make between 20 and 30 separate measurements of systolic and diastolic pressure. For each data point all the values for each measurement were averaged together. Mean arterial pressure was calculated by adding one third of the pulse pressure to the diastolic pressure. These measurements were made in addition to those specified under overall experimental outline.

Experimental Protocol for Investigation of Forearm Arteries using Ultrasound

Again three experiments were carried out on each subject at 38°C, 24°C and 12°C. Ultrasound measurements were made at the brachial, radial and palmar sites every 10 minutes during the first 90 minutes of these experiments and the measurements on radial and brachial arteries were continued every 5 minutes during the hand immersion phase. It was not possible to make digital artery measurements during the period of hand immersion since the ultrasound probe was not designed for underwater use. These measurements were made in addition to those specified under overall experimental outline.

Experimental Protocol for Direct Investigation of Forearm Blood Pressure

The cannulae were inserted as soon as the subjects arrived so as to allow time for the artery to recover from any spasm due to insertion of the cannula. Arterial diameter and arterial blood velocity were also measured using ultrasound as specified earlier, as was finger artery blood pressure with the Finapres, these measurements were made every 15 minutes during the first 90 minutes and then every five minutes during the hand immersion. The arterial blood pressure was recorded continuously at 100 Hz on a personal computer. The subjects were instrumented with three additional heat flow

sensors one on the palm of the hand and two heat flow sensors on the back of the hand. This procedure was also carried out on an additional subject LC a long distance swimmer with known ability to survive immersion in cold water (Keatinge, 1989).

Blood pressure measured using the Finapres was recorded via the serial link to a computer and the pressure waveform was also recorded via the Cambridge Electronic Devices 1401 to a personal computer.

RESULTS

EFFECTS OF 90 MINUTES EXPOSURE TO AIR AT 38°C, 24°C AND 12°C ON FOREARM ARTERY PARAMETERS DERIVED FROM ULTRASOUND MEASUREMENTS AND ON MEAN ARTERIAL PRESSURE AND CORE TEMPERATURE

Results

These results show the effect of 90 minutes exposure to moving air at either 38°C, 24°C or 12° on brachial and radial artery parameters measured by ultrasound and derived from ultrasound measurements. 12 male subjects (Table 1) volunteered aged between 19 to 33 years of age (average 24 years), height 1.73 to 1.92 m (average 1.79 m), weight 68.2 to 94.2 Kg (average 75.4 Kg), surface area 1.9 to 2.3 m^2 (average 1.9 m^2) and mean subcutaneous fat thickness 3.8 to 6.9 mm (average 5.1 mm).

Table 1
Mean and individual anthropometric measurements of subjects who took part in the main series of experiments

Subject (Initials)	Age (years)	Height (m)	Weight (Kg)	Surface Area (m^2)	Fat Thickness (mm)
AC	20	1.92	94.2	2.3	5.5
CD	29	1.85	84.4	2.1	4.9
CJ	23	1.75	70.9	1.9	6.6
DA	24	1.75	70.7	1.9	3.9
DD	33	1.77	72.3	1.9	6.9
EJ	24	1.83	76.6	2.0	6.1
JT	20	1.79	77.5	2.0	4.0
LW	25	1.76	77.0	1.9	4.4
MC	19	1.80	68.2	1.9	3.8
RB	22	1.77	71.0	1.9	4.6
RP	27	1.78	69.9	1.9	5.4
RR	20	1.73	72.1	1.9	4.6
Mean	**24**	**1.79**	**75.4**	**1.9**	**5.1**

The subjects were exposed on each occasion to nominal air temperatures of 12°C, 24°C.

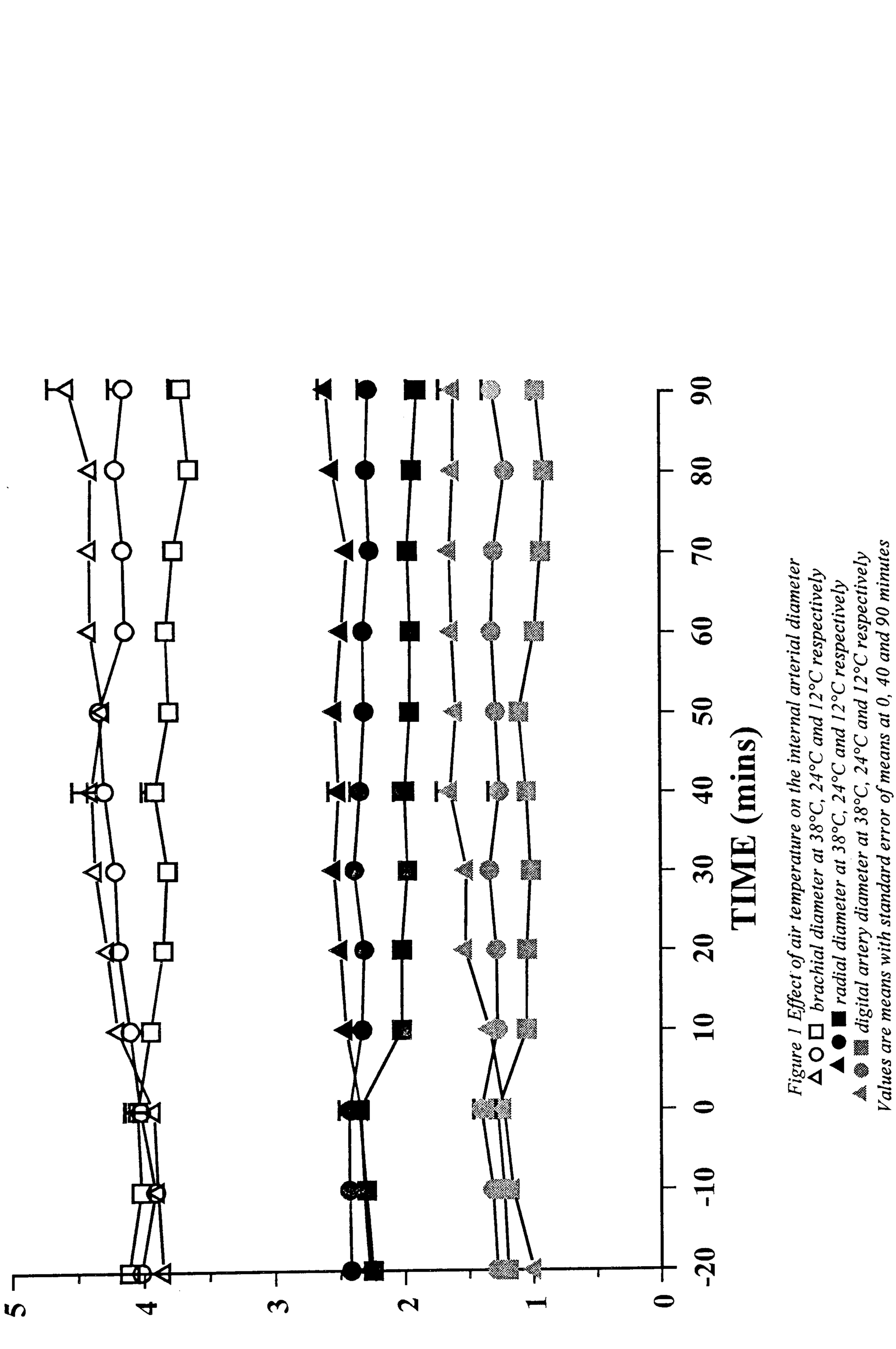

Figure 1 Effect of air temperature on the internal arterial diameter
△○□ brachial diameter at 38°C, 24°C and 12°C respectively
▲●■ radial diameter at 38°C, 24°C and 12°C respectively
▲●■ digital artery diameter at 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 0, 40 and 90 minutes

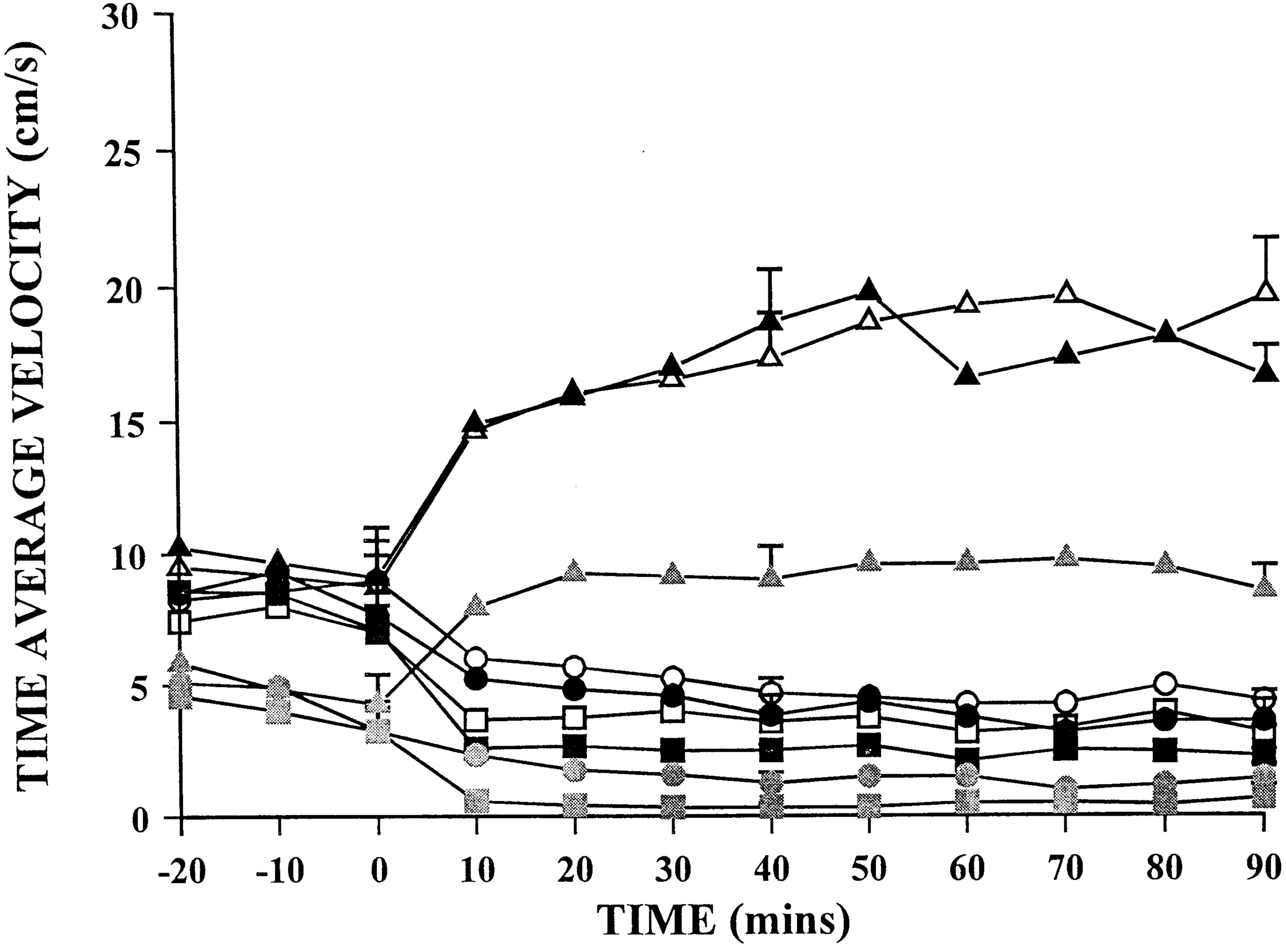

Figure 2 Effect of air temperature on the time average velocity of arterial blood
△ ○ □ *brachial time average velocity at 38°C, 24°C and 12°C respectively*
▲ ● ■ *radial time average velocity at 38°C, 24°C and 12°C respectively*
▲ ● ■ *digital time average velocity at 38°C, 24°C and 12°C respectively*
Values are means with standard error of means at 0, 40 and 90 minutes

and 38°C the actual air temperatures measured were 12.53 ± 0.04°C, 24.59 ± 0.03°C and 38.13 ± 0.04°C; before each exposure the subjects lay supine outside the chamber in the laboratory at a nominal air temperature of 24°C which was measured at 24.18 ± 0.14°C, 24.11 ± 0.10°C and 24.55 ± 0.21°C respectively for each exposure.

Arterial Diameters and Arterial Blood Time Average Velocity

Figure 1 shows the mean arterial diameters and Figure 2 the mean time average velocity of the arterial blood during the 20 minutes before entering the climatic chamber, and then during the first ninety minutes in moving air at either 12°C, 24°C or 38°C. Table 2 and 3 give the mean arterial diameter and mean time average velocity respectively after 90 minutes exposure at each temperature. These tables also show the percentage value, with t-test comparisons of each parameter after 90 minutes in air at 38°C and 12°C compared against the value of that parameter after 90 minutes at 24°C.

Table 2
Arterial diameters after 90 minutes of exposure to moving air, as a percentage of the control exposure value and t-test results

Exposure Temperature	Brachial	Radial	Digital
Diameter at 38°C (mm)	4.55 ± 0.15	2.58 ± 0.06	1.60 ± 0.12
(as % of 24°C value)	(110.2% p=0.032)	(113.7% p=0.002)	(122.1% p=0.027)
Diameter at 24°C (mm)	4.13 ± 0.11	2.27 ± 0.07	1.31 ± 0.07
Diameter at 12°C (mm)	3.69 ± 0.09	1.89 ± 0.08	0.97 ± 0.04
(as % of 24°C value)	(89.3% p=0.001)	(83.3% p<0.001)	(74.1% p<0.001)

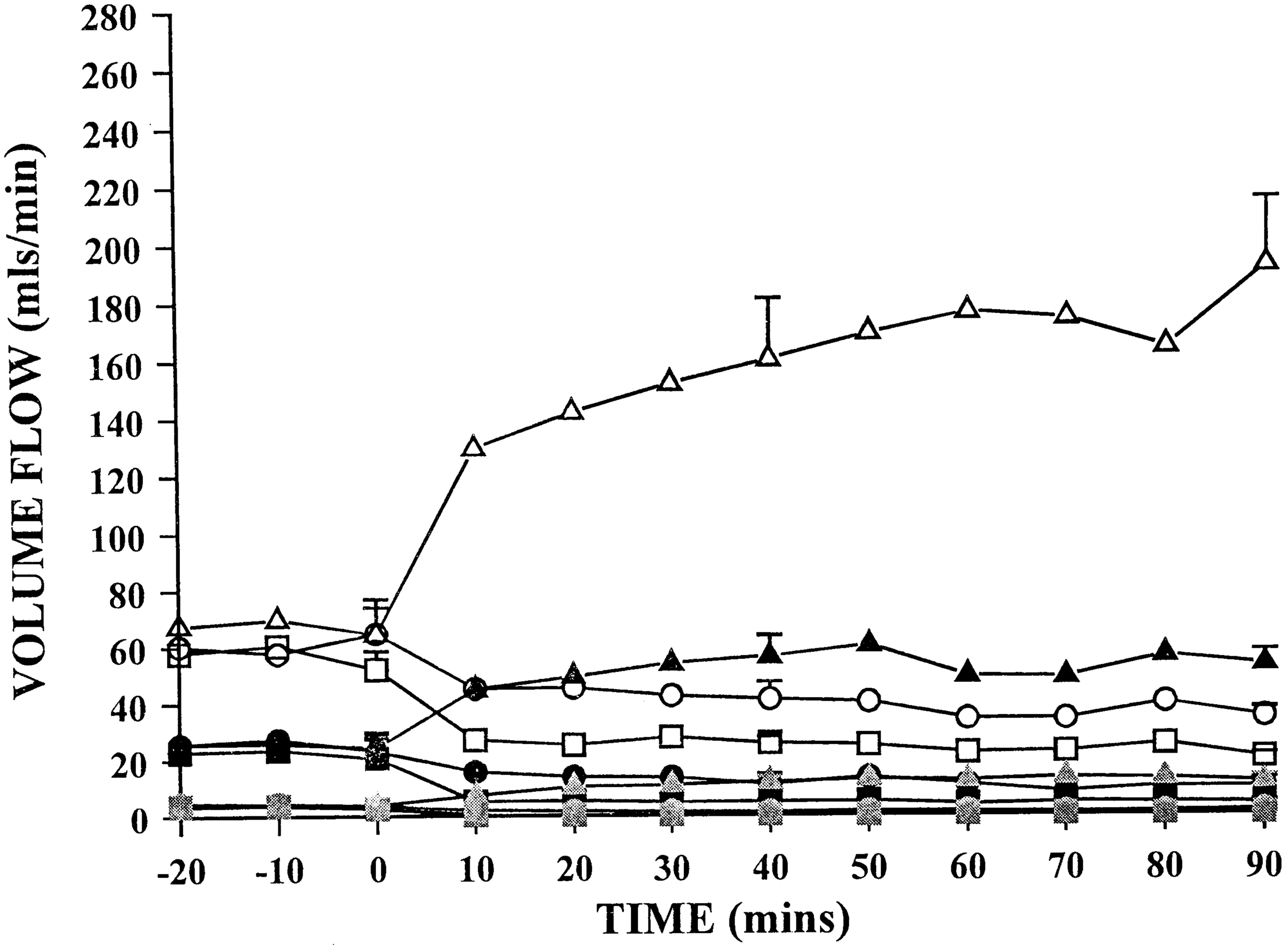

Figure 3 Effect of air temperature on arterial blood flow
△ ○ □ *brachial flow at 38°C, 24°C and 12°C respectively*
▲ ● ■ *radial flow at 38°C, 24°C and 12°C respectively*
▲ ● ■ *digital flow at 38°C, 24° and 12°C respectively*
Values are means with standard error of means at 0, 40 and 90 minutes

Table 3
Blood Velocity (TAV) after 90 minutes of exposure to moving air, as a percentage of the control exposure value and t-test result

Exposure Temperature	Brachial	Radial	Digital
Velocity at 38°C (cm/s)	19.58 ± 2.07	16.58 ± 1.12	8.50 ± 0.99
(as % of 24°C value)	(452.2% p<0.001)	(463.1% p<0.001)	(598.6% p<0.001)
Velocity at 24°C (cm/s)	4.33 ± 0.38	3.58 ± 0.79	1.42 ± 0.53
Velocity at 12°C (cm/s)	3.17 ± 0.21	2.25 ± 0.25	0.67 ± 0.50
(as % of 24°C value)	(73.2% p=0.015)	(62.8% p=0.067)	(47.2% p=0.339)

Just before exposure to the three different air temperatures the mean baseline velocities were the same, for each of the three arteries. All brachial, radial and digital arteries showed an initial rapid dilatation and increase in blood velocity in warm air, and constriction and decrease in blood velocity in cold air, with only a small further change in either case during the rest of the 90 minutes before hand immersion. They showed little change in air at 24°C.

The changes in diameter were on average slower in the brachial than in the radial and digital arteries and these differences were relatively smaller in the large than the small arteries. The absolute values of the mean time average velocity of blood in the brachial and radial arteries was very similar after 90 minutes at any given temperature.

Arterial Blood Flow

Figure 3 shows arterial blood flow in the brachial, radial and digital arteries calculated from the time average velocity and the arterial diameter, during the time before entering the chamber and the time in the chamber but before hand immersion. Table 4 gives, for

each experiment, the mean blood flow at 90 minutes and compares the blood flow at this time in the warm and cold experiment against that for the control experiment as described earlier for the time average velocity and diameter changes.

Table 4
Blood Flow after 90 minutes of exposure to moving air, as a percentage of the control exposure value and t-test results

Exposure Temperature	Brachial	Radial	Digital
Flow at 38°C (mls/min)	192.11 ± 23.26	52.89 ± 5.14	11.53 ± 2.15
(as % of 24°C value)	(556.4% p<0.001)	(544.7% p<0.001)	(748.7% p<0.001)
Flow at 24°C (mls/min)	34.53 ± 3.14	9.71 ± 3.29	1.54 ± 0.85
Flow at 12°C (mls/min)	20.15 ± 1.31	4.00 ± 0.68	0.39 ± 0.30
(as % of 24°C value)	(58.4% p=0.002)	(41.2% p=0.068)	(25.3% p=0.240)

Just before exposure to the three different air temperatures the mean baseline flows were the same, for each of the three arteries. In all three arteries the blood flow shows an initial rapid increase in the warm and decrease in the cold followed by only a small subsequent change. The percentage change in the radial and brachial artery time average velocity is very similar in both the warm and cold exposure compared to that during the control exposure.

Arterial Resistance

Table 5 gives, for each experiment, the calculated arterial resistance at 90 minutes and the comparison between the resistance at the end of the warm and cold experiment against that for the control experiment.

Table 5
Arterial resistance after 90 minutes of exposure to moving air, as a percentage of the control exposure value and t-test results

Exposure Temperature	Brachial	Radial	Digital
Resistance at 38°C (dyn sec/cm^5) (as % of 24°C value)	41.64 ± 6.94 (55.5% p=0.014)	342.54 ± 32.89 (42.1% p=0.001)	3843.5 ± 1029.5 (40.8% p=0.007)
Resistance at 24°C (dyn sec/cm^5)	75.03 ± 8.86	812.96 ± 100.97	9428.8 ± 1824.9
Resistance at 12°C (dyn sec/cm^5) (as % of 24°C value)	119.09 ± 11.43 (158.7% p=0.003)	3393.01 ± 535.92 (417.4% p<0.001)	no data

The digital artery resistance during the cold exposure cannot be calculated since the blood temperature and hence viscosity are not known under these conditions . There was no significant difference in arterial resistance for any of the three arteries at 0 minutes in any of the experiments. The arterial resistance in all arteries shows an increase at the end of 90 minutes in the cold compared to the control and an decrease in the warm, the percentage changes being larger in the radial artery than the brachial artery with the change, in the warm, in the digital artery being similar to that in the radial artery.

Calculated Arterial Pressure Gradient

Table 6 gives, for each experiment, the calculated arterial pressure gradient at 90 minutes and compares the pressure gradient at the end of the warm and cold experiments against that for the control experiment.

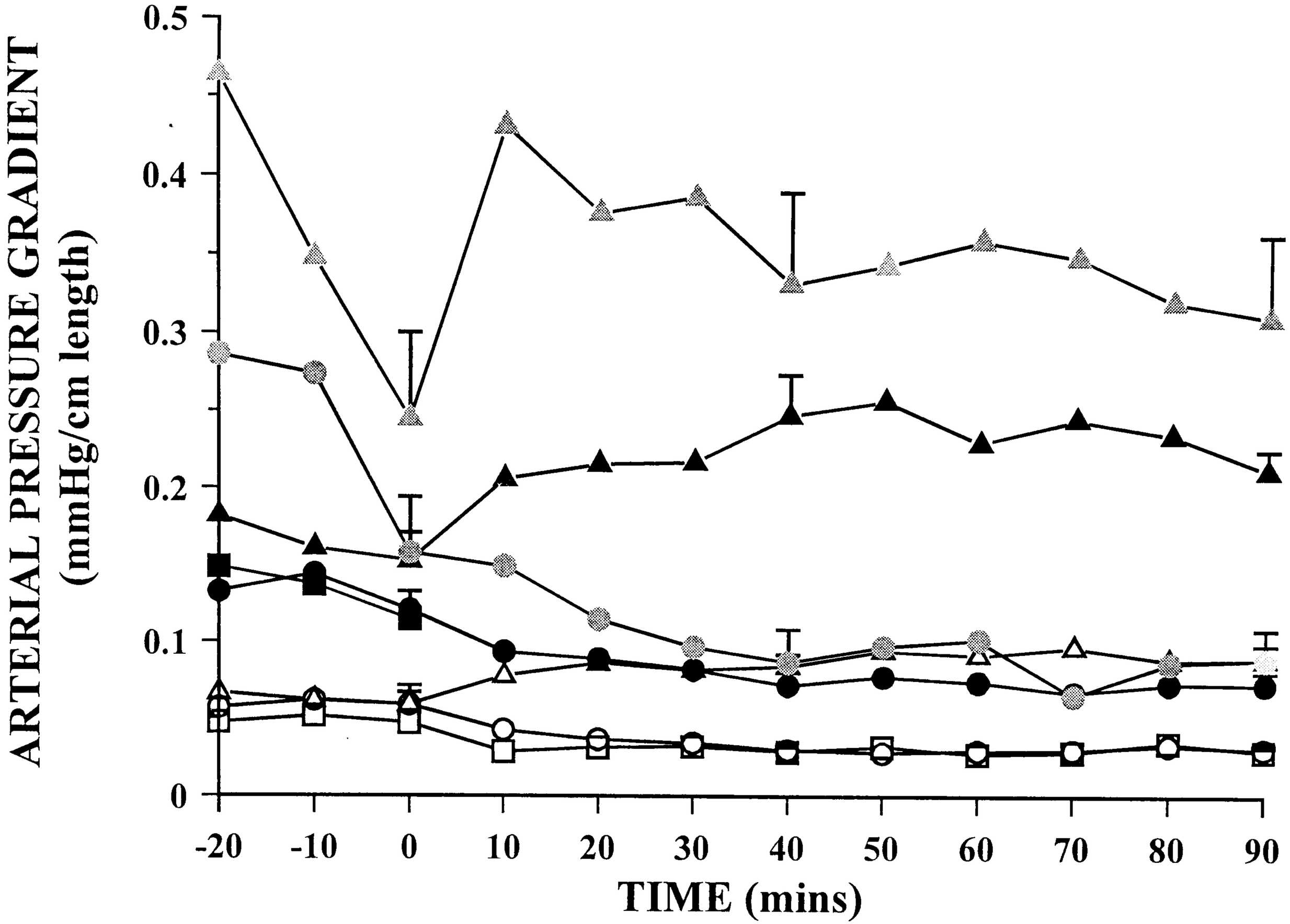

Figure 4 Effect of air temperature on the calculated arterial pressure gradient
△ ○ □ *brachial pressure gradient at 38°C, 24°C and 12°C respectively*
▲ ● ■ *radial pressure gradient at 38°C, 24°C and 12°C respectively*
◍ ◭ *digital pressure gradient at 38°C and 24°C respectively*
Values are means with standard error of means at 0, 40 and 90 minutes

Table 6
Calculated arterial pressure gradient after 90 minutes of exposure to moving air, as a percentage of the control exposure value and t-test results

Exposure Temperature	Brachial	Radial	Digital
Pressure gradient at 38°C (mmHg/cm) (as % of 24°C value)	0.0887 ± 0.0097 (288.8% p<0.001)	0.2112 ± 0.0135 (290.7% p<0.001)	0.3049 ± 0.0521 (348.5% p=0.002)
Pressure gradient at 24°C (mmHg/cm)	0.0308 ± 0.0029	0.0727 ± 0.0078	0.0890 ± 0.0195
Pressure gradient at 12°C (mmHg/cm) (as % of 24°C value)	0.0293 ± 0.0027 (95.1% p=0.624)	0.1313 ± 0.0115 (180.6% p=0.001)	no data

The calculated pressure gradient in the brachial, radial and digital artery is shown in Figure 4. There was no significant difference in calculated arterial pressure gradients for any of the three arteries at 0 minutes in any of the experiments. The calculated arterial pressure gradient in all three arteries increased about three fold in the warm compared to that during the control, the greatest increase being in the digital, radial and brachial arteries. There was no significant difference in the brachial artery pressure gradient after 90 minutes of cold exposure compared to after the same time in the control exposure. The radial artery pressure gradient was higher after 90 minutes exposure to cold air than after the same time in the control environment but the increase was about half of that seen after this period in the warm. Again no data is calculated in the cold for the digital artery due to the unknown blood temperature.

Calculated Arterial Pressure Drop

Calculated arterial pressure drop is the average of the calculated pressure gradient at the

brachial and radial site of measurement multiplied by the distance between the two sites. The calculated pressure drops for each subject and the means at the end of 90 minutes exposure to warm, control and cold air are shown in Table 7.

Table 7
Calculated pressure drop between brachial and radial sites of measurement for each subject

Subject	Distance between Brachial and Radial Site (cm)	After 90 minutes exposure to air at 38°C (mmHg)	After 90 minutes exposure to air at 24°C (mmHg)	After 90 minutes exposure to air at 12°C (mmHg)
AC	26.5	3.79	1.57	2.06
CD	25.3	4.40	2.19	2.03
CJ	25.0	5.20	1.27	2.88
DA	25.0	4.63	1.13	2.13
DD	24.5	3.08	1.47	2.29
EJ	25.0	3.25	1.17	1.18
JT	24.6	3.50	1.16	2.69
LW	25.1	3.41	1.48	1.50
MC	24.9	4.33	0.97	2.45
RB	26.0	3.70	1.23	1.50
RP	25.2	3.91	1.57	2.00
RR	25.0	2.20	0.44	1.49
Average	**25.2**	**3.78 ± 0.23**	**1.30 ± 0.12**	**2.02 ± 0.15**

The estimated pressure drop between the brachial and radial sites of measurement after 90 minutes of exposure to air at 38°C, 24°C and 12°C was 3.78 ± 0.23 mmHg (range 2.20-5.15 mmHg), 1.30 ± 0.12mmHg (range 0.44-2.19 mmHg) and 2.02 ± 0.15 mmHg (range 1.18-2.88 mmHg) respectively.

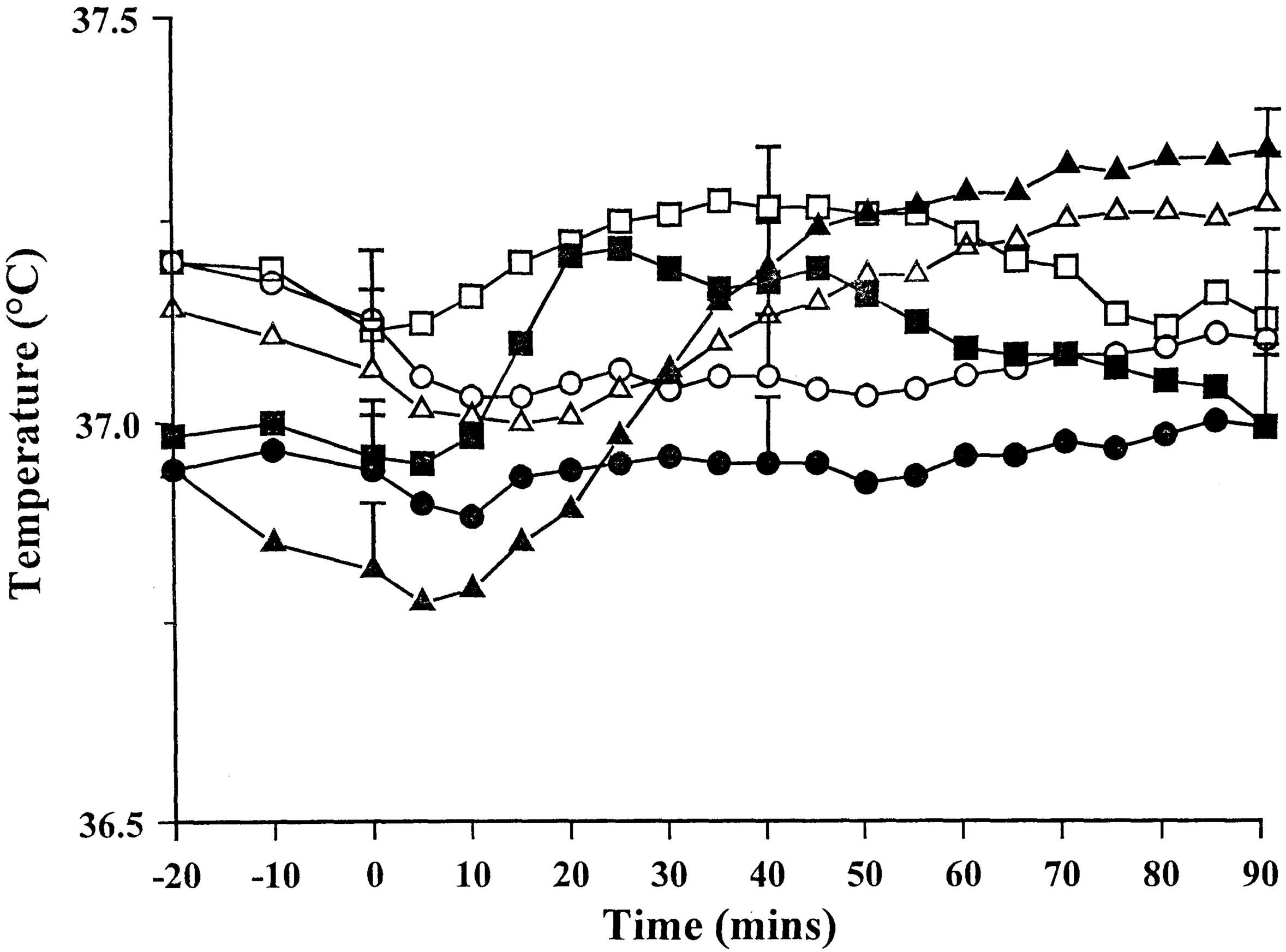

Figure 5 Effect of air temperature on aural and rectal temperature
▲ ● ■ *Aural temperature at 38°C, 24°C and 12°C respectively*
△ ○ □ *Rectal temperature at 38°C, 24°C and 12°C respectively*
Values are means with standard error of means

Core Temperature

The average aural and rectal temperature during the period before entering the chamber and during the first 90 minutes of exposure are shown in Figure 5. The rectal and aural temperatures after 90 minutes exposure are shown in table 8; also given are the p values for the t-test between the core temperature measured at the end of the warm and cold exposure compared to that at the end of the control exposure and for the t-test between the core temperature just prior to entering the chamber compared to that after 90 minutes exposure to a particular temperature.

Table 8
Core temperature after 90 minutes of exposure to moving air, with t-test results for comparison with control value at 90 minutes and for comparison with value at time 0

Exposure Temperature °C	Rectal Temperature °C	Aural Temperature °C
38°C (compared with control) (compared with time 0)	37.27 ± 0.06 (p=0.145) (p=0.005)	37.33 ± 0.05 (0.002) (p<0.001)
24°C (compared with time 0)	37.10 ± 0.08 (p=0.614)	36.99 ± 0.09 (p=0.432)
12°C (compared with control) (difference with time 0)	37.13 ± 0.11 (p=0.858) (p=0.917)	36.99 ± 0.10 (p=1.000) (p=0.702)

There was no significant difference in aural or rectal temperature at 0 minutes in any of the experiments at time 0. The changes in aural temperature occur slightly sooner and are larger in magnitude than those in rectal temperature otherwise both core temperatures follow the same general pattern. In the warm there is a slight initial fall in temperature on entering the chamber followed by a fairly rapid rise which then tends towards a

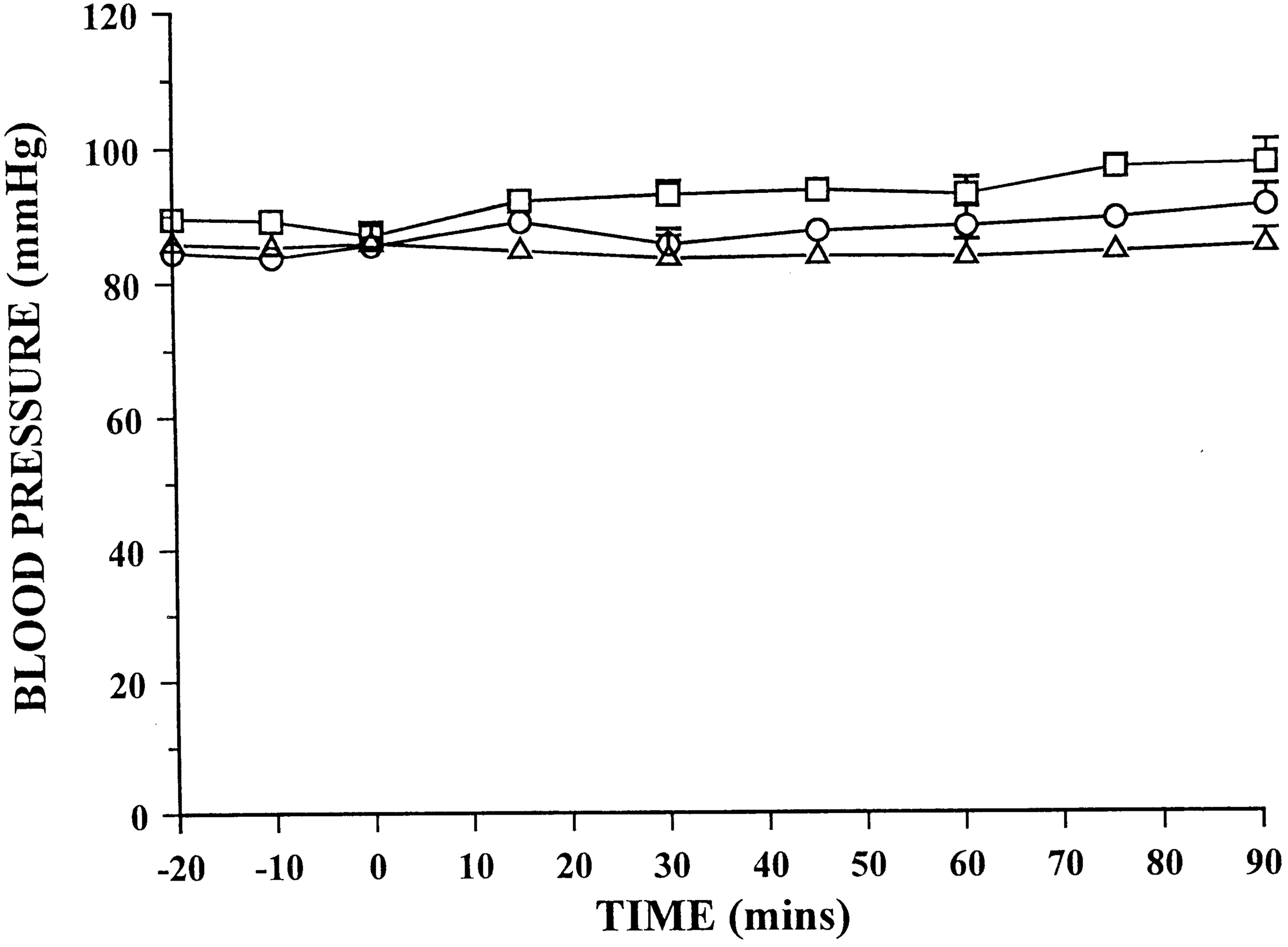

Figure 6 Effect of air temperature on the mean arterial blood pressure measured by an Oscillometric Technique
△ ○ □ blood pressure at 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 0, 30, 60 and 90 minutes

plateau. The control temperature does not produces very little change in either core temperature measurement. The cold exposure produces a rise in temperature for the first 20 to 30 minutes this is followed by a gradual fall tending towards a stable value. After 90 minutes exposure to warm air the rectal and aural temperature were significantly higher than just before entering the chamber, additionally the aural temperature was significantly higher than the aural temperature after 90 minutes exposure to the control air temperature. There were no other significant differences in aural or rectal temperature comparing between the 90 minute reading for the different temperature exposures or between the 90 minute values and the 0 minute values at any given temperature.

Arterial Pressure Measured by Oscillometric Technique

The arterial blood pressure measured in the dominant arm by an oscillometric technique (Dinamap) is shown in Figure 6. Table 9 gives the mean arterial pressure and the t-test result for the comparison between the 90 minute measurement in the cold and warm compared against the control.

Table 9
Mean Arterial Blood Pressure Measured by an Oscillometric Technique after 90 minutes exposure to moving air at different temperatures with t-test result for comparison with control value at 90 minutes

Exposure Temperature °C	Mean Blood Pressure (mmHg)
38°C (comparison with control)	85.0 ± 2.4 (p=0.004)
24°C	91.0 ± 3.0
12°C (comparison with control)	97.3 ± 3.4 (p=0.159)

The mean arterial blood pressure in the cold tended to go up slightly although, after 90

minutes it did not differ significantly from that measured after 90 minutes at the control temperature. In the warm the mean blood pressure went down slightly and was significantly lower than that at the same time in the control exposure.

Conclusion

Brachial, radial and digital arteries became more constricted and the blood time average velocity lower the colder the environment. The more distal the artery the greater the percentage change in diameter. The calculated pressure gradients in all these arteries were very small, being least in the brachial artery and progressively greater in the radial and digital artery. The calculated pressure drop from the brachial to radial site was small in all subjects ranging from 0.44 to 5.15 mmHg at 90 minutes including all subjects and all exposures, the average pressure drop at 90 minutes was greatest in the warm exposure and least in the control with the cold being intermediate.

EFFECTS OF 120 MINUTES EXPOSURE TO AIR AT 38°C, 24°C AND 12°C AND 30 MINUTES HAND IMMERSION IN ICE WATER ON FOREARM ARTERY PARAMETERS DERIVED FROM ULTRASOUND MEASUREMENTS AND ON MEAN ARTERIAL PRESSURE, CORE TEMPERATURE AND HAND HEAT FLOW

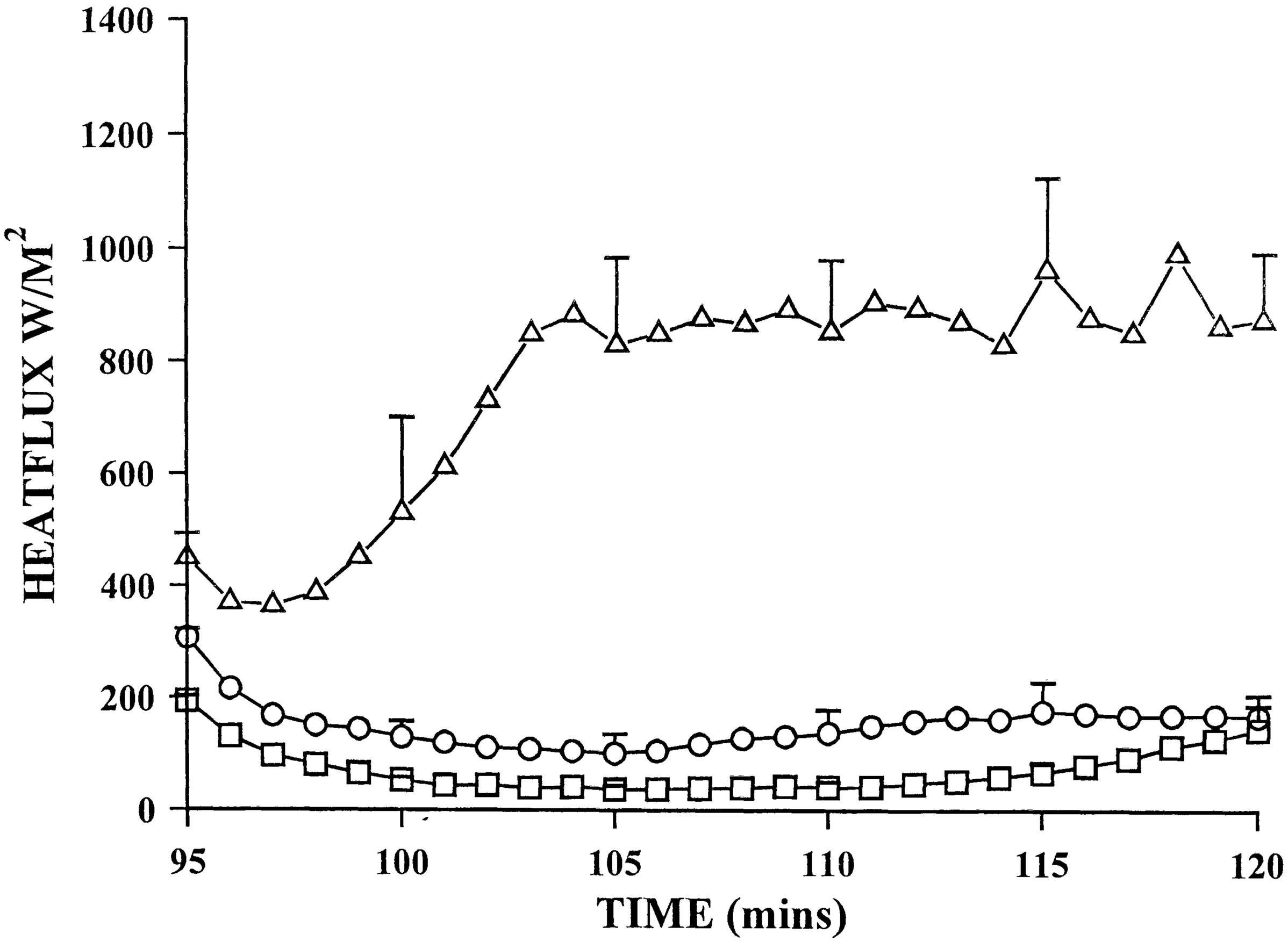

Figure 7 Effect of air temperature on hand heatflux during hand immersion in ice water
△ ○ □ heat flux at 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 5 minute intervals

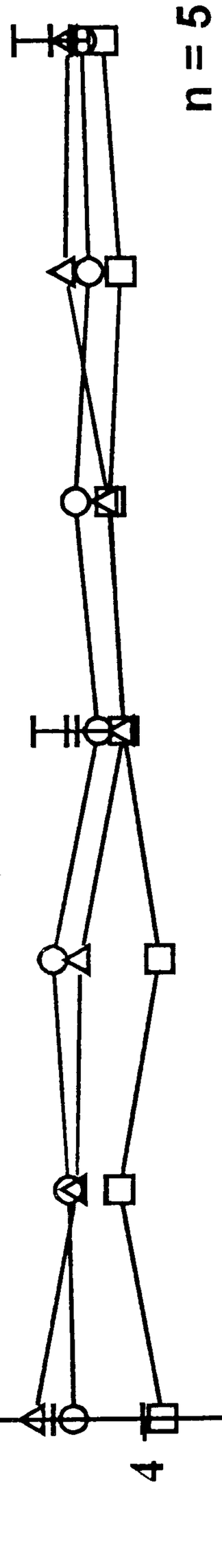

Figure 8 Effect of air temperature on the internal brachial artery diameter during hand immersion in ice water
△ ○ □ diameter at air temperature of 38°C, 24°C and 12°C respectively
Values are means for 5 subjects with standard error of means at 90, 105 and 120 minutes

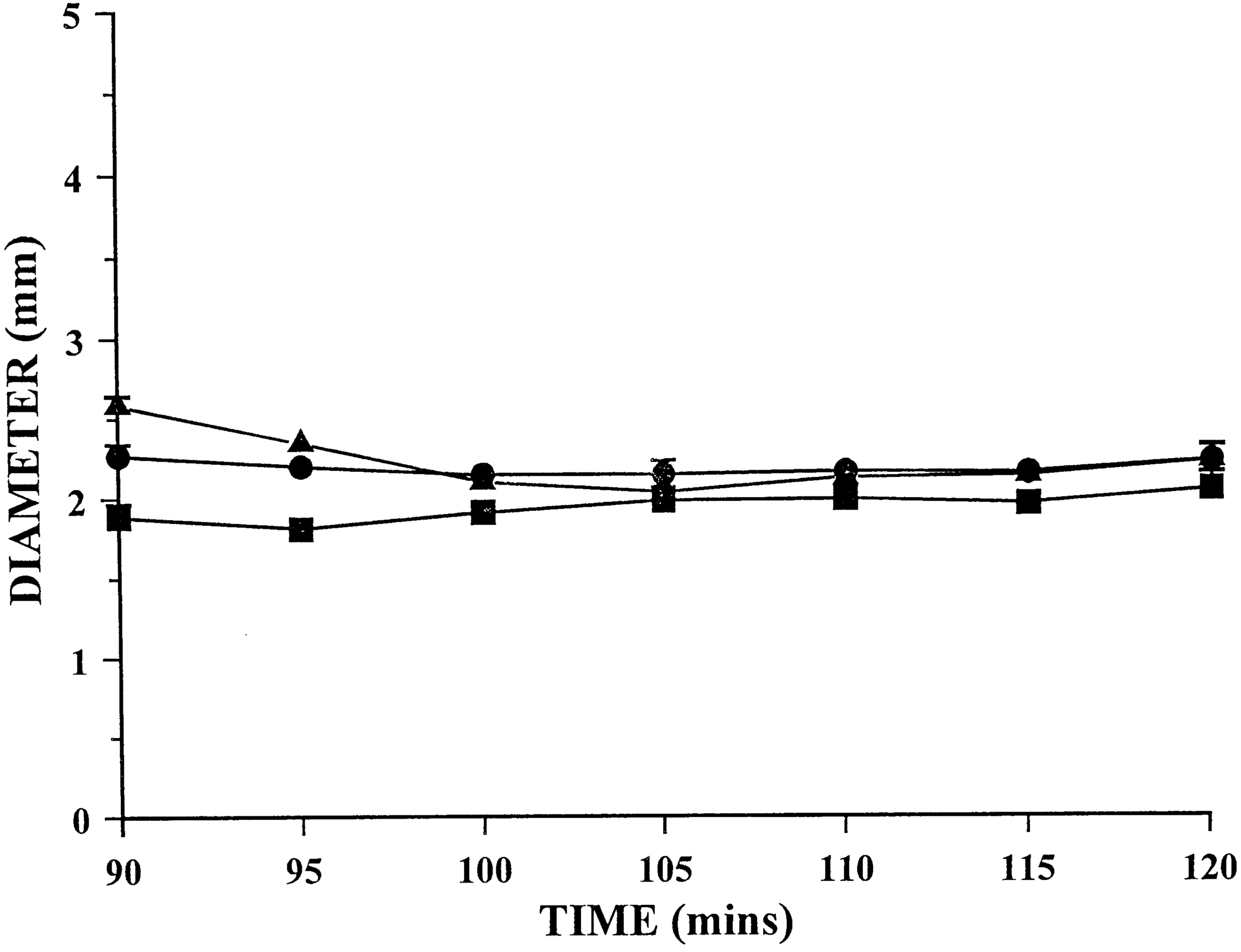

Figure 9 Effect of air temperature on the radial artery internal diameter during hand immersion in ice water
▲ ● ■ diameter at air temperature of 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 90, 105 and 120 minutes

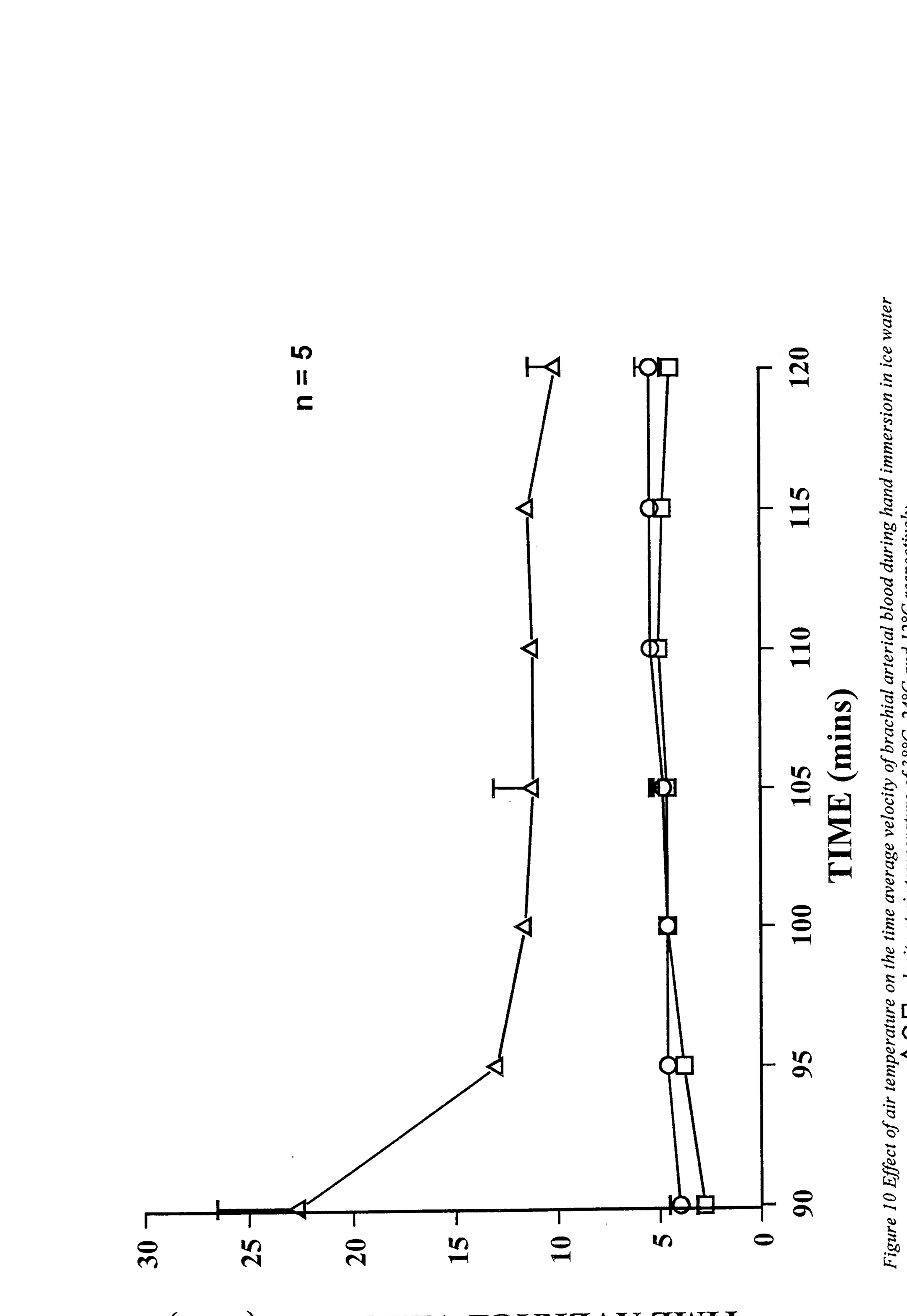

Figure 10 Effect of air temperature on the time average velocity of brachial arterial blood during hand immersion in ice water
△ ○ □ velocity at air temperature of 38°C, 24°C and 12°C respectively
Values are means for 5 subjects with standard error of means at 90, 105 and 120 minutes

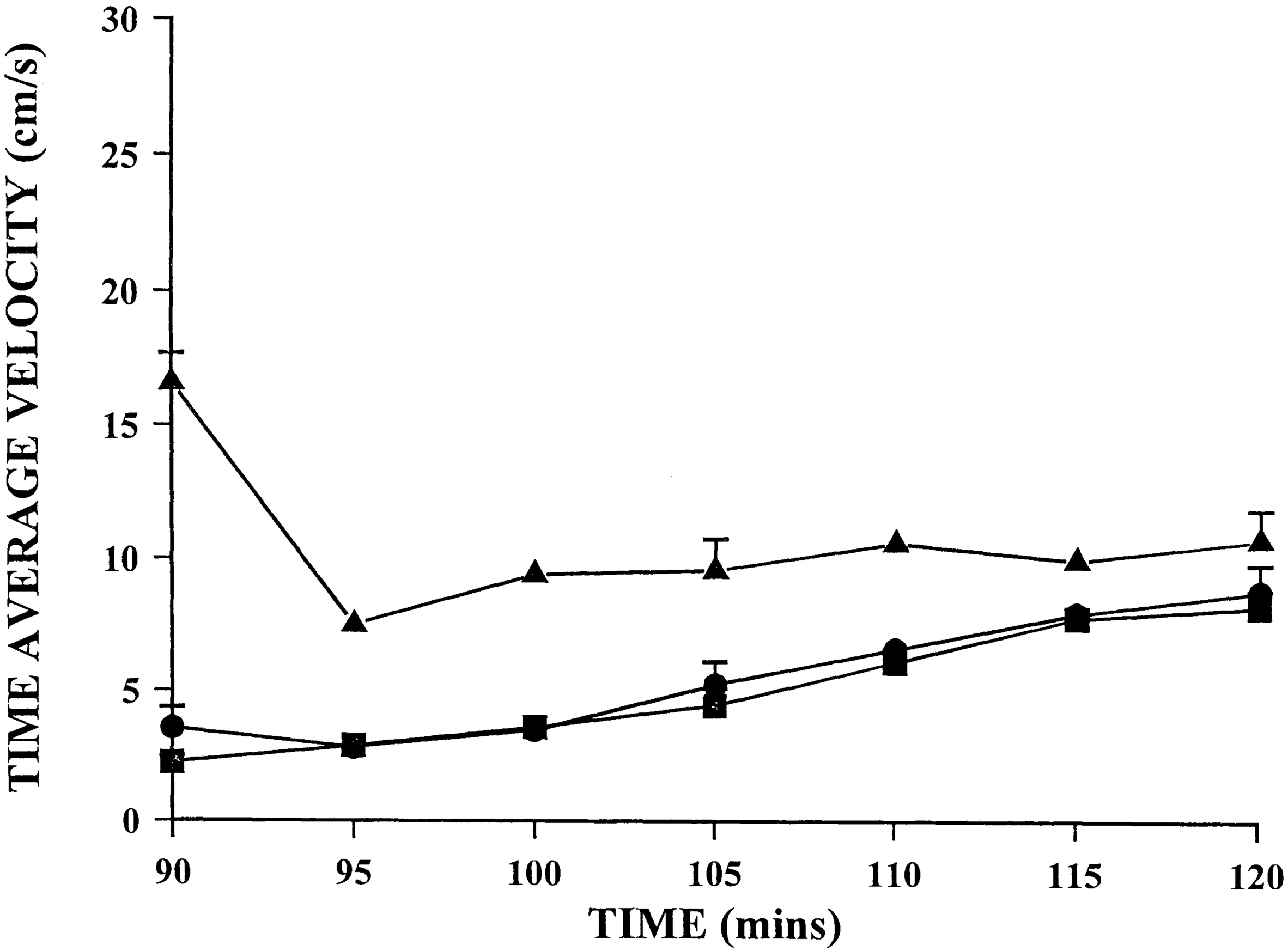

Figure 11 Effect of air temperature on the time average velocity of radial artery blood during hand immersion in ice water
▲ ● ■ velocity at air temperature of 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 90, 105 and 120 minutes

Results

These results refer to the last thirty minutes of exposure to moving air at 38°C, 24°C or 12°C during which the subjects also immersed their non dominant hand in a mixture of stirred ice and water. The average water temperature was measured as 0.21 ± 0.14°C.

Average Hand Heat Flow

The average heat flow from the hand and fingers after the initial five minutes of hand immersion is shown in Figure 7. In the warm exposure heat flow goes up rapidly after less than 10 minutes of hand immersion. In the control exposure heat flow starts to increase but only gradually compared to the warm exposure after about 15 minutes immersion. The heat flow in the cold exposure does not start to rise until about 20 to 25 minutes after the start of the hand immersion.

Arterial Diameters and Arterial Blood Time Average Velocity

Figures 8 and 9 show the mean arterial diameter and Figures 10 and 11 show the mean time average velocity of the arterial blood in the brachial and radial arteries respectively during the last half hour of each experiment, the 90 minute data point is just prior to hand immersion and the subsequent points are during hand immersion in a stirred mixture of ice and water. Table 10 gives the brachial and radial artery diameters at 120 minutes and the arterial diameters in the warm and cold environments expressed as a percentage of the value in the control environment. Table 10 also gives the diameter of the arteries at the end of hand immersion at all three temperatures as a percentage of the value just before hand immersion.

Table 10
Arterial diameters after 120 minutes of exposure to moving air in conjunction with 30 minutes of hand immersion in ice water, as a percentage of the control exposure value and as a percentage of the value just prior to hand immersion with t-test result

Exposure Temperature	Brachial (n = 5)	Radial
Diameter at 38°C (mm) (as % of 24°C value) (as % of 90 minute value)	4.32 ± 0.26 (101.6% p=0.663) (95.4% p=0.399)	2.22 ± 0.09 (100.0% p=0.978) (86.0% p=0.002)
Diameter at 24°C (mm) (as % of 90 minute value)	4.25 ± 0.15 (97.7% p=0.486)	2.22 ± 0.09 (97.8% p=0.576)
Diameter at 12°C (mm) (as % of 24°C value) (as % of 90 minute value)	4.15 ± 0.15 (97.6% p=0.469) (106.1% p=0.067)	2.05 ± 0.10 (92.3% p=0.059) (108.5% p=0.142)

At the end of the period of hand immersion whilst the subjects were exposed to air at 38°C and 12°C the brachial and radial artery diameters were not significantly different from the diameters recorded at the same stage of the control experiment. The radial diameter at the end of the 38°C exposure was slightly more constricted compared to the diameter just prior to hand immersion, otherwise there was no significant difference in diameters at the end of the period of hand immersion compared to just before hand immersion at any air temperature.

Table 11 shows the time average velocity of the arterial blood during the period of hand immersion with the same comparisons as were made for diameter.

Table 11
Blood velocity (TAV) after 120 minutes of exposure to moving air in conjunction with 30 minutes of hand immersion in ice water, as a percentage of the control exposure value and as a percentage of the value just prior to hand immersion with t-test result

Exposure Temperature	Brachial (n = 5)	Radial
Velocity at 38°C (cm/s) (as % of 24°C value) (as % of 90 minute value)	10.00 ± 1.30 (185.2% p=0.017) (44.3% p=0.028)	10.67 ± 1.13 (121.9% p=0.034) (64.4% p<0.001)
Velocity at 24°C (cm/s) (as % of 90 minute value)	5.40 ± 0.68 (135.0% p=0.005)	8.75 ± 1.02 (244.4% p=0.002)
Velocity at 12°C (cm/s) (as % of 24°C value) (as % of 90 minute value)	4.40 ± 0.51 (81.5% p=0.142) (157.1% p=0.078)	8.17 ± 0.61 (93.4% p=0.659) (363.1% p<0.001)

At the end of hand immersion in the warm environment the time average velocity of the blood in the brachial and radial artery was greater than at that time in the control exposure, the difference being greater in the brachial than the radial artery. There was no significant difference in either artery between the average values at the end of the hand immersion in the control environment compared to those measured at that time in the cold environment. After 30 minutes of hand immersion in the warm environment the time average velocity of the blood in both arteries was less than that recorded at 90 minutes in the same experiment. At the end of the period of hand immersion in the control environment the arterial blood time average velocity in the brachial and radial artery was higher than just before hand immersion the increase being much greater in the radial than the brachial artery. In the cold environment the radial artery time average velocity increased considerably by the end of the 30 minute hand immersion compared to just before the immersion but the brachial artery velocity did not show a significant change.

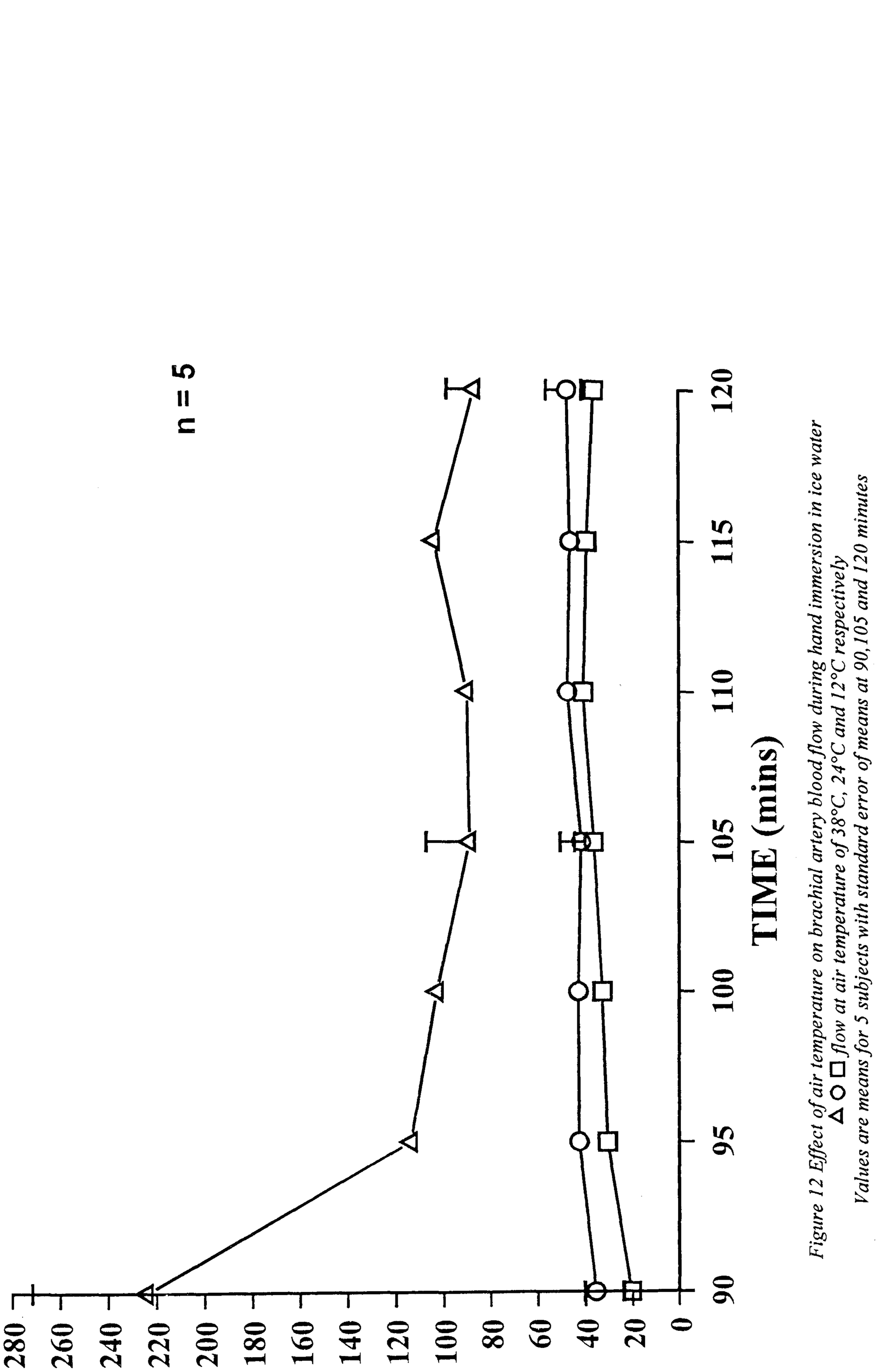

Figure 12 Effect of air temperature on brachial artery blood flow during hand immersion in ice water
△ ○ □ flow at air temperature of 38°C, 24°C and 12°C respectively
Values are means for 5 subjects with standard error of means at 90,105 and 120 minutes

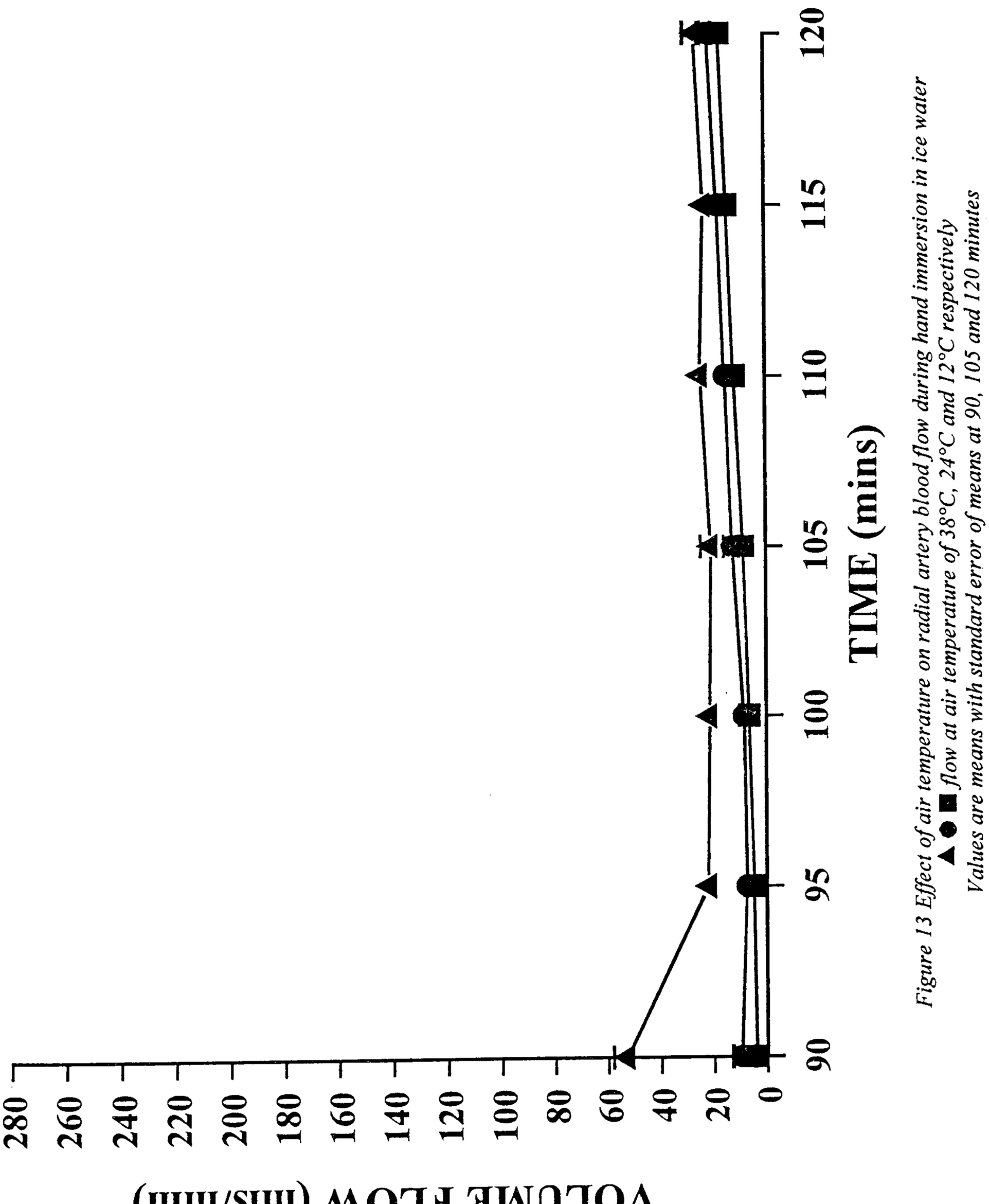

Figure 13 Effect of air temperature on radial artery blood flow during hand immersion in ice water
▲● ■ flow at air temperature of 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 90, 105 and 120 minutes

Arterial Flow

Figures 12 and 13 show the brachial and radial artery blood flows respectively during the period of hand immersion. Table 12 gives the arterial blood flow during the last half hour of each experiment during which time the subjects hand was immersed in ice water.

Table 12
Blood flow after 120 minutes of exposure to moving air in conjunction with 30 minutes of hand immersion in ice water, as a percentage of the control exposure value and as a percentage of the value just prior to hand immersion with t-test result

Exposure Temperature	Brachial (n = 5)	Radial
Flow at 38°C (mls/min) (as % of 24°C value) (as % of 90 minute value)	86.53 ± 11.44 (182.5% p<0.001) (38.6% p=0.020)	26.07 ± 4.09 (122.7% p=0.068) (49.3% p<0.001)
Flow at 24°C (mls/min) (as % of 90 minute value)	47.42 ± 8.81 (133.3% p=0.054)	21.25 ± 3.22 (218.8% p=0.003)
Flow at 12°C (mls/min) (as % of 24°C value) (as % of 90 minute value)	36.24 ± 5.05 (76.4% p=0.184) (177.4% p=0.028)	17.00 ± 2.44 (80.0% p=0.222) (425.0% p<0.001)

At the end of the period of hand immersion there was no significant difference between radial artery flow at any air temperature. The brachial artery flow at the end of the immersion phase of the warm experiment was significantly greater than at the corresponding time in the control experiment but there was no significant difference between the arterial flow in the cold and the control at this time. The brachial and radial artery flow decreased significantly by the end of hand immersion while the subject was in the warm air compared to just before hand immersion in the same environment. In the control environment the radial artery blood flow increased significantly during hand immersion but the brachial artery flow did not change significantly. In the cold experiment both the brachial and radial artery blood flow increased significantly with a

relatively greater change in the radial artery flow compared to the brachial artery flow.

Arterial Resistance

Table 13 gives the values for the brachial and radial resistances at the end of the period of hand immersion and shows the results of the comparisons between the control value and the warm and cold value and between the value just before hand immersion and the value at the end of hand immersion.

Table 13
Arterial resistance after 120 minutes of exposure to moving air in conjunction with 30 minutes of hand immersion in ice water, as a percentage of the control exposure value and as a percentage of the value just prior to hand immersion with t-test result

Exposure Temperature	Brachial (n = 5)	Radial
Resistance at 38°C (dyn sec/cm^5) (as % of 24°C value) (as % of 90 minute value)	57.20 ± 13.27 (91.1% p=0.511) (137.5% p=0.290)	774.85 ± 136.95 (102.2% p=0.892) (226.2% p=0.005)
Resistance at 24°C (dyn sec/cm^5) (as % of 90 minute value)	62.76 ± 9.29 (106.3% p=0.557)	758.19 ± 103.83 (93.3% p=0.559)
Resistance at 12°C (dyn sec/cm^5) (as % of 24°C value) (as % of 90 minute value)	71.21 ± 10.23 (113.5% p=0.419) (75.1% p<0.001)	1707.23 ± 295.66 (225.2% p=0.005) (50.3% p=0.014)

After 30 minutes of hand immersion in ice water with the subject exposed to air at 12°C and 38°C the brachial and radial artery resistance did not differ from that calculated at the same time in the control exposure with the exception of the radial artery in the 12°C exposure which had a significantly increased resistance at the end of hand immersion compared to at the end of hand immersion in the control experiment. In the cold

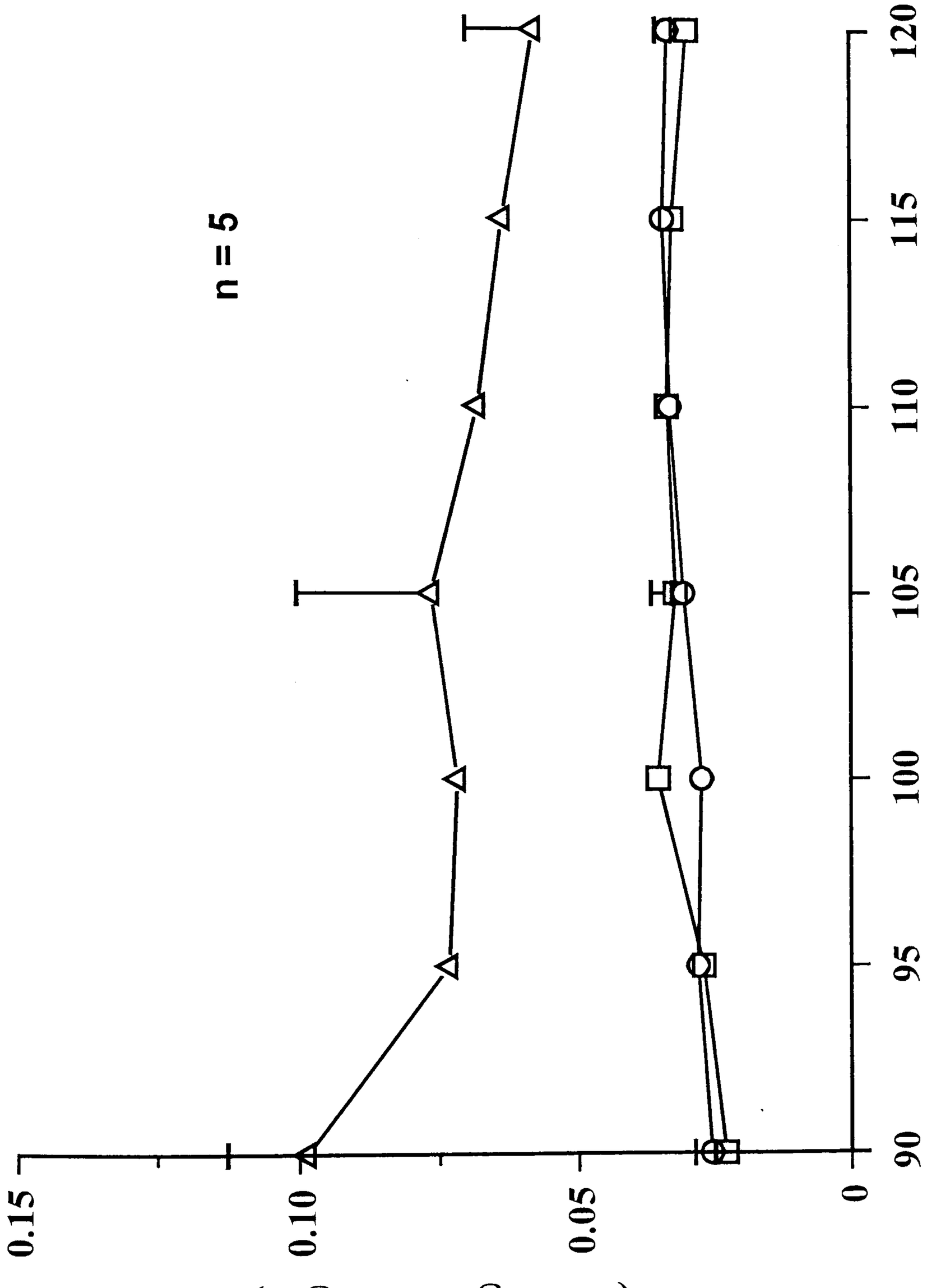

Figure 14 Effect of air temperature and hand immersion in ice water on the calculated brachial artery pressure gradient
△○□ pressure gradient at 38°C, 24°C and 12°C respectively
Values are means with standard error of means for five subjects at 90, 105 and 120 minutes

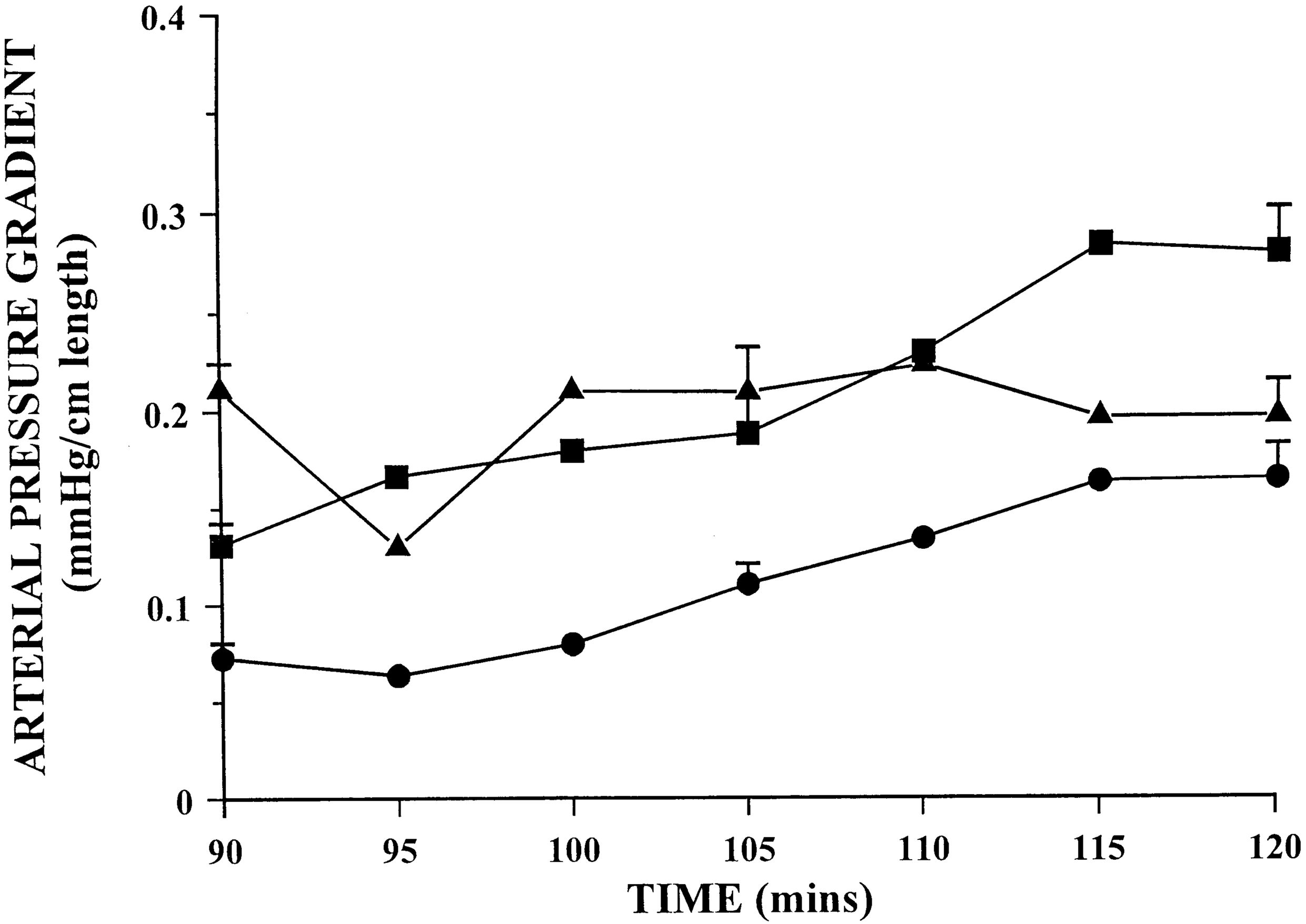

Figure 15 Effect of air temperature and hand immersion in ice water on the radial artery calculated pressure gradient
▲ ● ■ pressure gradient at 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 90, 105 and 120 minutes

environment hand immersion caused the brachial and radial artery resistance to decrease significantly the decrease being greatest in the radial artery. Hand immersion when subjects were exposed to air at 24°C and 38°C only produced an increase in radial artery resistance during the 38°C exposure; otherwise there was no change.

Calculated Arterial Pressure Gradient

Table 14 gives the brachial and radial calculated pressure gradients at the end of the period of hand immersion in each of the different environments with comparisons between the control and other air temperatures and between the pressure gradient at the end of hand immersion against that calculated just prior to hand immersion at each of the different environmental air temperatures. Figures 14 and 15 show the calculated pressure drop for the brachial and radial artery respectively during the period of hand immersion.

Table 14
Calculated arterial pressure gradient after 120 minutes of exposure to moving air in conjunction with 30 minutes of hand immersion in ice water, as a percentage of the control exposure value and as a percentage of the value just prior to hand immersion with t-test result

Exposure Temperature	Brachial (n = 5)	Radial
Pressure gradient at 38°C (mmHg/cm) (as % of 24°C value) (as % of 90 minute value)	0.0581 ± 0.0120 (172.8% p=0.095) (58.9% p=0.105)	0.01973 ± 0.0186 (119.3% p=0.168) (93.4% p=0.480)
Pressure gradient at 24°C (mmHg/cm) (as % of 90 minute value)	0.0337 ± 0.0022 (131.1% p=0.012)	0.1654 ± 0.0178 (227.6% p=0.001)
Pressure gradient at 12°C (mmHg/cm) (as % of 24°C value) (as % of 90 minute value)	0.0301 ± 0.0028 (89.4% p=0.129) (130.4% p=0.205)	0.2801 ± 0.0222 (169.4% p=0.001) (213.4% p<0.001)

The pressure drop per centimetre length of radial artery was significantly greater after hand immersion only in the 12°C exposure compared to after hand immersion in the control exposure, other than this there was no significant difference in the calculated arterial pressure gradient in either the brachial or radial artery, comparing between values calculated after the control exposure and hand immersion, and those calculated at the other temperatures after hand immersion. When the subjects were exposed to air at 24°C hand immersion produced a increase in the pressure gradient calculated in the brachial artery; in the cold and warm air temperatures no change in brachial artery pressure gradient occurred comparing the value just prior to immersion to that calculated at the end of hand immersion. The pressure gradient in the radial artery increased significantly during the period of hand immersion in both the control and cold air temperatures but not in the warm. The increase in the radial artery pressure gradient in the control exposure during hand immersion was greater than that which occurred in the brachial artery during the same time.

Calculated Arterial Pressure Drop

Calculated arterial pressure drop is the average of the calculated pressure gradient at the brachial and radial site of measurement multiplied by the distance between the two sites. The calculated pressure drops for each subject and the means at the end of 120 minutes exposure to warm, control and cold air during the last 30 minutes of which the subjects non-dominant hand was immersed in ice water are shown in Table 15. It was only possible to calculate pressure drop for five subjects since there was no brachial artery data for the other subjects during the hand immersion phase of the study.

Table 15

Calculated pressure drop between brachial and radial sites of measurement for each subject after 30 minutes of hand immersion in ice cold water at the end of the period of exposure

Subject	Distance between Brachial and Radial Site (cm)	After 120 minutes exposure to air at 38°C (mmHg)	After 120 minutes exposure to air at 24°C (mmHg)	After 120 minutes exposure to air at 12°C (mmHg)
cd	25.3	2.98	2.08	2.95
dd	24.5	3.20	2.36	4.63
ej	25.0	2.93	1.98	2.53
jt	24.6	3.89	3.42	4.81
mc	24.9	4.26	4.01	2.60
Average	**24.9**	**3.45 ± 0.26**	**2.77 ± 0.40**	***3.51 ± 0.50**

***Significantly higher than value before hand immersion for these subjects shown in Table 7**

The calculated pressure drop between the brachial and radial sites of measurement after 120 minutes of exposure to air at 38°C, 24°C and 12°C during the last 30 minutes of which the subjects non dominant hand was immersed in ice water was 3.45 ± 0.26 mmHg (range 2.93-4.25 mmHg), 2.77 ± 0.40 mmHg (range 1.98-4.01 mmHg) and 3.51 ± 0.50 mmHg (range 2.53-4.81 mmHg) respectively.

Change in blood flow during hand immersion

The change in blood flow during hand immersion is given in Table 16 in terms of the percentage of flow at the end of hand immersion compared to the flow just before hand immersion.

Table 16
Arterial blood flow after 90 minutes exposure to air at 38°C, 24°C and 12°C and percentage change after a further 30 minutes exposure in conjunction with 30 minutes hand immersion in ice water

Subject		Blood Flow (mls/min) (change after hand immersion %)		
		38°C	24°C	12°C
AC	brachial	178.6 (no data)	46.8 (no data)	20.8 (no data)
	radial	45.9 (25%)	6.0 (151%)	3.1 (417%)
CD	brachial	395.6 (32%)	51.5 (155%)	16.1 (305%)
	radial	97.5 (52%)	45.4 (94%)	9.4 (365%)
CJ	brachial	121.2 (no data)	50.7 (no data)	18.1 (no data)
	radial	33.2 (41%)	7.5 (115%)	2.0 (744%)
DA	brachial	135.6 (no data)	37.1 (no data)	21.8 (no data)
	radial	64.2 (33%)	4.2 (600%)	3.1 (484%)
DD	brachial	232.3 (35%)	39.9 (125%)	31.7 (131%)
	radial	68.1 (22%)	4.8 (207%)	2.4 (365%)
EJ	brachial	167.1 (49%)	33.3 (113%)	12.4 (161%)
	radial	43.5 (77%)	7.3 (188%)	1.7 (905%)
JT	brachial	112.0 (52%)	23.8 (119%)	21.9 (184%)
	radial	43.6 (43%)	6.6 (302%)	3.9 (350%)
LW	brachial	167.1 (no data)	21.8 (no data)	17.7 (no data)
	radial	46.6 (80%)	6.0 (522%)	4.7 (547%)
MC	brachial	213.1 (39%)	29.5 (141%)	20.1 (150%)
	radial	60.5 (85%)	8.1 (371%)	4.6 (159%)
RB	brachial	216.6 (no data)	31.7 (no data)	20.8 (no data)
	radial	45.9 (31%)	7.3 (164%)	1.4 (1794%)
RP	brachial	257.6 (no data)	28.9 (no data)	20.5 (no data)
	radial	52.3 (32%)	10.3 (196%)	7.3 (336%)
RR	brachial	108.6 (no data)	19.7 (no data)	20.1 (no data)
	radial	33.5 (88%)	3.1 (1044%)	4.6 (159%)
average	**brachial**	**192.1 ± 23.3 (42 ± 4%)**	**34.5 ± 3.1 (131 ± 8%)**	**20.2 ± 1.3 (186 ± 31%)**
	radial	**52.9 ± 5.1 (51 ± 7%)**	**9.7 ± 3.3 (330 ± 80%)**	**4.0 ± 0.7 (552 ± 129%)**

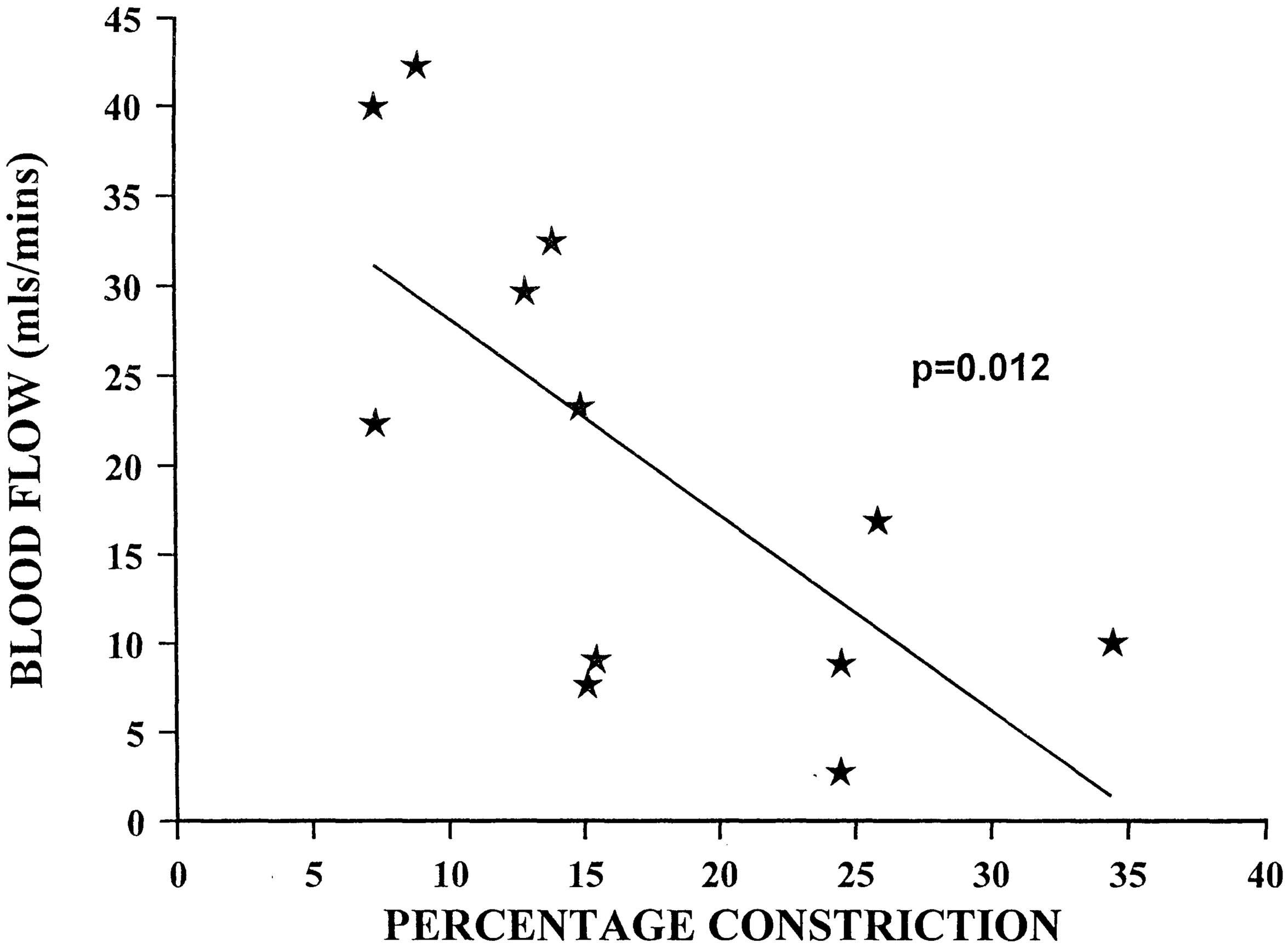

Figure 16 Linear regression of the percentage constriction of the radial artery against radial artery blood flow at the end of 30 minutes of hand immersion in ice water and 120 minutes of exposure to air at 12°C

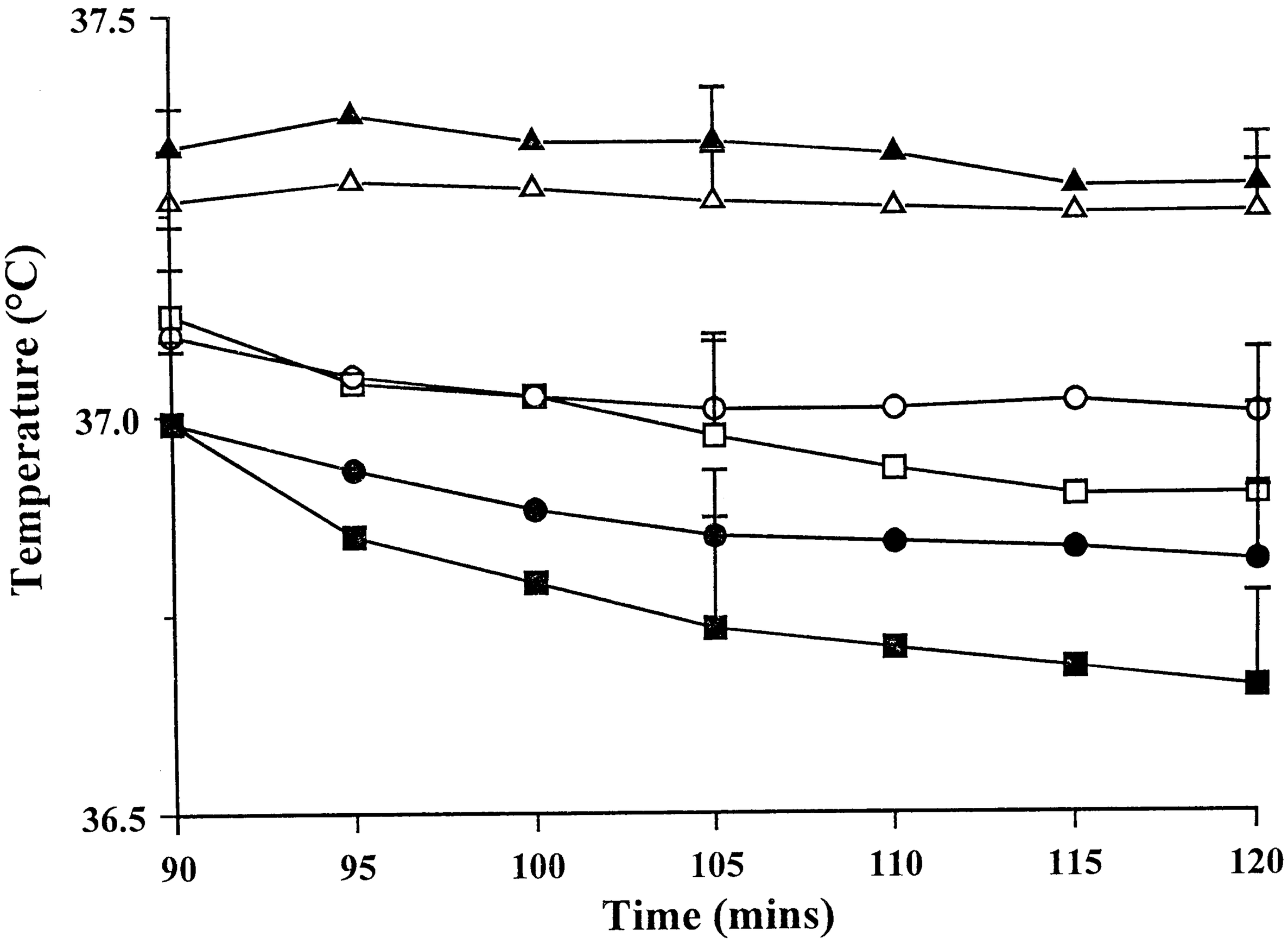

Figure 17 Effect of air temperature and hand immersion in ice water on aural and rectal temperature
▲ ● ■ *Aural temperature at 38°C, 24°C and 12°C respectively*
△ ○ □ *Rectal temperature at 38°C, 24°C and 12°C respectively*
Values are means with standard error of means

During the hand immersion in the cold and control exposures there was an average change in blood flow in the brachial artery of 186 ± 31% (range 131-305%) and 131 ± 8% (range 113-155%) and in the radial artery of 552 ± 129% (range 159-1794%) and 330 ± 80% (range 94-1044%) respectively. In the warm, hand immersion caused a change in blood flow in the brachial and radial artery of 42 ± 4% (range 32-52%) and 51 ± 7% (range 22-88%) respectively.

Relationship between cold induced vasodilatation and arterial constriction

Figure 16 shows the Pearson's linear regression of the percentage constriction of the radial artery at the end of the period of cold induced vasodilatation at the end of the cold exposure compared against the blood flow at this time. The percentage constriction was calculated as the percentage difference between the fully dilated radial artery diameter after 90 minutes in the warm environment compared to the constricted diameter at the time for which the regression was performed. This regression was designed to show if the blood flow in the radial artery was related to the degree of constriction. A negative linear correlation exists the equation for which is:

$$Y = -1.0985X + 39.131$$

Where Y is blood flow in mls/min and X is percentage arterial constriction. The relationship has an R^2 value of 0.4811 and a p value of 0.012.

Body Core Temperature

Rectal and aural temperatures during hand immersion are shown in Figure 17. Table 17

gives the core temperature at the end of period of hand immersion in the three different environments. The table also gives the results of the t-tests for comparisons between the control value and the warm and cold value at 120 minutes and comparisons between the 90 minute and 120 minute value at any given temperature.

Table 17
Core temperature after 120 minutes of exposure to moving air in conjunction with 30 minutes hand immersion in ice water, with t-test results for comparison with control value at 120 minutes and for comparison with value at 90 minutes

Exposure Temperature °C	Rectal Temperature °C	Aural Temperature °C
38°C (compared with control) (compared with time 90)	37.25 ± 0.06 (p=0.013) (p=0.615)	37.28 ± 0.06 (p<0.001) (p=0.293)
24°C (compared with time 90)	37.00 ± 0.08 (p=0.011)	36.82 ± 0.09 (p<0.001)
12°C (compared with control) (compared with time 90)	36.90 ± 0.11 (p=0.499) (p=0.001)	36.66 ± 0.12 (p=0.174) (p<0.001)

Although there is a tendency for both the aural and rectal temperature to fall throughout the period of hand immersion there is no significant difference between the rectal temperature at 120 minutes comparing the control against either the warm or cold exposure and in addition the rectal temperature did not change significantly during the period of hand immersion at any exposure temperature. The aural temperature fell significantly in both the control and cold exposures but not the warm exposure during hand immersion. At the end of hand immersion in the cold air the aural temperature was significantly lower than at the end of hand immersion in the control environment.

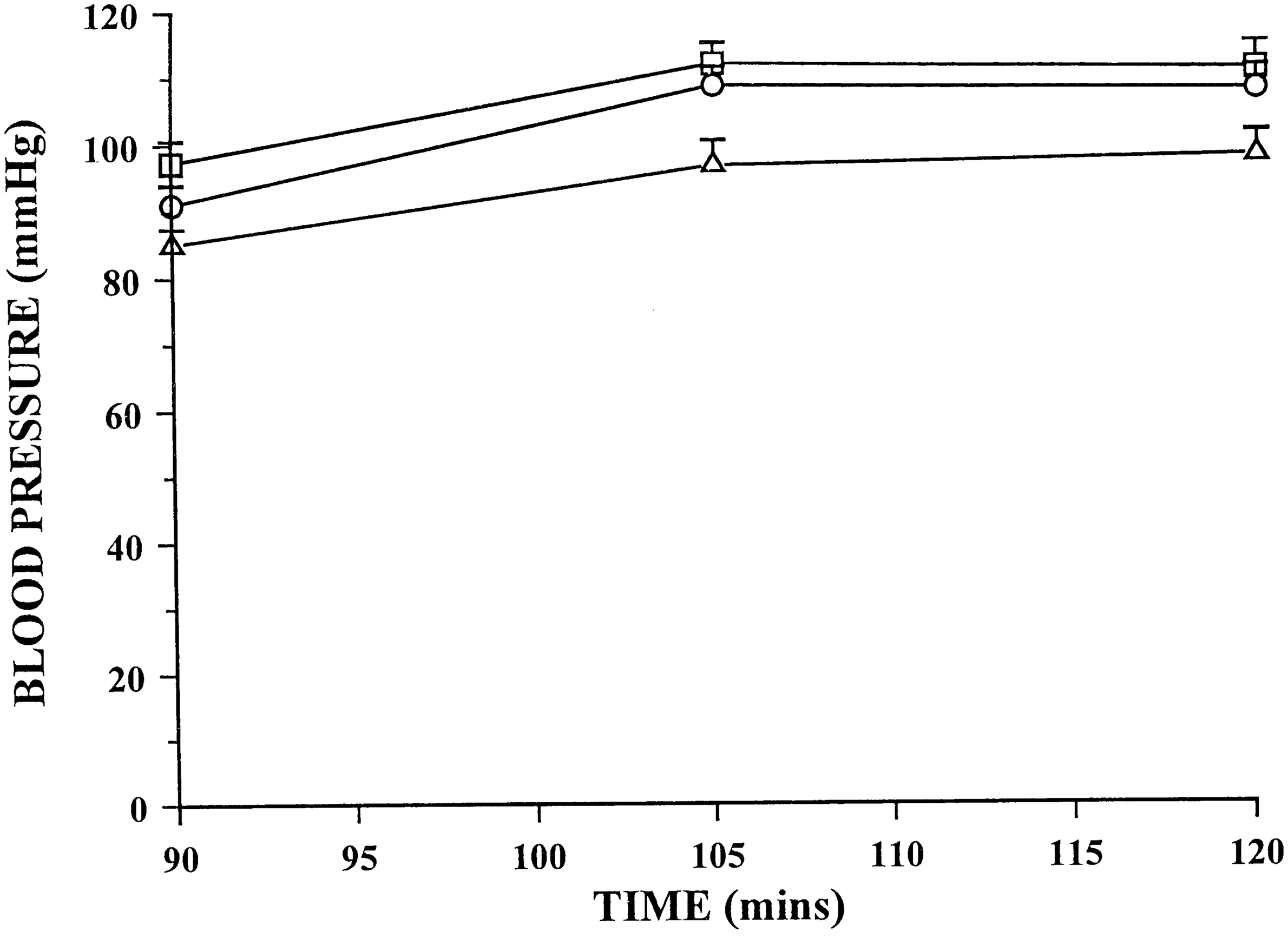

Figure 18 Effect of air temperature and hand immersion on the mean arterial blood pressure measured by an Oscillometric Technique during ultrasound measurements
△ ○ □ blood pressure at 38°C, 24°C and 12°C respectively
Values are means with standard error of means at 90, 105 and 120 minutes

Arterial Pressure Measured by Oscillometric Technique

The arterial blood pressure measured in the dominant arm by an oscillometric technique (Dinamap) is shown in Figure 18. Table 18 gives the mean arterial pressure and the t-test result for the comparison between the 120 minute measurement in the cold and warm compared against the control.

Table 18
Mean Arterial Blood Pressure Measured by an Oscillometric Technique after 120 minutes of exposure to moving air in conjunction with 30 minutes hand immersion in ice water, with t-test result for comparison with control value at 120 minutes

Exposure Temperature °C	Mean Blood Pressure (mmHg)
38°C (comparison with control)	97.83 ± 3.69 (p=0.001)
24°C	107.83 ± 3.55
12°C (comparison with control)	110.94 ± 4.03 (p=0.374)

The mean arterial blood pressure tended to go up slightly during the period of hand immersion during all the exposures, at the end of the period of hand immersion the mean pressure was significantly less in the in the warm than in the control but there was no significant difference between the control and cold values at this time.

Conclusion

The period of hand immersion in the warm exposure caused a significant constriction in the radial artery comparing its diameter at the end of the immersion to that just before immersion; no other significant changes in brachial or radial artery diameters occurred during hand immersion. The time average velocity of the brachial and radial blood was higher at the end of the hand immersion in the warm than at the end of the control

exposure otherwise there was no significant difference at this time between the brachial or radial blood time average velocity at the end of the control exposure compared to the warm or cold exposure. In the warm exposure the time average velocity in both arteries fell during the period of hand immersion, in the control exposure brachial and radial velocity increased and in the cold exposure only radial artery velocity increased.

Blood flow was higher at the end of hand immersion compared to just before hand immersion in the brachial and radial arteries in the cold exposure and in the radial artery in the control exposure. Blood flow fell during hand immersion in the warm exposure in both the brachial and radial artery and remained higher in the brachial artery than at the end of the control exposure.

The pressure gradient in both arteries increased during hand immersion in the control exposure and in the radial artery in the cold exposure the value was higher than at the same point in the control exposure.

The pressure drop at the end of the period of hand immersion including all exposure temperatures and all subjects ranged from 1.84 to 4.24 mmHg, the average in the cold, control and warm exposures being 3.09 ± 0.44 mmHg, 2.57 ± 0.37 mmHg and 3.20 ± 0.25 mmHg.

The change in blood flow produced by immersing the hand in ice water in the warm, control and cold exposures was 42 ± 4% (range 32-52%), 131 ± 8 (117-155%) and 186 ± 31% (range 131-305%) in the brachial artery and 51 ± 7% (range 22-88), 330 ± 80% (range 94-1044%) and 552 ± 129% (range 159-1794%) in the radial artery respectively.

A negative correlation exists between the percentage constriction of the artery and blood flow with a p value of 0.012 using Pearson's linear regression analysis.

The aural temperature was higher at the end of the warm exposure than at the same point in the control exposure and fell significantly during the period of hand immersion in both the cold and control exposures.

Blood pressure was not significantly different at the end of any of the exposures after the hand immersion.

EFFECT OF 120 MINUTES EXPOSURE TO MOVING AIR AT 12°C AND HAND IMMERSION IN STIRRED ICE WATER ON BLOOD PRESSURE MEASURED INDIRECTLY IN THE BRACHIAL, RADIAL AND DIGITAL ARTERIES

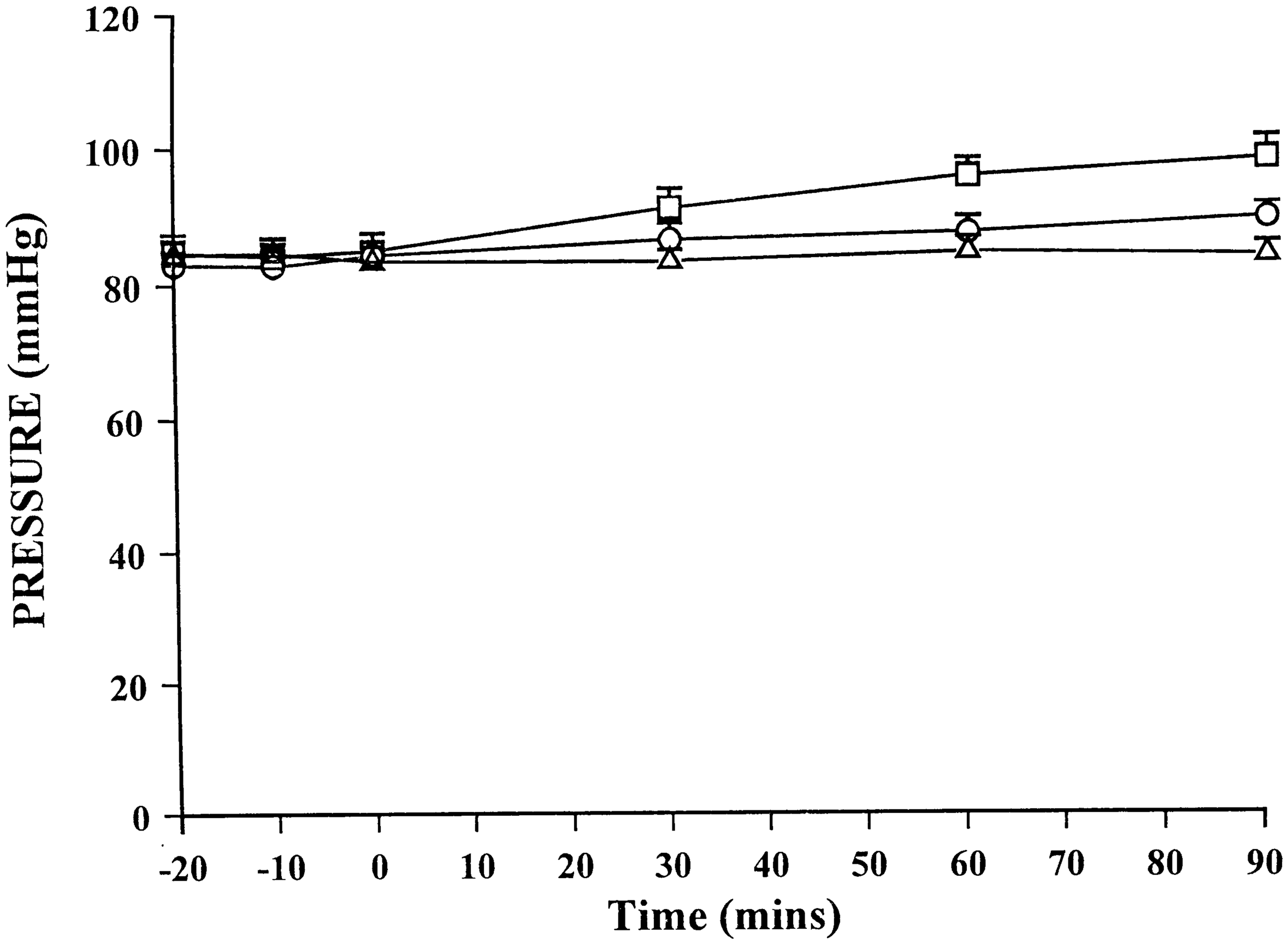

Figure 19 Effect of air temperature on mean brachial artery pressure measured indirectly by auscultation
△ ○ □ Mean pressure at 38°C, 24°C and 12°C respectively
Values are means with standard error of means

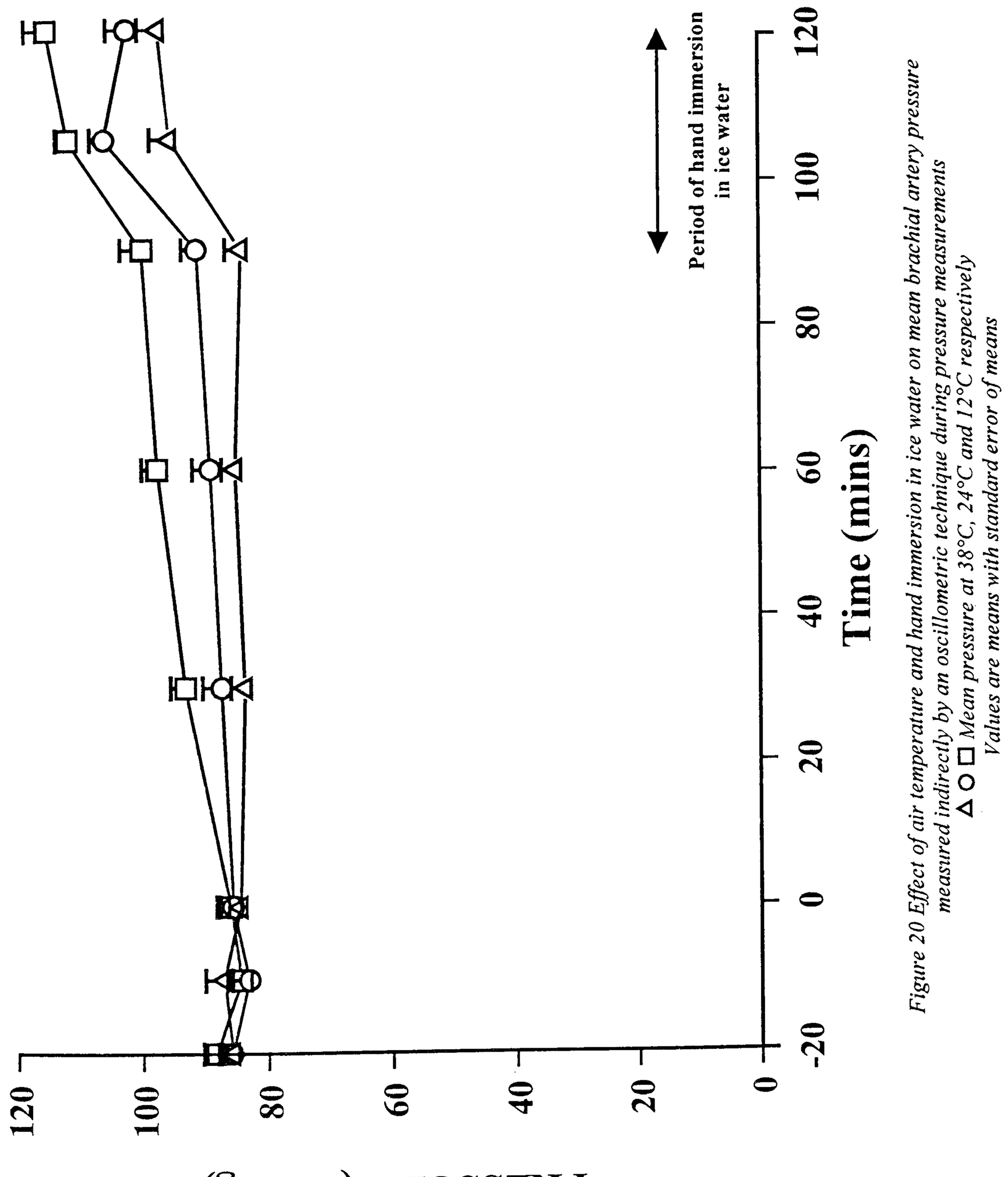

Figure 20 Effect of air temperature and hand immersion in ice water on mean brachial artery pressure measured indirectly by an oscillometric technique during pressure measurements
△ ○ □ Mean pressure at 38°C, 24°C and 12°C respectively
Values are means with standard error of means

Results

These results show the effect of exposure to air at 38°C, 24°C and 12°C for 120 minutes during the last 30 minutes of which the non dominant hand was immersed in a mixture of stirred ice and water on the blood pressure measured in the brachial and radial artery and the digital artery.

The subjects were exposed on each occasion to a nominal air temperatures of 12°C, 24°C and 38°C the actual air temperatures measured were , and; before each exposure the subjects lay supine outside the chamber in the laboratory at a nominal temperature of 24°C which was measured at , and respectively for each exposure. The water temperature for the warm, control and cold exposures was measured at , and respectively.

Brachial Artery Pressure measured by Auscultation

The brachial artery pressure was measured by auscultation in the first 90 minutes in the non dominant arm. The mean pressure measured is displayed in Figure 19.

There was a slight tendency for the mean pressure measured during the cold and control exposure to rise but very little change occurred in the warm exposure.

Brachial Artery Pressure measured by an Oscillometric Technique

Figure 20 shows the mean brachial artery pressure in the dominant arm measured by an oscillometric technique during the three different exposures including the time the hand of the non dominant arm was immersed in ice water.

The pressure during the cold exposure went up slightly compared to that during the

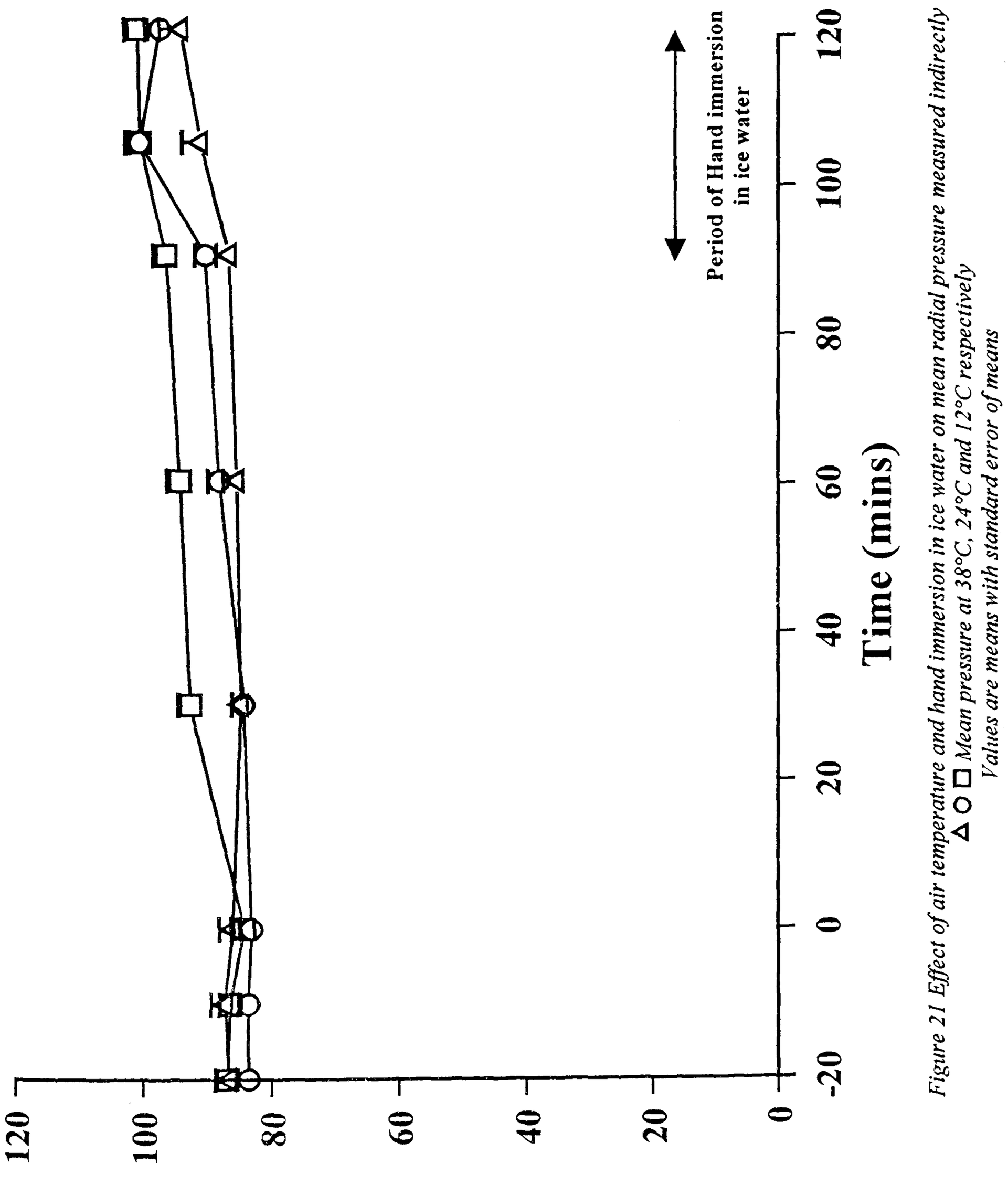

Figure 21 Effect of air temperature and hand immersion in ice water on mean radial pressure measured indirectly
△ ○ □ Mean pressure at 38°C, 24°C and 12°C respectively
Values are means with standard error of means

control exposure and that in the warm exposure went down slightly. On immersing the hand of the non dominant arm in ice cold water the pressure measured at all exposure temperatures went up but the difference between the pressures measured at the different temperatures was maintained. At the end of 120 minutes the pressure in cold exposure appeared to still be rising whereas in the control and warm exposures the arterial pressure seemed to have stabilised.

Radial artery Pressure measured by auscultation

The mean radial artery pressure measured in the non dominant arm during exposure to different air temperatures including the period when the hand of the same arm is immersed in ice water is displayed in Figure 21.

The mean radial artery pressure tended to go up slightly in the cold and control and remain fairly constant in the warm before hand immersion. During the hand immersion at all exposure temperatures the mean radial artery pressure showed a tendency to rise.

Digital Artery Pressure measured by Volume Clamp Technique

The Finapres device proved to be very unreliable in the cold and during hand immersion in ice water. In most subjects it ceased to be able to detect the arterial pulse in the cold exposure particularly during the period of hand immersion. In the control and warm exposures the device again gave results that were highly questionable. In general terms it was observed that the Finapres had most difficulty working with those who had low blood flows and when blood flow increased during cold induced vasodilatation the device sometimes managed to detect the arterial pulse which it had previously lost. The device had most problems in the cold exposure and least in the warm exposure with the control

being intermediate.

Conclusion

The brachial and radial artery pressure measured indirectly tended to go up in the cold and control exposure before hand immersion. The pressure tended to increase further in all exposures during the hand immersion phase of the experiment. Due to systematic problems using this method of pressure measurement no further analysis of these results was made.

EFFECT OF 120 MINUTES EXPOSURE TO MOVING AIR AT 12°C AND HAND IMMERSION IN STIRRED ICE WATER ON THE PRESSURE DROP BETWEEN THE BRACHIAL AND RADIAL ARTERIES AS MEASURED BY INDWELLING ARTERIAL CANNULAE

Results

These results are for a further set of experiments carried out on 6 of the original volunteers selected randomly. 6 male subjects (Table 19) volunteered aged between 19 to 25 years of age (average 22 years), height 1.75 to 1.92 m (average 1.81 m) weight 68.2 to 94.2 Kg (average 76.3 Kg), surface area 1.9 to 2.3 m^2 (average 2.0 m^2) and mean subcutaneous fat thickness 3.8 to 6.1 mm (average 4.7 mm).

These results show the effect of cold air exposure and hand immersion in ice water on the pressure drop between the brachial and radial artery as measured directly by indwelling arterial cannulae.

Table 19
Mean and individual anthropometric measurements of subjects who took part in the cannulation experiments

Subject (Initials)	Age (years)	Height (m)	Weight (Kg)	Surface Area (m^2)	Fat Thickness (mm)
AC	20	1.92	94.2	2.3	5.5
DA	24	1.75	70.7	1.9	3.9
EJ	24	1.83	76.6	2.0	6.1
LW	25	1.76	77.0	1.9	4.4
MC	19	1.80	68.2	1.9	3.8
RB	22	1.77	71.0	1.9	4.6
Mean	**22**	**1.81**	**76.3**	**2.0**	**4.7**

The subjects were exposed to a nominal air temperature of 12°C, the actual air temperatures measured was 12.18 ± 0.05°C; before each exposure the subjects lay supine outside the chamber in the laboratory at a nominal temperature of 24°C which was measured at 24.39 ± 0.16°C.

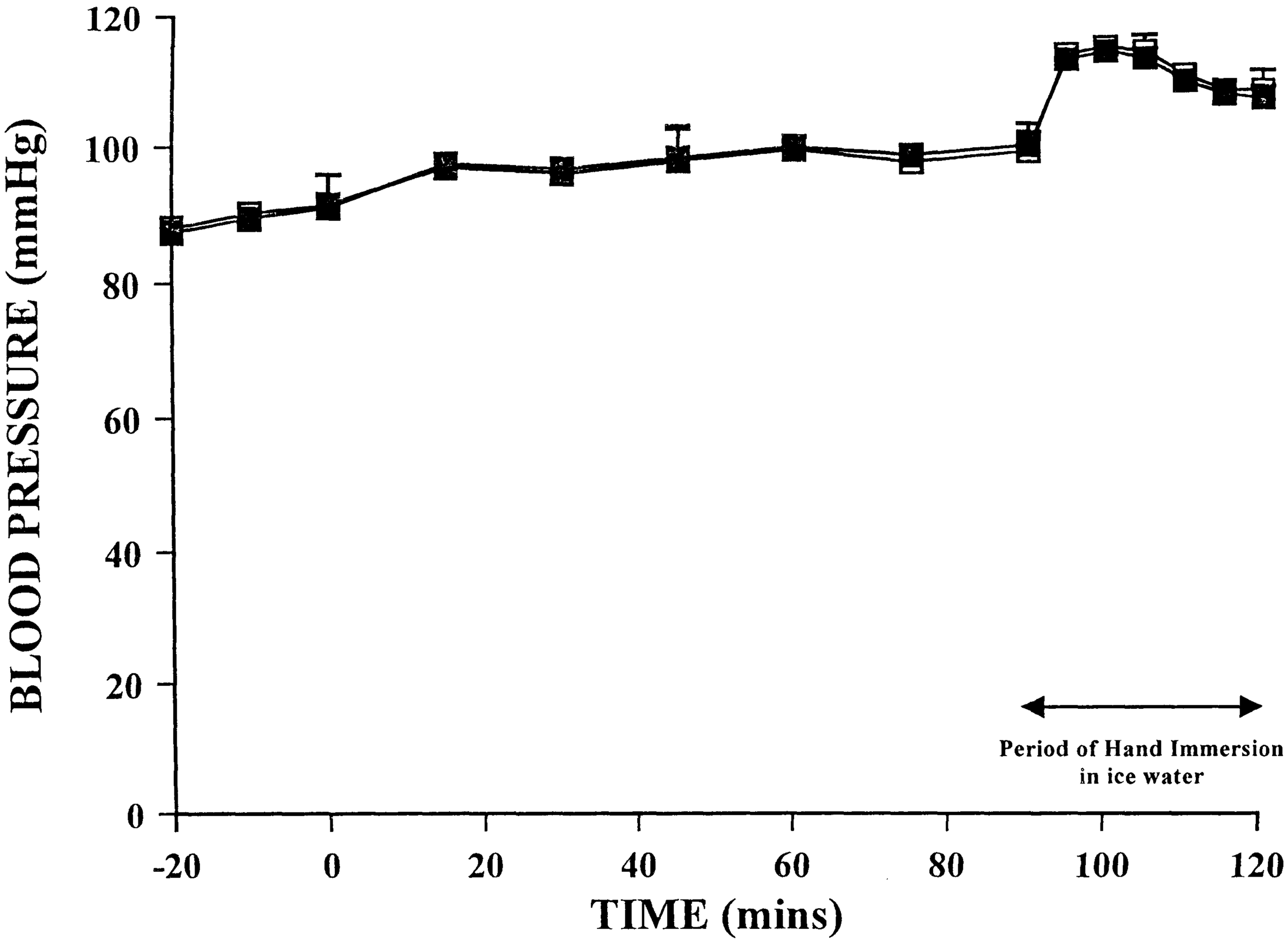

Figure 22 Effect of air at 12°C and hand immersion in ice water on directly measured arterial blood pressure
□ *average brachial pressure at 12°C*
■ *average radial pressure at 12°C*
Values are means with standard error of means at 0, 45, 90, 105 and 120 minutes

Direct Arterial Pressure Measurements

The direct measurements of pressure recorded at the brachial and radial sites using intra arterial cannulae are shown in Figure 22. The average directly measured mean blood pressures at 0, 90 and 120 minutes are given in Table 20 with comparisons between the value at 0 minutes and 90 minutes, and between the value at 90 minutes and 120 minutes.

Table 20
Directly measured Blood Pressure during exposure to air at 12°C during Hand Immersion in ice water

Time (mins)	Brachial (mmHg)	Radial (mmHg)
0	91.7 ± 4.3	91.3 ± 4.8
90 (compared to time 0)	99.5 ± 2.9 (p=0.025)	100.3 ± 3.2 (p=0.039)
120 (compared to time 90)	108.5 ± 3.1 (p=0.030)	107.2 ± 1.9 (p=0.098)

The average directly measured blood pressure recorded from the brachial and radial sites did not differ significantly from each other at any time during the experiment. The brachial and radial artery pressures both rose significantly during the first 90 minutes of cold air exposure compared to the pressures recorded prior to entering the cold room. The brachial artery pressure rose further still during the period of hand immersion and although the radial artery pressure showed a tendency to rise during this time the rise was not significant.

Individual Variations in Blood Pressure determined by Intra Arterial Measurement

The mean blood pressure in the brachial and radial arteries of the individuals who took

part in this study are shown in Table 21.

Table 21
Directly measured Blood Pressure during exposure to air at 12°C and during hand immersion in ice water

Subject		Blood Pressure (mmHg)		
		0 (mins)	90 (mins)	120 (mins)
AC	brachial	79.30	94.68	113.94
	radial	76.41	95.04	113.93
DA	brachial	92.18	98.38	107.63
	radial	90.69	95.81	104.60
EJ	brachial	95.94	108.43	107.30
	radial	95.15	111.42	106.69
LW	brachial	109.89	108.10	119.91
	radial	111.40	108.25	112.20
MC	brachial	86.57	95.62	98.20
	radial	89.72	100.01	102.05
RB	brachial	86.19	91.58	103.87
	radial	84.33	91.30	103.87
average	**brachial**	**91.68 ± 4.31**	**99.47 ± 2.92**	**108.48 ± 3.11**
	radial	**91.28 ± 4.80**	**100.30 ± 3.24**	**107.22 ± 1.96**

The average brachial blood pressure at 0, 90 and 120 minutes was 91.68 ± 4.31 mmHg (range 79.03-109.89 mmHg), 99.47 ± 2.92 mmHg (range 91.58-108.43 mmHg) and 108.48 ± 3.11 mmHg (range 98.20-119.91 mm Hg) respectively and for the radial artery 91.28 ± 4.80 mmHg (range 76.41-111.40 mmHg), 100.30 ± 3.24 mmHg (range 91.30 ± 111.42 mmHg) and 107.22 ± 1.96 mmHg (range 102.05-113.93 mmHg).

Conclusion

Average brachial artery pressure never varied significantly from average radial artery pressure. Brachial and radial artery pressure both rose during the exposure before hand

immersion and brachial artery pressure continued to rise during the hand immersion. At the end of the hand immersion brachial artery pressure averaged 108.48 ± 3.11 mmHg (range 98.20-119.91 mmHg) and radial artery pressure averaged 107.22 ± 1.96 mmHg (range 102.05-113.93 mmHg).

EFFECTS OF COLD STRESS AND HAND IMMERSION IN ICE WATER ON ARTERIAL PARAMETERS OF A LONG DISTANCE SWIMMER.

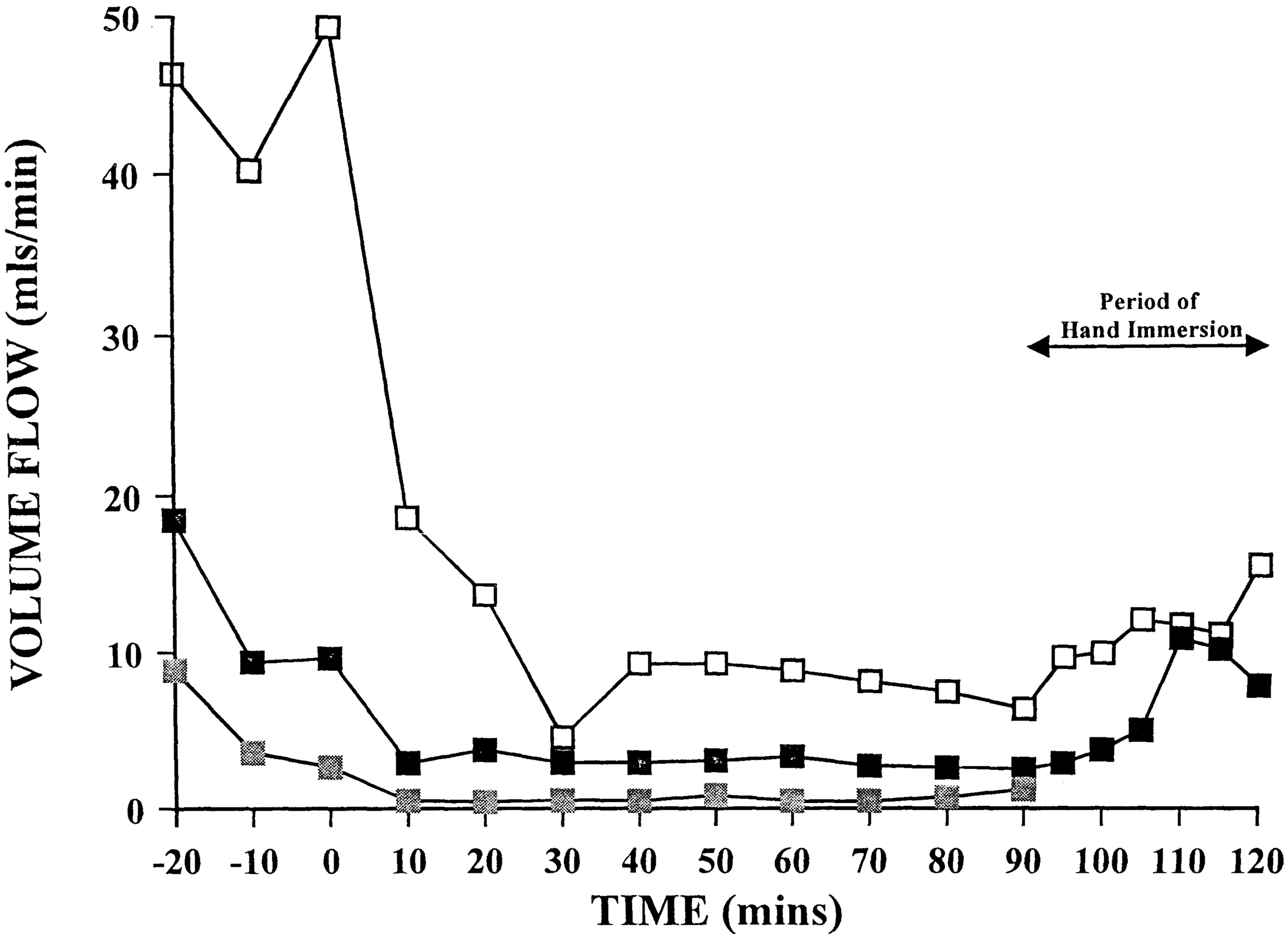

Figure 23 Effect of air at 12°C and hand immersion on the arterial flow of subject LC
□ *brachial flow*
■ *radial flow*
▩ *digital flow*

Arterial Blood Flow, Calculated Pressure Gradient and Directly Measure Pressure

The long distance swimmer Lynne Cox (LC) has previously been followed during two long distance swims (Keatinge *et al.* 1989; 1990).

These results show the effect of 120 minutes of exposure to air at 12°C, during the last thirty minutes of which the subject's non dominant hand was immersed in a stirred mixture of ice and water, on arterial parameters measured by ultrasound and values derived from those measurements and on the arterial pressure measured by indwelling cannulae. The subject was aged 36 years, height 1.67 m, weight 84.3 Kg, surface area 1.9 m^2 and had mean subcutaneous fat thickness of 13.8 mm.

The subject was exposed to a nominal air temperature of 12°C which was measured at 12.08 ± 0.19°C and before each exposure the subject remained supine outside the chamber at a nominal air temperature of 24°C measured at during the hand immersion the subject immersed her hand in a mixture of stirred ice and water measured at a temperature of 1.19 ± 1.34°C.

Figure 23 shows the brachial, radial and digital blood flow during the 90 minutes of exposure to air at 12°C and brachial and radial blood flow during a further 30 minutes during which the subject's hand was immersed in a mixture of stirred ice and water. All three flows show a large drop on entering the cold chamber and then brachial and radial flow show an increase during hand immersion.

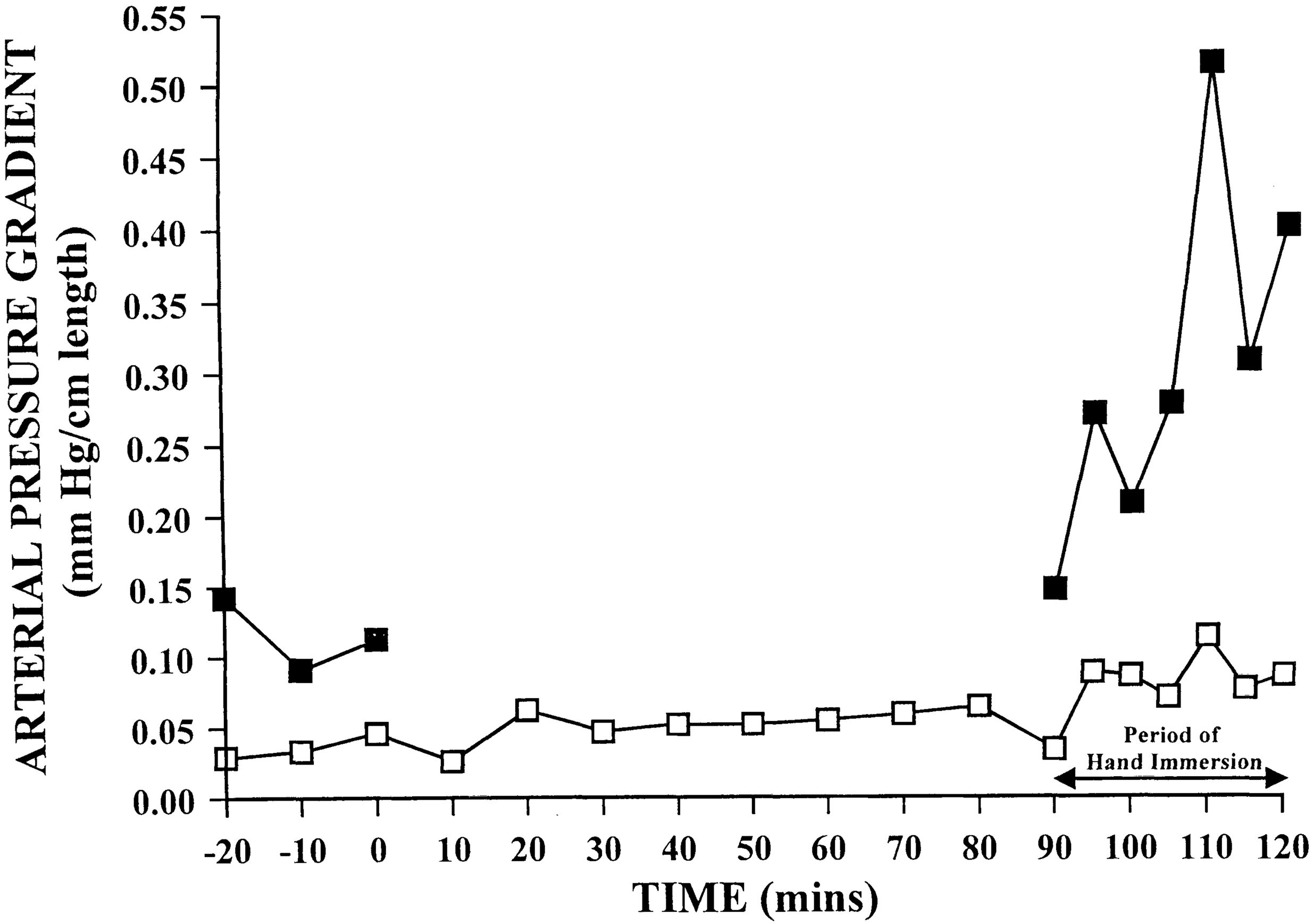

Figure 24 Effect of air at 12°C and hand immersion on the calculated arterial pressure gradient
□ *brachial pressure gradient*
■ *radial pressure gradient*

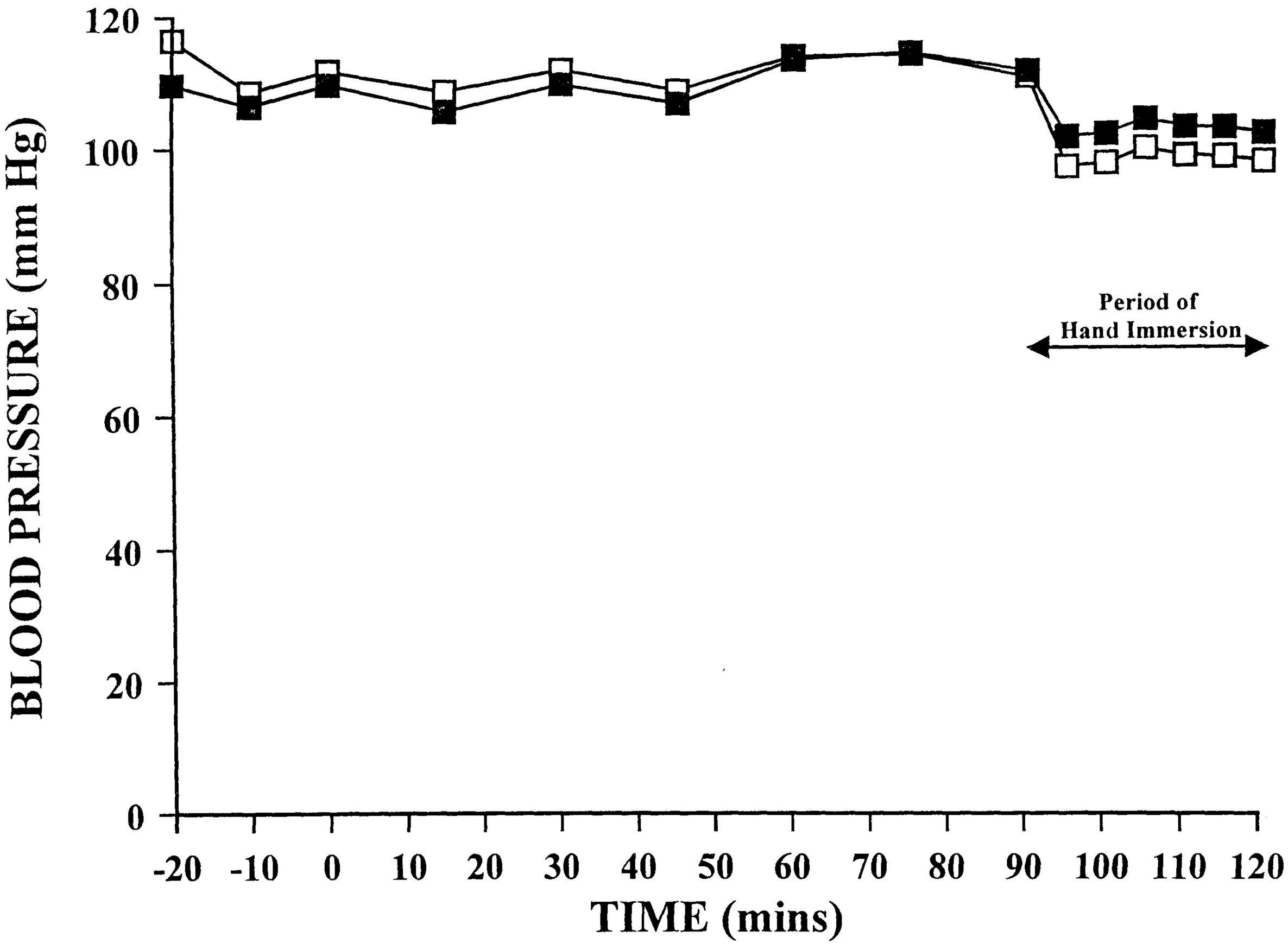

Figure 25 Effect of air at 12°C and hand immersion on the mean arterial pressure of subject LC measured directly by indwelling cannulae
□ *brachial pressure*
■ *radial pressure*

Figure 24 shows the calculated pressure gradient in the brachial and radial arteries during the cold exposure and subsequent hand immersion. Brachial pressure gradient shows little change but radial gradient starts to increase during the hand immersion. Just before hand immersion in ice water the calculated pressure drop between the brachial and radial sites is 2.09 mm Hg and at the end of hand immersion this value has risen to 5.89 mm Hg.

The mean directly measured pressures at the brachial and radial sites are shown in Figure 25. Both pressures remained almost the same until the period of hand immersion when they both dropped, just before hand immersion the brachial and radial pressures were 110.76 mm Hg and 111.70 mm Hg respectively and at the end of the period of hand immersion 97.93 mm Hg and 102.10 mm Hg respectively.

Conclusion

Subject LC showed a decrease in arterial blood flow on entering the cold room and then during hand immersion in ice water an increase in blood flow occurred, this gave rise to a slight increase in pressure drop between brachial and radial arteries but the difference for calculated and measured pressure drops remained small throughout.

DISCUSSION

Forearm artery diameter has been shown to be affected by a number of different factors. Arteries are directly relaxed by heat and contracted by moderate cold, are under the influence of sympathetic nerve activity, respond to changes in shear stress, and respond to circulating levels of noradrenaline (Boutouyrie, 1994). All these factors may contribute to the decrease in arterial diameter in the cold as described by Anderson and Mark (1989), Perret *et al.* (1989) and Corretti *et al.* (1995) and to the increase in diameter in the heat. It has also been shown that large arteries can completely shut off blood flow when traumatised due to external damage (Kinmouth, 1949; Cohen, 1944; Freeman, 1949).

The sympathetic nervous system and circulating levels of catecholamines play a role in controlling the diameter of large arteries (Anderson & Mark, 1989; Nabel *et al.*, 1988; London *et al.* 1990; Laurent *et al.*, 1988; Corretti *et al.*, 1995). Cold stress causes an increase in sympathetic activity and in circulating levels of adrenaline and noradrenaline (Frank, 1994). However Anderson and Mark (1989) infused adrenaline into the brachial artery of some of their subjects which produced slight changes in heart rate and blood pressure but no change in brachial artery diameter so it is unlikely circulating levels of adrenaline are important in controlling large artery diameter. Noradrenaline is likely to be important, Laurent *et al.* (1988) showed a significant decrease in brachial artery diameter upon administration of noradrenaline. This change was not necessarily due to the effects of the noradrenaline since they showed a decrease in blood velocity which may have caused an endothelial shear stress mediated response. However Anderson & Mark (1989) showed that sympathetic activity occasioned by cold stress resulted in the constriction of the brachial artery. They occluded the brachial artery of their subjects

distal to the site of diameter measurement which resulted in a decrease in velocity and diameter, the subjects then performed the cold pressor test with their contra lateral hand which resulted in a further decrease in brachial artery diameter without any further change in blood velocity. Additionally it has been shown that brachial artery diameter increases in subjects in whom sympathetic activity has decreased, although there was a slight non significant increase in blood velocity which may also have played a part through increased shear stress (London *et al.*, 1990). Other studies have also shown either a decrease in compliance or a decrease in diameter of large arteries due to either an increase in sympathetic nervous activity, direct application of noradrenaline or an enhancement of sympathetic response (Dobrin *et al.*, 1969; Boutouyrie *et al.*, 1994; Lyons *et al.*,1995). Local cooling to approximately 20°C increases the response of arteries to noradrenaline and will have been important at least in the radial and digital arteries in the present study (Ekenvall *et al.* 1988).

The myogenic response of arteries describes the contraction which reduces passive dilation produced by a rise in transmural pressure. In this study there is a stretching stimulus caused by the increase in mean arterial pressure in the cold and the decrease in mean arterial pressure in the warm. Both the passive stretch and myogenic response are unlikely to be of importance since the stretching stimulus is small with mean blood pressure seldom changing more than 10 mmHg. These blood pressure changes occurred gradually which tends to reduce myogenic response (Johnson, 1980), and large arteries generally show little such response (Anderson & Mark, 1989).

Shear stress is likely to be a more important factor affecting arterial diameter during this

study. The diameter of the large arteries has been shown to be dependent on the velocity and viscosity of the blood flowing through them (Anderson & Mark, 1989; Melkumyants & Balashov, 1990; Melkumyants *et al.*, 1989). Melkumyants *et al.* (1989; 1990) showed that the diameter of a cats femoral artery was dependent on the shear stress, which is the product of blood viscosity and velocity, on the endothelial lining. They showed that the change in diameter of the artery was directly proportional to both the viscosity of the blood (Melkumyants *et al.*,1989) and to the velocity of the blood (Melkumyants & Balashov, 1990). They further demonstrated that these shear stress induced changes were dependent on intact endothelium indicating that shear stress on the endothelium was probably the effective stimulus. Large bore arteries in the cat have been shown to respond to changes in endothelium-derived relaxing factor (EDRF) (Ekelund & Mellander, 1990) which is thought to be identical to nitric oxide (NO) (Cremona *et al.*, 1990). Ekelund & Mellander (1990) showed that infusing N^G-monomethyl-L-arginine (L-NMMA) which is a specific inhibitor of NO formation caused a 138% increase in the resistance of large arteries (>25μm diameter). These findings are supported by a very recent study in humans (Joannides *et al.*, 1995) that assesses the affects of L-NMMA infusion on the diameter of the radial artery. Joannides *et al.* (1995) demonstrated that the radial artery diameter is not influenced at rest by the infusion of L-NMMA but the response during hyperaemia is very much affected by such an infusion. They interpreted this to mean that the basal release of NO is minimal but that the dilatation that occurs with high blood flows such as during hyperaemia or those observed by Melkumyants *et al.* (1990) is intimately associated with the release of NO. Flow mediated responses almost certainly play a part in the changes in diameter during the present study since clear changes in blood velocity were observed.

In the present study the decrease in brachial artery diameter in the cold might be partly attributable to the decrease in shear stress due to the decrease in blood velocity, which the study of Bazett (1948) indicates would not be accompanied by important changes in temperature. Apparent reduction in velocity in the radial and digital arteries in the cold was not statistically significant and any effect of this on shear stress will be countered by increases in viscosity (Rand, 1964) due to decrease in blood temperature that occurs in the radial artery during such cold stress (Bazett, 1948). Joannides *et al.* (1995) showed that in subjects exposed to roughly the same thermal conditions as in the control experiments of the present study there was a minimal release of endothelium derived relaxing factor (EDRF); when they inhibited synthesis of EDRF no change was seen in radial artery diameter. Overall it therefore seems unlikely that the cold exposure causes much decrease in diameter due to reduced shear stress in the arteries under investigation, except possibly in the brachial artery.

During the cold exposure the decrease in the diameter of the arteries measured in this study is likely to be mainly brought about by an increased sympathetic tone to the large arteries (Anderson & Mark, 1989). The largest percentage decrease in arterial diameter was seen in the digital artery then the radial artery and least in the brachial artery. The increase in tone would be augmented by the local decrease in temperature of the radial and digital arteries resulting in enhanced sensitivity to noradrenaline (Ekenvall *et al.*, 1988). This increase in sensitivity could account for the graded response from the brachial, which showed least to the digital arteries, which showed most percentage reduction in diameter. The greater degree of constriction in the more peripheral arteries could also be due, in part, to the increase in the amount of smooth muscle associated with

more peripheral arteries (Rhodin, 1980).

The increases in diameter of the brachial, radial and digital arteries during the warm experiments in air at 38°C, were all associated with approximately five fold increases in blood velocity. Such an increase in blood velocity is likely to contribute substantially to the increased arterial diameter through the EDRF shear stress mediated mechanism. The increased diameter is also likely to be partly brought about by a decrease in sympathetic tone associated with decreased cold stress (Anderson & Mark, 1989). London *et al.* (1990) produced evidence that there is sympathetic constrictor tone in the brachial artery under thermal conditions similar to the controls of the present study, since leg raising produced reflex dilation.

The pressure drop between the brachial and radial site calculated using the ultrasound recordings (Simon *et al.*, 1990) measured at the end of the different temperature exposures was too small to be important in controlling blood flow. The changes in diameter in these large arteries and the changes in viscosity of the blood due to temperature did result in very significant changes in resistance of the arteries; the radial artery resistance almost quadrupled and the brachial artery resistance increased by half. There are two main reasons these increases were not important: not only was the resistance and pressure drop in the large arteries very small in absolute terms, so that even the quadrupling in the radial artery resistance produced little change in total resistance, but as the resistance of the large arteries increased, other downstream resistive elements in the arterial tree also increased their resistance even more to contribute a larger proportion of the total resistance.

The pressure of blood entering the right atrium is a few centimetres of water (Milnor, 1989) and in terms of the overall mean arterial pressure can be taken as zero, leaving mean arterial pressure as a direct measure of the total driving force for the flow through the systemic circulation, and the pressure drop down any given arterial section relative to mean arterial pressure as a measure of the relative importance of that arterial section in controlling blood flow through that branch of the arterial tree. Mean arterial pressure was slightly higher during the cold exposure and lower during the warm exposure compared to the control exposure as has been previously recorded (Bonde-Petersen *et al.*, 1992). In the present study the mean calculated pressure drop between the brachial and radial site at the end of the warm exposure was 3.78 ± 0.23 mmHg (range 2.20-5.15 mmHg), at the end of the control exposure 1.30 ± 0.12 mmHg (range 0.44-2.19 mmHg) and at the end of the cold exposure 2.02 ± 0.15 mmHg (range 1.18-2.88 mmHg). At the same time in the warm, control and cold exposure mean arterial pressure was respectively 85.0 ± 2.4 mmHg, 91.0 ± 3.0 mmHg and 97.3 ± 3.4 mmHg. These results show that the largest calculated pressure drop for any individual result amounts to only a small part (five percent at the very most) of the mean arterial pressure. These figures also demonstrate that these arteries exert their greatest effect when they are at their most dilated, after the warm exposure, when both the largest pressure drop and largest measured diameter were observed. The calculated pressure drop was at its lowest after 90 minutes of the control exposure and the cold exposure produced a calculated pressure drop intermediate to the control and warm exposures. These findings can be explained when the branch of the arterial system of the arterial tree under investigation is considered in terms of all its resistive elements. No individual produced a large calculated drop in pressure along their large arteries, suggesting that no particular individual's large

arteries has a markedly greater ability to control blood flow than the average during general cold stress.

Cold induced vasodilatation in fingers is usually indicated by either measuring changes in finger temperature (Lewis, 1930) or changes in finger heat flow (Greenfield, 1950) both these methods are indirect. Cold vasodilatation refers to the dilatation of the cold paralysed resistance arteries which allows an increase in warm blood flow giving rise to the local increase in temperature and heat flow. In the present study actual measurement of blood flow to the locally cooled area was made and therefore it was possible to make a more direct assessment of cold vasodilatation than by inferring a change in blood flow from a change in temperature or heat flow.

The radial artery blood flow is more representative of the changes in blood flow to the hand since the brachial artery supplies blood to the tissue of the forearm as well as to the hand. Radial artery blood flow should therefore be a good measure of cold induced vasodilatation in the hand. It has been shown that blood flows through the radial and ulnar arteries are generally almost identical and that 36% of the combined ulnar and radial artery blood flow goes to the fingers (Blair *et al.*, 1991). Blair *et al.* (1991) do not state the thermal condition of their subjects but presumably they were thermoneutral, so that the arteries would be in a basal state of constriction.

Both increases in radial artery blood flow during hand immersion in ice water, and in brachial artery blood flow, in generally cold subjects, show that all subjects experienced cold induced vasodilatation. There was a large degree of variation as indicated by radial

artery blood flow, in different subjects. The change in flow comparing with the flow just before hand immersion was on average 552 ± 129% and individual changes ranged from 159% to 1794%. This is in accordance with previous findings which showed the highest rate of heat loss during cold induced vasodilatation to be between 2.6% and 36.0% of a maximally vasodilated value (Keatinge, 1957). The hand immersion in ice water in the control experiment produced an increase in radial and brachial artery blood flow in all subjects except one, again with a large degree of variability between subjects, blood flow in the radial artery changing by between 94% and 1044%, mean 330 ± 80%. The hand immersion in ice water during the warm exposure produced a decrease in brachial and radial artery blood flow in all cases, the percentage decrease in radial artery flow by the end of hand immersion being between 22% and 88%, mean 51 ± 7%. In the warm exposure blood flow to the hand probably remained too high for the local tissue to cool to the point at which the smooth muscle of the arteries became insensitive to catecholamines and cold induced vasodilatation occurred. The drop in blood flow during hand immersion in the warm was presumably due to increased sympathetic activity, the effect of which was further enhanced by local tissue cooling increasing the sensitivity of the adrenoceptors.

The increased volume blood flow produced in brachial and radial arteries during cold induced vasodilatation in generally chilled subjects was as a result of an increase in the time average velocity of the arterial blood, which was almost a four fold increase in the radial artery. Immersion of an extremity in ice water produces an increase in sympathetic activity which is due both to the pain stimulus and the cold stimulus (Fagius *et al.*, 1989; Kreh *et al.*, 1984). The increase in arterial diameter usually seen therefore probably

resulted from increased velocity, and consequent shear stress leading to an EDRF mediated dilatation of the artery. It is possible that the sympathetic tone was already at a maximum so that hand immersion produced no further increase in arterial tone; previous studies showing that severe cold stress (Fagius *et al.*, 1989; Kreh *et al.*, 1984) produces an increase in sympathetic tone were on initially comfortably warm subjects. When subjects immersed their hand in ice water during the control experiment there was a tendency for both arteries to constrict but the change was again not significant despite highly significant and large increases in arterial blood time average velocity, presumably because the tendency of increased sympathetic tone to cause a constriction was countered by an increase in EDRF mediated dilatation. When subjects immersed their hand in ice water during the warm exposure the diameter of the brachial artery showed a tendency to decrease and the diameter of the radial artery decreased significantly; in both cases the time average velocity of the blood dropped significantly. In this case, both the decrease in time average velocity leading to a decrease in shear stress mediated EDRF release and an increase in sympathetic tone, are likely to have contributed to the constriction.

The small arterial diameter produced by hand immersion in ice water, in generally chilled subjects were nevertheless sufficient, despite increases in viscosity related to the decline in velocity of the blood (Barbee, 1973; Merrill, 1963) to decrease brachial and radial artery resistance significantly. The resistance of the radial artery halved and that of the brachial artery decreased by a quarter. This decrease in blood viscosity will also reduce the increase in shear stress on the endothelial lining caused by the increase in velocity of the blood during cold vasodilatation but only slightly, as it was much smaller.

The large arteries are most likely to affect blood flow during the peak of cold induced vasodilatation, whilst the large arteries are at their most constricted, and flow through them is high, this peak was at the end of the last immersion, during general chilling. However in practice in this study the contribution that the large arteries make to the control of blood flow remained negligible, the mean calculated pressure drop between the brachial and radial site after the hand immersion with the subjects generally cold stressed being only 3.50 ± 0.50 mm Hg, with a mean arterial pressure of 111 ± 4 mmHg, at that time. There was little difference in the calculated pressure drop comparing between different individuals, the minimum calculated pressure drop being 2.53 mmHg and the maximum 4.81 mmHg. The calculated pressure drops at the end of the period of hand immersion were similar in the warm and control exposures, 3.45 ± 0.26 mmHg (range 2.93-4.25 mmHg) and 2.77 ± 0.40 mmHg (range 1.98-4.01 mmHg) respectively. Again these figures show very little variation between different individuals despite the large variation in the amount of cold induced vasodilatation seen between different individuals. The average calculated pressure drop between the brachial and radial sites was greater after hand immersion during exposure to warm air than after hand immersion during exposure to cold air despite the greater constriction in the cold environment because the velocity of the blood was greater in the warm. This increased velocity must reflect a greater dilation elsewhere in the arterial tree during the warm exposure than the cold exposure thereby giving a marginally greater pressure drop along the large arteries in the warm.

The percentage decrease in radial artery diameter in cold air showed a significant negative linear correlation against the degree of cold vasodilatation assessed by radial

artery blood flow at the end of hand immersion in ice water. This indicates that those who experienced most arterial constriction developed least cold induced vasodilatation, although the arterial constriction did not make an important contribution to restraining blood flow.

All these measurements are dependent on the reliability and accuracy of the ultrasound system. The frequency of ultrasound used for measuring arterial diameter was 10 MHz this gives a theoretical resolution equal to one wavelength in this case 0.15 mm assuming a velocity of sound of 1500 ms^{-1}. Accurate measurement of diameter is crucial to flow measurements since the square of the diameter is used to derive the flow. Error was minimized by repeating each diameter measurement three times; the random error reduces as the square root of the number of measurements made. Other sources of possible error are if the vessel is not truly circular in cross section and if the vessel diameter varies with the pulse wave. Arteries generally have a circular cross section due to the relatively high internal pressure compared to the external pressure (Milnor, 1989) and the degree of non circularity has been measured as being very small (Oates *et al.*, 1990). Care was taken to measure the arterial diameter during diastole, the increase in diameter caused by the greater pressure during systole is in any case relatively small and has been measured as about 1.5% in one study (Mooser *et al,*. 1988) and less than 1% in another study (Joannides *et al.*, 1995) in the radial artery. Trager *et al.* (1993) recorded far greater differences in arterial diameter during the cardiac cycle but this was using a colour Doppler system which tends to give large errors in the measurement of diameter (Sheikh *et al.*, 1991; Nelson & Pretorius, 1988).

Errors may occur in the measurement of the velocity of the blood if the vessel is not uniformly insonated. If the sample volume is therefore too small, the Doppler shifted frequencies detected will lead to an overestimation of blood flow since it will be the velocity of the centre of the flow stream that is detected, which during laminar flow will be higher than the average for the vessel. Equally if the sample volume is too large Doppler shifted frequencies from other vessels may be included in the estimate. In this study the brachial, radial and digital vessels were within the adjustment range of the sample volume and they were also close to the surface and not in close proximity to any other vessels of any significance making accurate adjustment of the sample volume relatively easy. The ultrasound has a high pass "wall thump" filter which was set to its lowest setting of 100 Hz; this is designed to remove the low frequency Doppler shifted frequencies caused by movement of the arterial wall. If the ultrasound reflected signals exceed the "Nyquist limit" (which is a frequency equal to one half of the pulse repetition rate of the pulsed Doppler) then the frequency of that component will be changed and appear to be a completely different frequency a phenomenon known as aliasing. Aliasing only tends to occur at very high velocities such as during cardiac measurements and low pulse repetition frequencies. In this study velocities were comparatively low and pulse repetition frequencies were high (usually 10.4 KHz or 15.6 KHz) and therefore "aliasing" will not occur. The error in measurement of the Doppler shifted frequencies also depends on the angle of approach between the direction of flow and the direction of the ultrasound beam; the closer this gets to 90° the greater the error and at 90° such measurements theoretically become impossible. During this study the angle of approach was generally about 50° and the system would not allow velocity measurements to be made if the angle exceeded 70°. A number of studies have been made to assess the accuracy of ultrasound

systems. In general duplex ultrasound systems of the kind used in this study are more accurate than colour ultrasound systems (Nelson & Pretorius, 1988) which tend to underestimate diameter (Ranke *et al.*, 1992). Ranke *et al.* (1992) showed a mean error of -1.2% in diameter measurements for a DRF 400 using a 7.5 MHZ small parts probe which is essential the same system as used in this study but with a slightly lower resolution probe. They performed their experiments using a flow phantom consisting of silicon tubes of known diameter which had a pulsatile flow of animal blood pumped through them and were mounted in animal tissue. Flow rates were calculated by measuring the volume collected over a given time. The DRF 400 showed good correlation with the actual flow rates and a correlation coefficient of 0.973 was obtained with a mean volume flow error of -11.2%. Zierler *et al.* (1992) studied the accuracy of a duplex ultrasound system *in vivo* measuring the femoral artery blood flow of baboons and comparing it against timed collection, they obtained a percentage error of 13 ± 8%.

Gill (1985) and Hoskins (1990) review a number of studies and conclude that peripheral measurements such as those made in this study are less prone to error than deeper measurements such as for the abdominal aorta. The major error was random error in the measurement of arterial diameter, and accuracy can be improved by repeated measurements. Gill (1985) states errors in flow are less than 6% with careful use of the technique and repeated measurements.

The indirect pressure measurements by the standard auscultatory technique provide only general confirmation of the small size of the pressure drop in the large arteries since they do not provide the accuracy to detect the small changes in pressure that occurred between

the brachial and radial artery. The other major problem with the auscultatory technique is that occlusion of flow with a sphygmomanometer cuff, itself changes the haemodynamics. Other possible sources of error are that the technique is known to work effectively on the upper arm (Kirkendall *et al.* 1980; Petrie *et al.* 1986) making measurement in the brachial artery but is not widely used in the lower arm making measurements in the radial artery. It has also been shown that changes in distal vascular tone can result in changes in the amplitude of the Korotkoff sounds resulting in erroneous determination of blood pressure by this technique (Rabbany *et al.*, 1993) and during this study very marked large changes in vascular tone occur.

The volume clamp technique (Finapres) for the measurement of digital artery blood pressure is accepted by some to be an accurate method for the measurement of arterial pressure under the right conditions (Wesseling *et al.*, 1982; Van Egmond *et al.*, 1985; Pararti *et al.*, 1989; Gorback *et al.*, 1991). Others have shown unreliable results in vasoconstricted or vasodilated subjects (Tanaka & Thulesius, 1993; Nijboer *et al.*, 1988; Kurki *et al.*, 1987; Hilderbrandt *et al.*, 1991) and others report spurious problems (Kobler *et al.*, 1991; Kawahara, 1990; Gibbs *et al.*, 1991; Epstein *et al.*, 1991). In the cold and control experiments of the present study before hand immersion the system frequently ceased to be able to detect the arterial pulse; this problem usually became worse during the hand immersion phase of the experiment, though some subjects who developed large cold induced vasodilatation did re-establish a detectable pulse. The reason for disappearance of the pulse in the cold is likely to be low compliance of the wall of the constricted arteries rather than occlusion of the lumen by the constriction. Authors who report using the device successfully during peripheral vasoconstriction used drugs (Dorlas

et al., 1985) or only local cooling (Stroud *et al.* 1994) to cause constriction, which was presumably less intense than in the chilled subjects in this study.

The direct measurements of pressure using indwelling cannulae produced important confirmation of the calculations of arterial pressure gradient indicating that the large arteries played no important part in controlling blood flow. The difference between the average brachial and radial artery pressure measured just before entering the cold chamber, after 90 minutes of exposure to cold air and after 120 minutes of exposure to cold air during the last 30 minutes of which the subject's hand was immersed in stirred ice and water never exceeded 2 mmHg. The Bernoulli effect could theoretically result in a pressure change associated with change in blood velocity between the two sites of measurement. The Bernoulli effect describes the change in pressure that is seen as fluid passes along a tube of varying diameter and is due to the kinetic energy of the fluid being converted to potential energy, pressure, as its velocity falls or vice versa. In all these experiments the greatest difference in velocity measured at any time between the brachial and radial sites would produce a difference in pressure of less than 0.5 mmHg. The cannula were small enough to prevent them appreciably impeding blood flow by partially blocking the vessel. Taking the average radial artery diameter (2.26 mm standard deviation 0.04 mm) the 1.1 mm diameter cannula (manufacturers figures) will produce a mean pressure drop of 1.09 mmHg standard deviation 1.85 mmHg this is assuming the cannula lies along the axis of the artery, if the cannula lies next to the arterial wall, which is more likely this figure will reduce (Back, 1994).

The direct measurement of arterial pressure was subject to small amounts of error. The

transducers were calibrated after each experiment and a linear regression equation was determined for each device but this does not account for non-linearity, hysteresis or variation in sensitivity which the manufacturers state is no greater than 2% of the reading or 1 mmHg whichever is the greatest, since the pressures measured are about 100 mmHg the error should not be greater than ±2 mmHg. The cannulae used in this study all faced upstream with their opening facing into the flow, which can result in a slight increase in the measured pressure. In this study although the average velocity in both vessels is usually the same the velocity that impinges on the cannula opening may be different. This difference in velocity comes about since the velocity profile across the artery is not constant. At the walls the blood velocity is zero and along the axis the blood velocity is twice the average blood velocity assuming Newtonian flow. It is impossible to determine exactly where the cannula lies in relation to the axis of the vessel so although the average blood flow at both sites is much the same one cannula may be lying against the artery wall and the other may be midstream, but with the flows being measured during this experiment this will result in a maximum error of no more than about ± 3 mmHg (Milnor, 1989). Comparing the measurements of arterial diameter at different stages during the cannulation experiment with the diameters recorded during the cold experiment showed that the cannula did not cause arterial spasm. No potential error seems able to put in question the conclusion that pressure drops in the large arteries were small.

At the end of the period of hand immersion the average brachial and radial pressure measured directly was 108.48 ± 3.11 mmHg and 107.22 ± 1.96 mmHg respectively, difference 1.26 mmHg. The individual variation in pressure difference was also small ranging from -3.84 to 7.76. The negative pressure difference denotes a value in which the

pressure measured at the radial artery site was higher than that measured in the brachial artery site, this discrepancy can be accounted for by the systematic errors previously described and has also been recorded by others (Hynson *et al.*, 1994).

The results of the direct pressure recordings were in agreement with those who have previously made direct simultaneous recordings of central pressure and radial artery pressure and showed differences of only a few millimetres of mercury despite various interventions (Kroeker & Wood, 1956; Heistad *et al.*, 1968; De Hert *et al.*, 1994; Pauca *et al.,* 1994; Hynson *et al.*, 1994). One of these studies (Pauca *et al.*, 1994) showed a very slight increase in the pressure difference when the hand was vasodilated this is in agreement with the pressure drops calculated from the ultrasound measurements in this study which were at their greatest during the warm exposure.

When subjects were exposed to cold air there was an initial rapid increase followed by a slow subsequent fall in both aural and rectal temperature, and in warm air there was an initial slight drop followed by a slow increase, the effect, in both cases was more marked in aural than rectal temperature and in line with earlier evidence (Bittel *et al.* 1988) which can be explained by over compensation of thermoregulation. The short period of hand immersion produced a drop in rectal and aural temperature in both the cold and control exposures. The aural temperature during the cold fell by 0.33°C and during the control by 0.17°C. The rectal temperatures also drop significantly during the hand immersion in both experiments but to a lesser extent presumably due to the lag seen in rectal temperature response compared to aural temperature (Keatinge and Sloan, 1975).

The experiments on the long distance swimmer LC also show similar results to the main set of subjects. At the end of the period of hand immersion in the cold environment the calculated pressure drop between the brachial and radial arteries was 5.89 mmHg which is higher than in any of the main set of subjects due to LC's smaller radial artery diameter. The measurements of radial artery blood flow showed that she did show cold induced vasodilatation with the flow tripling by the end of the period of hand immersion. The direct measurements of arterial pressure showed no pressure drop between the brachial and radial sites of measurement, the recorded brachial pressure being 4.2 mmHg lower than the recorded radial pressure at the end of the period of hand immersion in the cold. Although the calculated pressure drop down the large arteries of LC is slightly greater than the average it is still too small to have an important effect on flow.

The different degrees of cold induced vasodilatation seen in the hand in different individuals therefore could not be attributed to restriction of flow by arteries in the arm not exposed to local cooling to below 12°C and must be due to downstream resistance in arterioles and in veins or venules. The latter may be appreciable since enhanced sensitivity of cutaneous veins at low temperatures has been shown in dogs (Janssens & Vanhoutte, 1978) and humans (Harker *et al.*, 1994).

In conclusion the brachial, radial and digital artery all show a constriction in subjects when exposed to cold air and dilation when the subjects were exposed to warm air compared to during exposure to an intermediate control air temperature, probably due mainly to changes in sympathetic activity modified by effects of shear stress. When the subjects exposed to the cold and control air temperatures immersed their hand in ice

water an increase in blood flow was observed, this cold induced vasodilatation was not accompanied by an important change in arterial diameter. There was however a decrease in hand blood flow of warm subjects induced by placing the hand in ice water and this was accompanied by a small significant fall in radial artery diameter. The calculated or measured pressure drop between the brachial artery at the ante cubital fossa and the radial artery at the wrist never exceeded a few millimetres of mercury, despite there being large variations in the amount of cold induced vasodilatation between different individuals. The most important single point is that pressure measurement by indwelling cannulae never showed a pressure difference between the brachial and radial sites of measurement that was greater than 7.76 mmHg either during whole body cold stress or in conjunction with cold induced vasodilatation. The general conclusion is that large forearm arteries exerted only a small effect on blood flow in either cold or warm stressed subjects either before or during cold induced vasodilatation. Although the arterial diameters changed enough to produce large changes in resistance of the artery, the absolute resistance of the artery always remained small in relation to the resistance of the smaller vessels downstream. It therefore seems that the small vessels downstream are largely responsible for the variation in the degree of cold induced vasodilatation in different individuals, the most likely reason for the variation being a difference in the susceptibility of the downstream vessels to cold paralysis.

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